



Volume 28, No. 1 • Winter 2021

BIOPHARMACEUTICAL REPORT

Chair: Weili He Editors: Peter Mesenbrink, Herbert Pang, Kristi L Griffiths

CONTENTS

A Message from Weili He

Weili He (AbbVie).....2

Celebrating the 40th Anniversary of the Biopharmaceutical Section: The Early Years (1966-1990)

Richard C. Zink (Lexitas Pharma Services) and Meijing Wu (AbbVie).....2

Memories from past Biopharmaceutical Section Chairs in Commemoration of the 40th Anniversary of the ASA Biopharmaceutical Section Part I (1981-1990)

Winston Chinchilli and Karl Peace.....5

Test-Retest Reliability on the Sleep Quality Numeric Rating Scale for Patients with Fibromyalgia -- How Many Measurements Are Enough?

Joseph C. Cappelleri, PhD and Andrew G. Bushmakin, MS (Department of Biostatistics, Pfizer Inc.).....6

Report on the Non-clinical Biostatistics Scientific Working Group on P-Values

Stan Altan (Janssen), John Kolassa (Rutgers University), and Steve Novick (AstraZeneca).....10

Use of Non-Concurrent Common Control for Treatment Comparisons in Master Protocols

Rajeshwari Sridhara (Contractor, Oncology Center of Excellence, FDA), Olga Marchenko (Bayer), Qi Jiang (Seagen), Richard Pazdur (FDA)12

Data and Analytics – Put Your Expertise to Work to Address the COVID-19 Pandemic

Nevine Zariffa (NMD Group LLC), Jonas Haggstrom (Cytel Inc), Jaap Mandema (Certara).....14

Conferences.....15

JSM 2020 Biopharmaceutical Section Contributed Paper Award.....15

Note from the editors

As we enter the 3rd month of 2021 and get ready to commemorate the one-year anniversary when Europe and North America shut down due to the COVID-19 pandemic, we continue as statisticians to find ways to be innovative in our use of biostatistics to help find ways to save lives by developing new therapeutics and by better understanding the diseases for which there is no cure. This continues the mission that we started on when the Biopharmaceutical Section of the American Statistician Association (ASA) started 40 years ago. Throughout the year we will reflect on the many areas where the Biopharmaceutical Section has not only made an impact with ASA but in society as a whole by sharing thoughts from some of our past Section Chairs of the last 40 years.

In the first issue of 2021, we open with a message from our Section Chair, **Weili He** (AbbVie) which sets the vision of what we hope to achieve as a Section in 2021. We follow this with a general article by **Richard Zink** (Lexitas) and **Meijing Wu** (AbbVie) talking about the early years of the Biopharmaceutical Section, including those years when it was a subsection of the Biometrics Section from 1968-1981. This is followed by reflections from two of the Section Chairs from the first decade of BIOP, **Vernon Chinchilli** (Penn State) and **Karl Peace** (Georgia Southern University).

The lead scientific article in this issue is provided by **Joseph Cappelleri** (Pfizer) and colleagues who discuss test-retest reliability on the Sleep Quality Numeric Rating Scale for patients with fibromyalgia. This is followed by an article which we hope will be part of a regular column in the future for Biopharm Report on non-clinical statistics. The article in this issue from **Stan Altan** (Janssen), **John Kolassa** (Rutgers), and **Steve Novick** (AstraZeneca) discusses the work of the Non-clinical Biostatistics Scientific Working Group on P-values. Expect many interesting topics on non-clinical Biostatistics in future issues of the BIOP report.

In this issue, you will also find a summary report from the meeting organized by the ASA BIOP Statistical Methods in Oncology Scientific Working Group in coordination with the FDA Oncology Center of Excellence on 10-Dec-2020 that discussed the use of non-concurrent common controls for treatment comparisons in master protocols. Look for topics of this theme a lot in 2021, as we hope to have a special issue of the BIOP Report on complex innovative design topics later in 2021. We also are provided with an article by **Nevine Zariffa** (NMD Group LLC), **Jonas Haggstrom** (Cytel Inc), **Jaap Mandema** (Certara) discussing the work being done by the International COVID-19 Data Alliance (ICODA) with an appeal to the Biopharmaceutical Section to become more actively involved in the global effort of ICODEA in helping address the unanswered research questions related to COVID-19. We also share an update of upcoming conferences which may be of interest to the BIOP community and a brief note on the decision regarding the Contributed Paper Award from the Biopharmaceutical Section at JSM 2020. Let us hope that we are able to have in-person meetings at some point in time in 2021. We hope the information in this issue is useful to all and everyone remains healthy and safe in these complex times.

A MESSAGE FROM WEILI HE

Hello ASA Biopharmaceutical Section Members:

This message came as we mark the one-year anniversary since the COVID-19 pandemic started. We have seen the unprecedented changes with COVID-19 pandemic, both in our personal and professional lives. More than ever, the health of businesses is urgently and visibly linked with the health of workforces, the health of our society, and the health of our planet. It has been an all-hands-on-deck approach in the development of COVID-19 vaccines. We have seen the successful approvals of the Pfizer/BioNTech and Moderna vaccines, and the vaccines developed by AstraZeneca and Johnson & Johnson are on the horizon for regulatory considerations and approvals. It is a wonderful time to be a statistician. The role that statisticians play in drug and vaccine development and in public health in general has never been greater. As quantitative science has become more essential than ever to the decision-making process due to technological innovations and big data, our profession could play even a bigger role

in enhancing public health and serving patients through data-driven decisions and evidence-based healthcare.

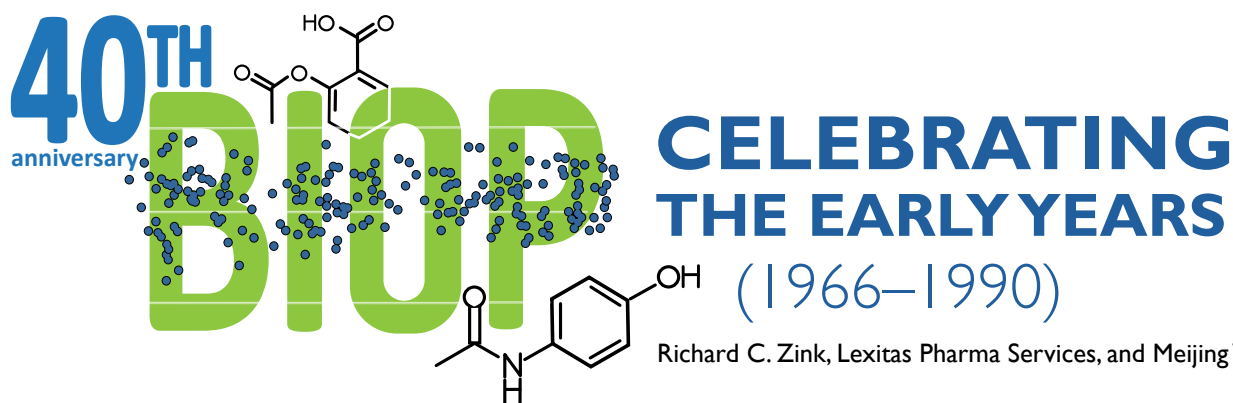
On a separate note, our section provides many services for the members. The BIOP Report is an excellent platform for sharing information and ideas with our colleagues and community. Anyone who has interest can get in touch with the editors. You can also refer to my January Newsletter to BIOP members for other services and opportunities that BIOP offers.

It is a great honor to serve as 2021 Chair of the Biopharmaceutical Section, and I will endeavor to reward the trust placed in me for this important role in serving the section. Please stay healthy and safe, and I look forward to meeting you all again in person in not-too-distant future!

Best Regards,

Weili He

2021 Chair, ASA Biopharmaceutical Section



Richard C. Zink, Lexitas Pharma Services, and Meijing Wu, AbbVie

Over its long history, the Biopharmaceutical (BIOP) Section of the American Statistical Association (ASA) has fostered community and created a shared sense of purpose among statisticians in the medical product industry. The year 2021 marks the 40th Anniversary of BIOP. It is a time to reflect on how the Section has grown from its humble roots, a time to celebrate the activities and accomplishments of the Section as it seeks to support its members, and a time to envision how the Section will continue to lead the way to address the challenges of medical product development in the 21st Century.

In the mid-to-late 1950s, thalidomide was shown to be well-tolerated, effective as a sedative, and effective as an anti-nausea medication for pregnant women suffering from morning sickness. Despite claims that thalidomide was a “nontoxic medication, with no side effects, and completely safe for pregnant women”, the drug became associated with instances of peripheral neuropathy and its ability to cause birth defects (Frisbee, 1990). The thalidomide disaster in other countries led to the 1962 Kefauver-Harris amendments of the 1938 Food, Drug, and Cosmetic Act in the United States (US

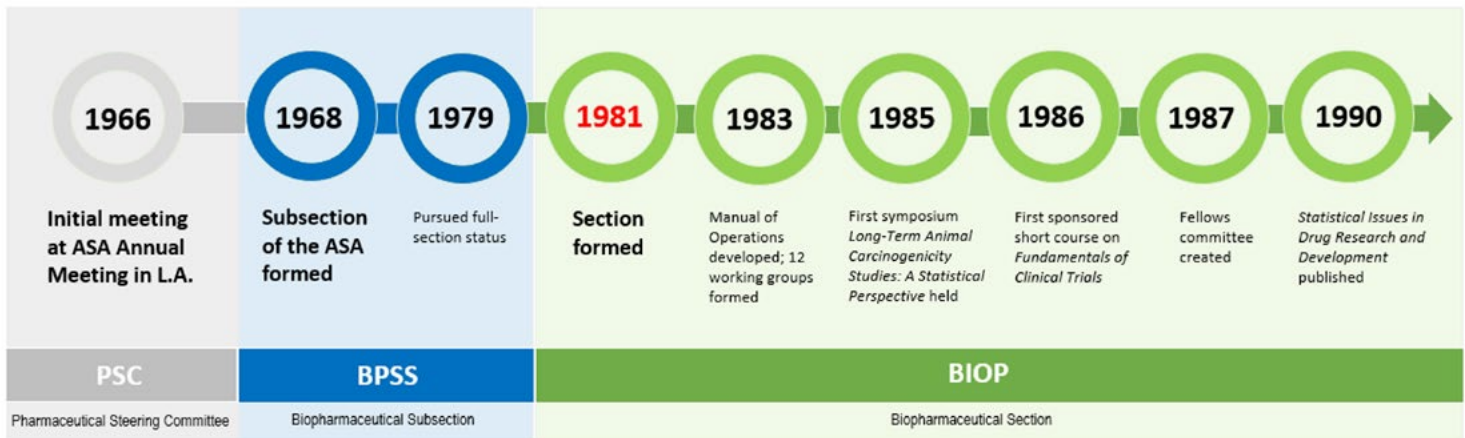


Figure 1. Timeline of Major Events

FDA, 2012). Notable authorities granted to the Food and Drug Administration (FDA) by this act include:

- The requirement that manufacturers prove effectiveness of drugs prior to marketing and disclose safety issues after marketing;
- The requirement that evidence be generated by adequate and well-controlled clinical studies;
- The mandate to review medications approved between 1938-1962.

These new requirements necessitated the hiring of a large number of statisticians, the development of statistical departments within pharmaceutical companies, and the training of statisticians about topics in the healthcare field. These statisticians found themselves in need of a professional venue to develop and share methodology and promote the field (Davis et al., 2005).

A formal group was initially discussed in 1966 at the ASA Annual Meeting in Los Angeles. The individuals present identified 5 professional organizations that could serve as a home for the new group (Free, 1990). Over time, the choices narrowed to the ASA and the Drug Information Association (DIA). Eventually, this Pharmaceutical Steering Committee (PSC) petitioned to join as the Pharmaceutical Subsection of the Biometrics Section of the ASA in 1968. The name was quickly changed to the Biopharmaceutical Subsection (BPSS) to help distinguish the group from the Pharmaceutical Manufacturers Association. BPSS was very successful, and it quickly grew in numbers from 100 statisticians in 1966 to approximately 1500 by 1979. Not surprisingly, by the mid-1970s, the need for full Section status was raised, and it involved many of the same culprits that

we see today in the birth of new Sections: a very active and large group, an ever-increasing scope of topics, the need for greater influence, the realization that there were potential fellows in BPSS who were not receiving proper consideration, and the increased frustration over space and visibility at conferences and meetings.

1979 began the year-long effort petitioning the membership of BPSS, the Biometrics Section (who was generally opposed to the split), and the larger ASA. Both sides presented their arguments at the February 1st, 1980 Board of Directors meeting, and a subsequent vote was in favor of the new Section. In a letter dated February 8th from ASA Executive Director **Fred Leone** to the Current Chair, Past Chair, and Chair-Elect of the Biometrics Section, the question of full Section status would be added to the national ballot in May of 1980. The new Biopharmaceutical Section would come into existence on January 1st, 1980 if 500 ASA members agreed to join (Leone, 1980). The Biopharmaceutical Section became the 8th Section after Biometrics (1938), Statistics and Data Science Education (1948), Business and Economic Statistics (1950), Social Statistics (1953), Physical and Engineering Sciences (1954), Statistical Computing (1972), and Survey Research Methods (1978).

Two notable events occurred early in the first decade (1981-1990). First, the first edition of the edited volume *Statistics in the Pharmaceutical Industry* (Buncher & Tsay, 1981) was published. Second, a reorganization occurred at FDA to form the Center for Drugs and Biologics. Both events would go a long way in clarifying the role of the professional statistician in the medical product industry and strengthening the relationships

between industry and regulatory statisticians (Davis et al., 2005). The first decade also saw the beginnings of many of the activities and policies that are still around today or would be formalized more concretely in later years. For example, the Manual of Operations which details the roles and responsibilities for Section officers and committees was developed in 1983; it continues to be updated annually. Further, a series of 12 Working Groups were formed on various topics specific to the medical product industry – their work would eventually be published as *Statistical Issues in Drug Research and Development* (Peace, 1990); the Section has a formalized process for forming Scientific Working Groups today. BIOP would hold its first symposium in 1985 entitled “Long-Term Animal Carcinogenicity Studies: A Statistical Perspective”; the Section would eventually go on to sponsor an annual Regulatory-Industry Statistics Workshop (RISW) and a biennial Nonclinical Biostatistics Conference (NCB). The year 1986 saw the first BIOP-sponsored short course Fundamentals in Clinical Trials; BIOP-sponsored short courses are a regular feature at the Joint Statistical Meetings (JSM), RISW, and NCB today. In 1987, a Fellows committee was created to help support BIOP members interested in achieving this important distinction; this committee exists today and just recently published an article in *Amstat News* (Dmitrienko A, Lipkovich I & Gallo, 2020). BIOP celebrated the ASA’s sesquicentennial (150th Anniversary) in 1989; we continue to celebrate important ASA milestones today (Sanchez-Kam, Bhattacharyya & Price D; 2014). These earlier years were foundational in starting BIOP on a path to offering many of the services and activities that members enjoy today.

A list of past chairs from initial committee through the first ten years of the Section is provided in Table 1, and a timeline of major events is summarized in Figure 1. For individuals interested in further reading, there are several sources of BIOP history available. Free (1990) summarizes a brief, early history of the Section in *The American Statistician*. Numerous BIOP members updated this history in very rich detail from Committee, Subsection, and early Section years through 1988 (Davis et al., 2005). As part of the ASA 175th Anniversary Celebrations, **Sanchez-Kam, Bhattacharyya & Price D** (2014) updated the BIOP history through 2014. Of course, more recent history is continually added to the *History* page under the *About Us* tab of the BIOP website (community.amstat.org/biop/aboutus/history). We encourage you to review this history, and ask you to consider how you may add to this amazing legacy

Group	Year	Chair
Section	1990	Karl Peace
	1989	Vern Chinchilli
	1988	John Schultz
	1987	Charlie Goldsmith
	1986	Paula Norwood
	1985	David Gaylor
	1984	Kathleen Lamborn
	1983	Wanzer Drane
	1982	Roger Flora
	1981	Ralph Buncher
Subsection	1980	Carl Metzler
	1979	Charlie Sampson
	1978	Wilf Westlake
	1977	Dave Salsburg
	1976	Marti Hearron
	1975	Bob Assenzo
	1974	Joe Meyer
	1973	Ted Colton
	1972	Joe Ciminera
	1971	David Bray
	1970	Charlie Dunnett
	1968–1969	Joe Dresner
Committee	1966–1967	Joe Dresner

Table 1: List of Past Chairs From Initial Committee Through the First Ten Years of the Section

of activity.

There are numerous activities planned for 2021. Panel discussions among past chairs are planned for both JSM in Seattle and RISW in Rockville. The mixer at the Open Business Meeting at JSM as well as the mixer at RISW will feature food, fun, and reminiscing. The Biopharmaceutical Report will feature 4 quarterly articles highlighting the activities and successes of BIOP over 10-year increments (this being the first). Finally, be on the lookout for activities and podcasts broadcast through ASA Connect throughout the year. While we are planning for in-person activities, we will adapt as needed due to any lingering safety concerns surrounding COVID-19.

We hope you join us as we celebrate the 40th Anniversary of the Biopharmaceutical Section!

References

- Buncher CR & JY Tsay (eds). (1981). *Statistics in the Pharmaceutical Industry*. New York: Marcel Dekker, Inc.
- Davis RL, Free SM, Gulyas SW, Hearron MS, Lindborg SR, O'Neill R & Sampson CB. (2005). The History of the Biopharmaceutical Section of the American Statistical Association (ASA), 1966-1988. *The Biopharmaceutical Report 13: 2-7*. Available at: https://higherlogicdownload.s3.amazonaws.com/AMSTAT/fa4dd52c-8429-41d0-abdf-0011047bfa19/UploadedImages/BIOP%20Report/2005_Winter_BR.pdf.
- Dmitrienko A, Lipkovich I & Gallo P. (June 2020). Biopharmaceutical Section Offers Advice for ASA Fellow Nomination. *Amstat News*. Available at: magazine.amstat.org/blog/2020/06/01/advice-for-asa-fellow-nomination/.
- Free SM. (1990). Some History for the Biopharmaceutical Section. *The American Statistician* 44: 80-82.
- Frisbee, J. (2004). Thalidomide. In S. Loue, & M. Sajatovic (Eds.), *Encyclopedia of Women's Health*, pp 643-644.
- Leone FC. (1980). Board Action on Biopharmaceutical Subsection Petition.
- Peace K (ed). (1990). *Statistical Issues in Drug Research and Development*. New York: Marcel Dekker, Inc.
- Sanchez-Kam M, Bhattacharyya A & Price D. (2014). The History of the Biopharmaceutical Section of the American Statistical Association. Poster presented at the 2014 Regulatory-Industry Statistics Workshop. Available at: https://higherlogicdownload.s3.amazonaws.com/AMSTAT/fa4dd52c-8429-41d0-abdf-0011047bfa19/UploadedImages/Biopharm_History_Poster_for_JSM_FINAL_16JUL14.pdf.
- US Food and Drug Administration (2012). Kefauver-Harris Amendments Revolutionized Drug Development. Available at: <https://www.fda.gov/consumers/consumer-updates/kefauver-harris-amendments-revolutionized-drug-development>.

MEMORIES FROM PAST BIOPHARMACEUTICAL SECTION CHAIRS IN COMMEMORATION OF THE 40TH ANNIVERSARY OF THE ASA BIOPHARMACEUTICAL SECTION PART I (1981-1990)

Throughout 2021, to remember all of the achievements of the Biopharmaceutical Section over the last 40 years, in each of the issues this year of the Biopharm Report, we plan to share reflections from past Section Chairs over this period.

The Section Chairs during this first decade were the following:

- **1981** *Ralph Buncher*
- **1982** *Roger Flora*
- **1983** *Wanzer Drane*
- **1984** *Kathleen Lamborn*
- **1985** *David Gaylor*
- **1986** *Paula Norwood*
- **1987** *Charlie Goldsmith*
- **1988** *John Schultz*
- **1989** *Vern Chinchilli*
- **1990** *Karl Peace*

In this issue, we share remembrances from **Winston Chinchilli** and **Karl Peace**.

Winston Chinchilli (Section Chair 1989)

In 1989, the Joint Statistical Meetings (JSM) were held August 06-10 in Washington DC. Although the theme of the 1989 JSM was Statistics in Society, the ASA leadership was very excited about, and distracted by, 1989 being the sesquicentennial celebration of its founding in 1839. The ASA leadership submitted a proposal to the US Postal Service requesting that it issue a commemorative stamp in honor of the ASA sesquicentennial. **Fred Leone**, the ASA Executive Director at that time, was very disappointed when the US Postal Service rejected the proposal. He complained that if the US Postal Service could issue a stamp commemorating Enrico Caruso, an Italian opera singer, then it should issue a stamp commemorating the ASA sesquicentennial.



Winston Chinchilli

Karl Peace (Section Chair 1990)

In 1983, when I was working at Smith, Kline and French labs in Philadelphia, I placed an invitation in AMSTAT NEWS, for those interested in working on one or more of 16 statistical issues (within the pharmaceutical industry, some of which were controversial at that time), to contact me. Eventually 16 working groups were formulated and began work on the issues/ topics – which



Karl Peace

I identified and provided. As expected, some groups were more productive than others.

I was subsequently made Chair of Work Group Activity within the Biopharmaceutical Section of the ASA. In that capacity, we had several invited sessions or round table discussions on the topics at JSM from 1984-1988, with presentations by Work Group Members.

Marcel Dekker asked me to develop a book with the title: Statistical Issues in Drug Research and Development. I did so, selecting the issues on which the work groups were farthest along. The book was published in 1990, during my term as Chair of the Biopharmaceutical Section.

TEST-RETEST RELIABILITY ON THE SLEEP QUALITY NUMERIC RATING SCALE FOR PATIENTS WITH FIBROMYALGIA – HOW MANY MEASUREMENTS ARE ENOUGH?

Joseph C. Cappelleri and Andrew G. Bushmakin, Department of Biostatistics, Pfizer Inc.

Contact: Joseph C. Cappelleri, Pfizer Inc, 445 Eastern Point Road, MS 8260-2502, Groton, CT 06340; phone: (860) 389-8107; e-mail: joseph.c.cappelleri@pfizer.com

The authors are employees and stockholders of Pfizer Inc. This study was sponsored by Pfizer.

Acknowledgment: The authors are grateful to the past and current editors —Xiaofei Wang, Peter Mesenbrink, and Herbert Pang—for their helpful feedback.

Clinicaltrials.gov identifiers: NCT00645398 and NCT00230776.

Key Points:

- Research is needed on how many daily measurements need to be averaged to obtain acceptable test-retest reliability (intraclass correlation coefficient of at least 0.70) on the Sleep Quality Numeric Rating Scale (NRS) for patients with fibromyalgia.
- At least two daily measurements need to be averaged to obtain acceptable reliability on the Sleep NRS.

Categories: intraclass correlation coefficient; measurement; psychometrics; reproducibility; Spearman-Brown prophecy formula; stability

SLEEP QUALITY NUMERIC RATING SCALE: WHAT AND WHY?

In the last issue of the *Biopharmaceutical Report*, we provided estimates of test-retest reliability that ranged from 0.58 for a single daily measurement to 0.91 for an average of 7 daily measurements on a 11-point pain intensity numeric rating scale for patients with fibromyalgia (Cappelleri and Bushmakin, 2020). In this article, an analogous undertaking is performed on the Sleep Quality Numeric Rating Scale (Cappelleri et al., 2009; Martin et al., 2009).

Specifically, we address the following question: How many daily measurements need to be averaged to obtain acceptable test-retest reliability on the Sleep Quality Numeric Rating Scale (NRS) for patients with fibromyalgia? A number of self-report measures of sleep quality have been developed for use in different populations (Cappelleri et al., 2009; Kurtis et al., 2018;

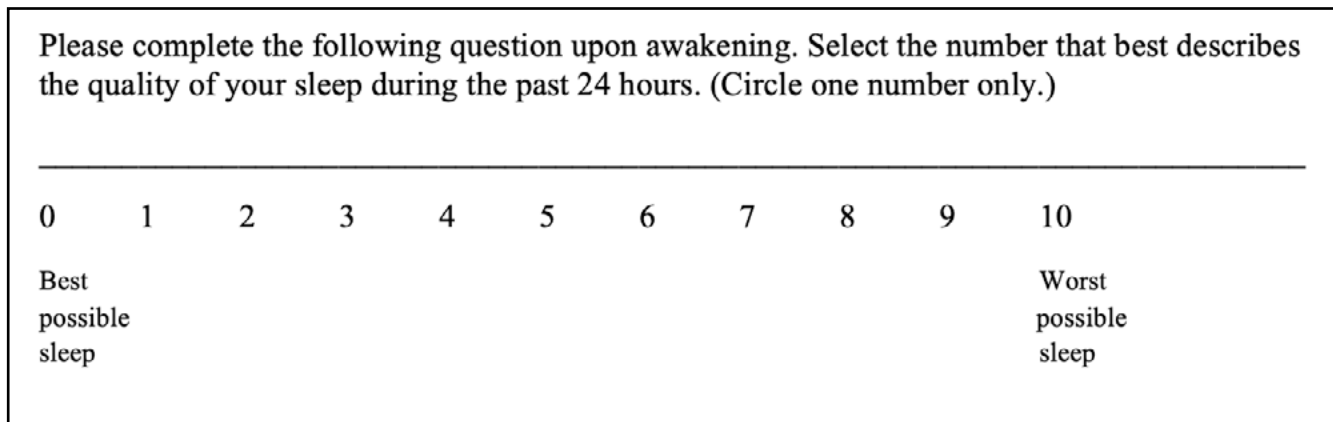


Figure 1. Sleep Quality Numeric Rating Scale

Lomeli et al., 2008; Martin et al., 2009; Snyder et al., 2018; Yi et al., 2006). One of them is the Sleep Quality NRS that consists of an 11 point numeric rating scale, with a recall period of the past 24 hours, ranging from zero (best possible sleep) to 10 (worst possible sleep), with self-assessment performed daily upon awakening (Cappelleri et al., 2009; Martin et al., 2009) (Figure 1). Therefore, patients rate their sleep quality during the past 24 hours by choosing the appropriate integer number between 0 and 10.

The instrument has been validated and used in clinical studies for patients with fibromyalgia (Arnold et al., 2008; Cappelleri et al., 2009; Martin et al., 2009; Mease et al. 2008). Specifically, this particular measure has been used as a daily diary measure of sleep quality whose responses are averaged over the past seven days in order to obtain a weekly average score. *Yet there has been no definitive published assessment on many daily measurements need to be averaged in order to achieve acceptable test-retest reliability, defined here as an intraclass correlation of at least 0.70* (Cappelleri et al., 2013, Fayers and Machin, 2016; Prinsen et al., 2018; Reeve et al., 2013).

HOW TO ASSESS TEST-RETEST RELIABILITY?

This article uses pre-treatment data from two clinical trials of pregabalin (sponsored by Pfizer Inc) conducted in the United States for patients with fibromyalgia. The conduct, designs and results of these two trials have been described and published elsewhere (Arnold et al., 2008; Mease et al., 2008). For the purpose of assessing test-retest reliability, the mean sleep quality score was computed for the pre-treatment week, prior to subsequent randomization to treatment groups, and taken as the mean of all available pain diary entries.

Test-retest reliability for a single daily measurement of sleep quality was estimated using an intraclass correlation efficient (ICC), which reflects the proportion of total variability in observed scores that is due to true differences between subjects (between-subject variability), based on one week of pre-treatment data from a one-way random intercept model for absolute agreement on a single measurement (Cappelleri et al., 2009; McGraw and Wong, 1996; Schuck, 2004). Specifically, after estimation of a single daily ICC using the MIXED procedure in the SAS software (SAS, 2018), the Spearman-Brown prophecy formula was calculated to obtain a measure of ICC for two through seven daily averaged measurements: $m \cdot ICC / [1 + (m-1) \cdot ICC]$, where ICC is the reliability of a single daily measurement and m is the number of daily measurements averaged (Brown, 1910; Cappelleri et al., 2013; DeVellis, 2017; Spearman, 1910).

As noted previously (Cappelleri and Bushmakin, 2020), the pre-treatment period is the best juncture to collect data for the assessment of test-retest reliability (when it is expected that subjects are stable in their health state between screening and baseline, with no intervention of study drug). Post-treatment data can be considered but are not generally recommended as subjects are not expected to be in a period of stability, owing to the effect of the treatments received.

WHAT IS THE EVIDENCE?

For each of the 2 studies, Table 1 shows the number and percentage of subjects who completed a given number of sleep quality measurements (from as low as 1 to as high as 7) during the 7-day pre-treatment period, whose distribution happens to be identical to that of the pre-treatment pain intensity NRS measurements reported previously (Cappelleri and Bushmakin, 2020). In both studies, almost 90% of the patients completed all 7 measurements.

	# Measurements	Frequency	Percent	Cumulative Frequency	Cumulative Percent
STUDY 1					
	1	3	0.40	3	0.40
	4	1	0.13	4	0.53
	5	15	2.01	19	2.54
	6	57	7.62	76	10.16
	7	672	89.84	748	100.00
STUDY 2					
	1	5	0.67	5	0.67
	2	2	0.27	7	0.94
	5	16	2.15	23	3.09
	6	77	10.34	100	13.42
	7	645	86.58	745	100.00

Table 1. Number and percentage of subjects according to number of daily measurements completed during the 7-day pre-treatment period: Study 1 and Study 2

In Study 1 (n = 748), the estimated ICCs were 0.59 for a single measurement (daily score) and 0.91 $\{= (7*0.59 / [1 + (6)*(0.59)])\}$ for an average of 7 measurements; in Study 2 (n = 745), the estimated ICCs were 0.57 for a single measurement and 0.90 $\{= 7*0.57 / [1 + (6)*(0.57)]\}$ for an average of 7 measurements (Cappelleri and Bushmakin, 2009). What's new here is that, for both trials, Figure 2 shows estimates of ICC for an average of 2 through 6 measurements, as well as for a single measurement and an average of 7 measurements. As the figure shows, Study 1 and Study 2 gave estimated ICCs of 0.74 and 0.73, respectively, when 2 measurements were averaged to achieve test-retest reliability of at least 0.70.

WHAT IS LEARNED?

In medicine, daily assessments of sleep quality are known to fluctuate from day to day, even in the absence of no change in a patient's condition. It is common practice in these instances to average the results of the daily measurements, for example by taking the average (i.e., arithmetic or simple mean) of the last seven diary measurements on sleep quality scores to arrive at an average weekly score, in order to increase reliability.

In this brief exposition, the empirical evidence indicates that an average of at least 2 daily measurements are needed to achieve an acceptable level of test-retest

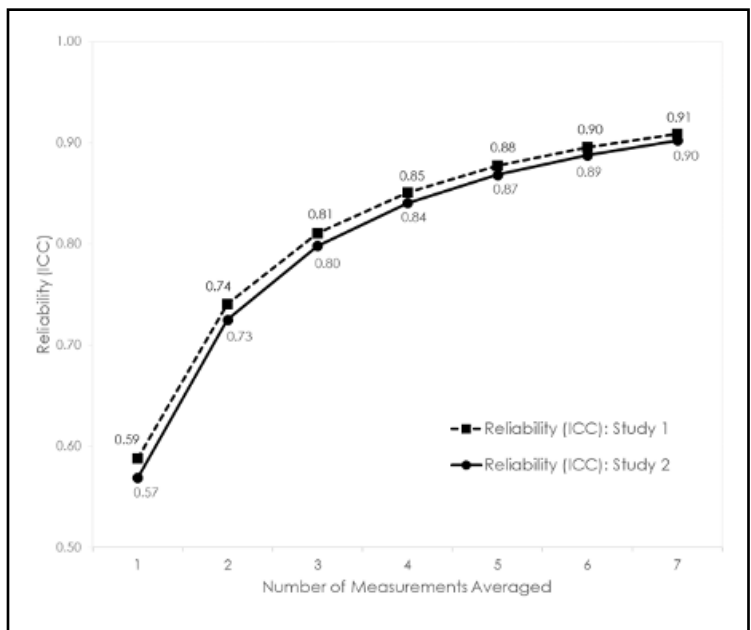


Figure 2. Test-retest reliability estimates of Intraclass Correlation Coefficient (ICC) for a single measurement and for measurements averaged on sleep quality scores in 2 fibromyalgia studies

reliability of at least 0.70 for patients with fibromyalgia responding on the Sleep Quality NRS. If instead an ICC reliability of at least 0.80 is being sought, then at least three measurements would need to be averaged. One consequence of these findings is that a minimum of a majority of daily measurements, at least 4 of 7, is not

necessarily required to be averaged for an individual to be included in a subsequent analysis on treatment effect, which should increase the sample size of individuals and hence precision of results. The same set of conclusions, with very similar results, was obtained for the 11-point pain intensity NRS used in the same 2 studies (Cappelleri and Bushmakin, 2020). More research is encouraged to support generalization of these findings on the Sleep Quality NRS for patients with other diseases or conditions.

DATA AVAILABILITY

Upon request, and subject to certain criteria, conditions and exceptions (see www.pfizer.com/science/clinical-trials/trial-data-and-results for more information), Pfizer will provide access to individual de-identified participant data from Pfizer-sponsored global interventional clinical studies conducted for medicines, vaccines and medical devices (1) for indications that have been approved in the US and/or EU or (2) in programs that have been terminated (i.e., development for all indications has been discontinued). Pfizer will also consider requests for the protocol, data dictionary, and statistical analysis plan. Data may be requested from Pfizer trials 24 months after study completion. The de-identified participant data will be made available to researchers whose proposals meet the research criteria and other conditions, and for which an exception does not apply, via a secure portal. To gain access, data requestors must enter into a data access agreement with Pfizer.

REFERENCES

- Arnold, L.M., Russell, I.J., Diri, E.W., Duan, W.R., Young Jr, J.P., Sharma, U., Martin, S.A., Barrett, J.A., & Haig, G. (2008). A 14-week, randomized, double-blinded, placebo-controlled monotherapy trial of pregabalin in patients with fibromyalgia. *Journal of Pain*, 9, 792-805.
- Brown. W. (1910). Some experimental results in the correlation of mental abilities. *British Journal of Psychology*, 3, 296-322.
- Cappelleri, J.C., Bushmakin, A.G., McDermott, A.M., Sadosky, A.B., Petrie, C.D., & Martin, S. (2009). Psychometric properties of a single-item scale to assess sleep quality among individuals with fibromyalgia. *Health and Quality of Life Outcomes*, 7, 54. Available from www.hqlo.com/content/7/1/54. Accessed May 15, 2020.
- Cappelleri, J.C., Zou, K.H., Bushmakin, A.G., Alvir, J.M.J., Alemayehu, D., & Symonds, T. (2013). *Patient-reported outcomes: Measurement, implementation and interpretation*. Boca Raton, Florida: Chapman & Hall/CRC Press.
- Cappelleri, J.C., & Bushmakin, A.G. (2020). Test-retest reliability of a 11-point pain intensity numerical rating scale for patients with fibromyalgia. *Biopharmaceutical Report*, 27, 15-19.
- DeVellis, R.F. (2017). *Scale development: Theory and applications*. Fourth edition. Thousand Oaks, California: SAGE Publications, Inc.
- Fayers, P.M., & Machin. D. (2016). *Quality of life: The assessment, analysis and reporting of patient-reported outcomes*. Third edition. Chichester, United Kingdom: John Wiley & Sons Ltd.
- Kurtis, M.M., Balestrino, R., Rodriguez-Blazquez, C., Forjaz João, M., & Martinez-Martin, P. (2018). A review of scales to evaluate sleep disturbances in movement disorders. *Frontiers in Neurology*, 9, 369. Available from www.frontiersin.org/articles/10.3389/fneur.2018.00369/full. Accessed May 15, 2020.
- Lomeli, H.A., Pérez-Olmos, I., Talero-Gutiérrez, C., Moreno, C.B., González-Reyes, R., Palacios, L., de la Peña, F., & Muñoz-Delgado, J. (2008). Sleep evaluation scales and questionnaires: A review. *Actas Españolas de Psiquiatría*, 36, 50-59.
- Martin, S., Chandran, A., Zografos, L., & Zlateva, G. (2009). Evaluation of the impact of fibromyalgia on patients' sleep and the content validity of two sleep scales. *Health and Quality of Life Outcomes*, 17, 64. Available from www.hqlo.com/content/7/1/64. Accessed May 15, 2020.
- McGraw, K.O. & Wong, S.P. (1996). Forming inferences about some intraclass correlation coefficients. *Psychological Methods*, 1, 30-46.
- Mease, P.J., Russell, I.J., Arnold, L.M., Florian, H., Young Jr, J.P., Martin, S.A., & Sharma U. (2008). A randomized, double-blind, placebo-controlled, phase II trial of pregabalin in the treatment of patients with fibromyalgia. *Journal of Rheumatology*, 35, 502-514.

- Prinsen, C.A.C., Mokkink, L.B., Bouter, L.M., Alonso, J., Patrick, D.L., de Vet, H.C.W., & Terwee, C.B. (2018). COSMIN guideline for systematic reviews of patient-reported outcome measures. *Quality of Life Research*, 27, 1147-1157.
- Reeve, B.B., Wyrwich, K.W., Wu, A.W., Velikova, G., Terwee, C.B., Snyder, C.F., Schwartz, C., Revicki, D.A., Moinpour, C.M., McLeod, L.D., Lyons, J.C., Lenderking, W.R., Hinds, P.S., Hays, R.D., Greenhalgh, J., Gershon, R., Feeny, D., Fayers, P.M., Cella, D., ... Zeeshan, B. (2013). ISOQOL recommends minimum standards for patient-reported outcome measures used in patient-centered outcomes and comparative effectiveness research. *Quality of Life Research*, 22, 1889-1905.
- SAS Institute Inc. (2018). *SAS/STAT®15.1 user's guide*. Cary, North Carolina: SAS Institute Inc.
- Schuck, P. (2004). Assessing reproducibility for interval data in health-related quality of life questionnaires: Which coefficients should be used? *Quality of Life Research*, 13, 571-586.
- Snyder, E., Cai, B., DeMuro, C., Morrison, M.F., & Ball, W. (2018). A new single-item sleep quality scale: Results of psychometric evaluation in patients with chronic primary insomnia and depression. *Journal of Clinical Sleep Medicine*, 14, 1849-1857.
- Spearman, C. (1910). Correlation calculated from faulty data. *British Journal of Psychology*, 3, 271-29.
- Yi, H., Shin, K., & Shin, C. (2006). Development of the sleep quality scale. *Journal of Sleep Research*, 15, 309-316.

REPORT ON THE NON-CLINICAL BIostatISTICS SCIENTIFIC WORKING GROUP ON P-VALUES

Stan Altan (Janssen), John Kolassa (Rutgers University), Steve Novick (AstraZeneca)

The Nonclinical Biostatistics Scientific Working Group was formed on the heels of the 2019 article by Wasserstein, Schirm and Lazar “Moving to a World Beyond $p < 0.05$ ”. It was the second of two position papers encouraging a re-thinking of the p -value amongst the larger statistical community. To some extent, these articles were a response to initiatives by the scientific community attenuating general use of p -values in scientific publications. See for example Harrington et al (*New England Journal of Medicine*, 2019), Carrol (JAMA Health Forum, 2016), and Editorial (*Nature*, 2019), among others.

A summary of important points is given below by way of introduction to the institutional direction being espoused by the ASA regarding p -values.

A. ASA’s Statement on p -Values (Wasserstein and Lazar, 2016)

[Wasserstein and Lazar (2016)]... articulate in nontechnical terms a few select principles that could improve the

conduct or interpretation of quantitative science, according to widespread consensus in the statistical community.

1. P -values can indicate how incompatible the data are with a specified statistical model.
2. P -values do not measure the probability that the studied hypothesis is true or the probability that the data were produced by random chance alone.
3. Scientific conclusions and business or policy decisions should not be based solely on whether a p -value passes a specific threshold.
4. Proper inference requires full reporting and transparency
5. A p -value does not measure the size of an effect or the importance of a result.
6. By itself, a p -value does not provide a good measure of evidence regarding a model or hypothesis.

B. “Moving to a World Beyond $p < 0.05$ ” (Wasserstein, Schirm & Lazar, 2019)

The ASA Symposium on Statistical Inference, held October 11-13, 2017, laid the foundations for this

special issue – 43 papers from leading statisticians mainly from academia.

1. Don't Say "Statistically Significant" - Regardless of whether it was ever useful, a declaration of "statistical significance" has today become meaningless. Similarly, we need to stop using confidence intervals as another means of dichotomizing (based, on whether a null value falls within the interval).
2. "Accept uncertainty. Be thoughtful, open, and modest." Remember "ATOM."

The essential challenge that confronts us is the conflation of " $p < 0.05$ " with the term "statistical significance". More generally, our aim is to revisit the rigid dichotomy of "statistical significance" at any level in applications specific to nonclinical statistics. The ASA position is not an outright ban on the calculation and reporting of p -values but rather a direction against the misuse of $p < 0.05$ as a decision rule. The special 2019 issue of the American Statistician also contains 43 articles by prominent statisticians, drawn from the 2017 Statistical Inference conference, proposing their own ideas and approaches to inference. Some of these papers may well serve as a basis for improving nonclinical statistical practice. Four papers which have good practical advice are:

1. Abandon Statistical Inference – McShane et al (2019)
2. Improving the use of p -values – Benjamin and Berger (2019)
3. Second generation p -values – Blume et al. (2019)
4. Predictive Inference and Scientific Reproducibility - Billheimer (2019).

Respecting the editorial position and the call for broad and committed support from the profession, a scientific working group was formed to consider the impact of the new perspectives specific to nonclinical statistical practices. Consequently, a call for volunteers was sent out and the scientific working group formed with three focus groups: 1. Discovery/-Omics, 2. Pre-clinical Pharmacology/Safety/Toxicology and 3. Chemistry, Manufacturing and Controls (Small and Large Molecules). The members of the working group are given in Table 1 whose time and efforts working on this project are deeply appreciated.

Focus Group	Name	Affiliation
Discovery/-Omics	Dhammika Amaratunga	Consultant
	Xavier Cabrera	Rutgers
	Jeonifer Garren	Pfizer
	Mariusz Lubomirski	Amgen
	Steven Novick (Chair)	AstraZeneca
	Charles Tan	Pfizer
Safety/Tox/Biomarkers	Helena Geys (Chair)	Janssen
	John Kolassa	Rutgers
	Dean Li	Pfizer
	Kanaka Tatikola	Janssen
	Fetene Tekle	Janssen
	Jennifer Thomas	Covance
	Stan Altan	Janssen
CMC	Dan Coleman	Genentech
	David LeBlond	Consultant
	Jason Liao	Merck
	Martin Otava	Janssen
	John Peterson	GSK
	Guillermo Miro-Quesada	AstraZeneca
	Katharina Reckermanns	Roche
	Tim Schofield (Co-Chair)	CMCSciences
	Kim Vukovinsky (Co-Chair)	Pfizer
	Yao Zhang	Pfizer
Stan Altan	Janssen	

Table 1 Membership of Nonclinical Biostatistics Scientific Working Group on p -values

It was proposed that the scientific working group carry out its activities in three stages.

Stage 1 :

1. A comprehensive survey to identify specific statistical applications which rely on a p -value criterion for decision making.
2. Assess the appropriateness of the p -value criterion for each application.
3. If the p -value decision rule is inappropriate, establish one or more alternative statistically appropriate procedures which mitigate a blind adherence to the p -value dichotomy.

Stage 2 : Achieve a consensus that embraces the ASA position as well as advancing statistical practice in the nonclinical statistics sphere.

Stage 3: Summarize the recommendations in the form of a white paper.

The scientific working group began its work in early 2020 and at the time of the writing of this report, the three focus groups have completed stages 1 and 2. The process of writing a white paper summarizing the discussions of the focus groups as the final deliverable of the scientific working group is currently in progress. It is expected that the White Paper will be issued within the next quarter.

John Kolassa acknowledges Grant NSF DMS 1712839 for partial funding of his research conducted as part of the working group.

References

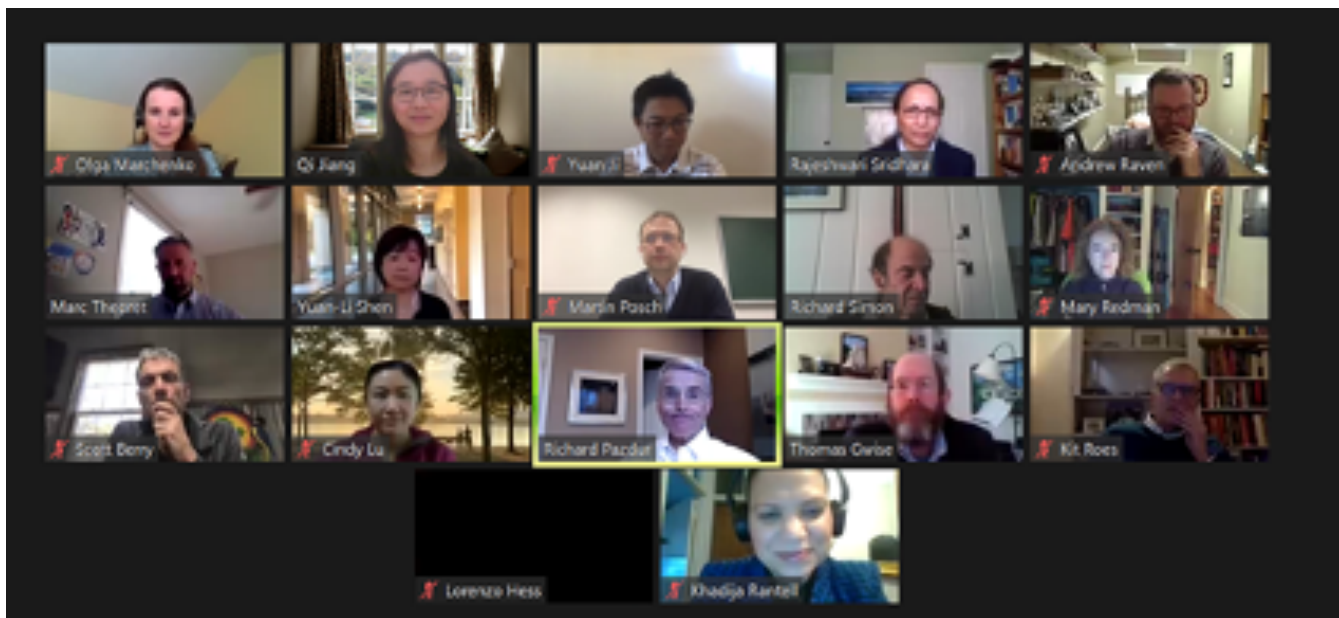
1. Benjamin, Daniel J.; Berger, James O. (2019). “*Three Recommendations for Improving the Use of P-Values*”. *American Statistician*, Issue 73: Suppl Pages: 186-191. DOI: 10.1080/00031305.2018.1543135
2. Billheimer, Dean (2019). “*Predictive Inference and Scientific Reproducibility*”. *American Statistician*. Issue 73: Suppl Pages: 291-295. DOI: 10.1080/00031305.2018.1518270
3. Blume, Jeffrey D.; Greevy, Robert A.; Welty, Valerie F.; Smith, Jeffrey R.; Dupont, William D. (2019). “*An Introduction to Second-Generation P-Values*”. *American Statistician*. Issue 73: Suppl Pages: 157-167. DOI: 10.1080/00031305.2018.1537893
4. Carroll A. Undue Influence: “*The P Value in Scientific Publishing and Health Policy*”. *JAMA Health Forum*. Published online June 22, 2016. DOI:10.1001/jamahealthforum.2016.0026
5. EDITORIAL “*It’s time to talk about ditching statistical significance*”. *Nature* 567, 283 (2019). DOI: <https://doi.org/10.1038/d41586-019-00874-8>
6. Harrington, D., D’Agostino, Sr., R.B., Gatsonis, C., Hogan, J.W., Hunter, D.J., Normand, S-L. T., Drazen, J. M., and Hamel, M.B. (2019). “*Editorial: New Guidelines for Statistical Reporting in the Journal*”. *New England Journal of Medicine*. 381(3):285-286 DOI: 10.1056/NEJMe1906559
7. McShane, Blakeley B.; Gal, David; Gelman, Andrew; Robert, Christian; Tackett, Jennifer L. (2019). “*Abandon Statistical Significance*”. *American Statistician*. Issue 73: Suppl Pages: 235-245. DOI: 10.1080/00031305.2018.1527253
8. Wasserstein, Ronald L. and Lazar Nicole A. (2016) “*The ASA Statement on p-Values: Context, Process, and Purpose*”, *The American Statistician*, 70:2, 129-133, DOI: 10.1080/00031305.2016.1154108
9. Ronald L. Wasserstein, Allen L. Schirm & Nicole A. Lazar (2019). “*Moving to a World Beyond $p < 0.05$* ”. *The American Statistician*, 73:sup1, 1-19, DOI: 10.1080/00031305.2019.1583913

USE OF NON-CONCURRENT COMMON CONTROL FOR TREATMENT COMPARISONS IN MASTER PROTOCOLS

Rajeshwari Sridhara (Contractor, Oncology Center of Excellence, FDA), Olga Marchenko (Bayer), Qi Jiang (Seagen), Richard Pazdur (FDA)

On December 10th of 2020, American Statistical Association (ASA) Biopharmaceutical Section (BIOP) gathered experts for the 2nd open forum organized by the ASA BIOP Statistical Methods in Oncology Scientific Working Group in coordination with the US FDA Oncology Center of Excellence. The topic of this forum was “Use of Non-concurrent Common Control for Treatment Comparisons in Master Protocols”. The

series of such forums was introduced by the ASA BIOP and the FDA as a part of the US FDA Oncology Center of Excellence Project SignifiCanT (Statistics in Cancer Trials), the goal of which is to promote collaboration and engagement among different stakeholders in design and analysis of cancer clinical trials to advance cancer drug development.



***Speakers/ Panelists:** Scott Berry (Berry Consultants), Thomas Gwise (FDA), Lorenzo Hess (SMC, Switzerland), Yuan Ji (University of Chicago), Qi Jiang (Seagen), Cindy Lu (Biogen), Olga Marchenko (Bayer), Richard Pazdur (Oncology Center of Excellence, FDA), Khadija Rantell (MHRA), Martin Posch (Medical Statistics at the Medical University of Vienna), Andrew Raven (HC, Canada), Mary Redman (Clinical Research Division, Fred Hutch), Kit Roes (EMA), Yuan Li Shen (FDA), Richard Simon (Consultant), Rajeshwari Sridhara (Contractor, Oncology Center of Excellence, FDA), Marc Theoret (Oncology Center of Excellence, FDA).

Oncology drug development is going through revolutionary changes both in terms of type of indications and type/class of drugs. Improvement in the way diseases are defined and classified based on a greater understanding of what is occurring at the molecular level has resulted in molecularly defined smaller patient subpopulations and rare disease subgroups. Small population clinical trials pose statistical challenges and opportunities for drug development. Many drugs have been approved based on single arm trials and smaller number of patients. However, randomized, controlled studies are the key to ensure that the observed clinical benefits and risks can be reliably attributed to the treatment under consideration and that estimate of treatment effect is unbiased. In a setting of rare disease or when limited number of potential patients to participate in clinical trials are available, the use of a Master Protocol design can provide efficiencies such as a common screening platform and a common/shared control and allow the conduct of randomized studies in such situations.

Master Protocols are used to establish an infrastructure to address multiple treatments and/ or disease specific questions within one protocol. Master protocols can be split into three distinct types: umbrella, basked, and platform designs. Depending on the trial objectives, different types of trials may benefit from a

Master Protocol. For example, platform trials in which different treatment arms are compared to a common/ shared control treatment may enter and exit the study at different times. Resources can be saved if concurrent and non-concurrent control data are used, in which case the assumption of independent inference may not hold. The focus of this virtual discussion was to understand the statistical properties of utilization of data from the non-concurrent control arm and its impact on Type I error rate in establishing treatment effect.

Generally, it is understood that if platform trials under a Master Protocol proceed over a long period of time, efficiency may be improved when multiple treatments, entering and leaving the platform trial over time, are randomized against a common control and non-concurrent control data are used for statistical inference. However, non-concurrent controls may introduce bias due to confounding factors that may depend on time. Methods to address potential bias are available, however, albeit all making specific assumptions.

The seventeen speakers/panelists* for the discussion included members of the BIOP Statistical Methods in Oncology Scientific Working Group representing pharmaceutical companies, representatives from International Regulatory Agencies (FDA, EMA, HC, MHRA and SMC), academicians and expert statistical con-

sultants. In addition, over 100 members attended the virtual meeting including representatives from other International Regulatory Agencies (e.g., from Japan, Australia, Singapore). The discussions were moderated by the BIOP Statistical Methods in Oncology Scientific Working Group co-chairs, Dr. Olga Marchenko from Bayer and Dr. Qi Jiang from Seagen, and Dr. Rajeshwari Sridhara, contractor from Oncology Center of Excellence, FDA.

The two-hour discussion was productive and covered different aspects of the use of concurrent and non-concurrent controls for platform trials. Examples discussed include platform trials I-Spy 2, GBM-AGILE, and Precision Promise that use concurrent and non-concurrent controls to analyze data and make comparisons by modeling time-dependent confounders using Bayesian “time machine”. There was some agreement that in a rare disease setting when it is impossible to run a large trial or in an exploratory setting, the use of non-concurrent control might be acceptable. For example, in a situation when the standard of care has not been changed for a long period of time and a time trend can be adequately modeled. In more common indications and in a confirmatory setting, an acceptance of treatment claims based on a non-concurrent control is unlikely. Non-concurrent control and historical data share several sources of potential bias. When we use historical data for comparisons in clinical trials, we accept that strict Type I error control is not possible. Non-concurrent control data are

collected within the same framework as a concurrent control data and patients are randomized and possibly blinded. However, because the data are collected at a different calendar time, randomization does not ensure exchangeability of the distribution of prognostic factors between non-concurrent control and experimental arms. Non-concurrent controls may introduce bias due to different factors related to time, changes in standard of care, changes in patient population, changes in recruiting strategies, changes in assessment of endpoints, etc. Methods to address potential bias are available, however, they rely on specific assumptions and make analysis less reliable. If non-concurrent data are utilized as a primary analysis, also the analysis using only concurrent control data should be presented as a sensitivity analysis. Some regulators also expressed a concern with the information leaks based on interim decisions that reveal treatment effects for arms that are still under study.

This forum provided an opportunity to have open scientific discussions among diverse stakeholder group – academicians, international regulators, and pharmaceutical companies focused on emerging statistical issues in cancer drug development. We plan to continue with similar open forum discussions in the future on a variety of important topics that include statistical aspects in cancer drug development involving different stakeholders and a multi-disciplinary approach.

DATA AND ANALYTICS – PUT YOUR EXPERTISE TO WORK TO ADDRESS THE COVID-19 PANDEMIC

Nevine Zariffa (NMD Group LLC), Jonas Haggstrom (Cytel Inc), Jaap Mandema (Certara)

The worldwide toll of the COVID-19 pandemic is substantial, so is the response of the many professionals in healthcare. Be it in the patient care, research or government sectors, many talented experts have joined together to advance the development of treatments to address infections from the virus, the development of vaccines to reduce the future morbidity caused by the virus, methods to monitor the use of therapeutics in real-world settings, and to generate additional scientific

insights to fuel even more progress in understanding the virus.

We invite the ASA Biopharmaceutical Section members to join the International COVID-19 Data Alliance (ICODA) community. ICODEA is an open global coordinated collaboration of leading life science, philanthropic and research organisations that have come together to harness the power of health data to respond to the COVID-19 pandemic. To join us is simple: either

advocate in your organization to share summary-level data from the trials of treatments of COVID-19 and other COVID-19 data sources available to you; or apply to be an accredited researcher to work with the data that continues to be aggregated from clinical trials and from other health data from around the world.

Accredited researchers can work with enriched summary-level data (*Data Dictionary*) from the most informative trials (Industry-sponsored trials, single- and multi-sponsor platform trials, larger academic trials). The summary-level data from these select trials are being provided to ICODA in harmonized fashion to allow side-by-side evaluation of all trials. We're also making available a digitized & curated data from public sources via the CODEx COVID-19 database (*info pack*) which contains summary level endpoint data from 340 studies reported in 329 references involving over 340,000 patients. The CODEx COVID19 database is immediate available and is a rich source of information: the most commonly reported efficacy and biomarker endpoints are death (305 studies), critical disease (169 studies), hospitalization (169 studies), hospitalization discharge (161 studies), and time in-hospital (147 studies).

Once you are an accredited researcher, you can evaluate a number of research hypotheses to aid in your work on COVID-19. For example, you can investigate the effect of a specific drug on multiple efficacy endpoints and across various subgroups. Another example would be to identify the most promising drug for a specific subset of the population. A third example would be to use the data provided in ICODA to inform the design new trials and to identify which populations remain underserved by available treatments. We ask you then share your findings, be they results or methods development work.

We thank the *REMAP CAP* platform trial team for agreeing to share their summary-level data in ICODA, and the following Pharma Companies: Amgen, Astra-Zeneca, Genentech, Gilead, GlaxoSmithKline, Novartis, Pfizer, Sanofi, Takeda, UCB – with more to come.

For more information on ICODA visit: [ICODA website](#)

For more information on the RCT data assets in ICODA visit: [ICODA DPI Project](#)

For general enquiries and to become an accredited researcher: Jonas.Haggstrom@hdruk.ac.uk

To join our mailing list: Mary.white@hdruk.ac.uk

CONFERENCES

2021 ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop

The *ASA Biopharmaceutical Section Regulatory-Industry Statistics Workshop* is sponsored by the ASA Biopharmaceutical Section in cooperation with the FDA Statistical Association. Each year, the conference lasts three days, with invited sessions co-chaired by statisticians from industry, academia, and the FDA and short courses on related topics offered the first day of the workshop.

Poster and roundtable proposal submission are now open. Roundtable discussion topic proposals are due March 30. Poster proposals are due April 14.

2021 Duke-Industry Statistics Symposium (DISS)

Theme: Emerging Clinical Initiatives in Pharmaceutical Development: Methodology and Regulatory Perspectives

The DISS is organized by the Department of Biostatistics and Bioinformatics, Duke University School of Medicine. The symposium was established seven years ago to discuss challenging issues and recent advances related to the clinical development of drugs, biologics and devices and to promote research and collaboration among statisticians from industry, academia, and regulatory agencies. All activities of DISS2021 will be hosted online from April 21 to April 23, 2021. You may register here: <https://sites.duke.edu/diss/register/>

The deadline for poster abstracts submission is April 7, 2021. For more information on poster session, visit this link: <https://sites.duke.edu/diss/poster-session/>

2021 DIA/FDA Biostatistics Industry and Regulatory Forum

The *DIA/FDA Biostatistics Industry and Regulator Forum* is focused on statistical thinking to inform policy, regulation, development, and review of medical products in the context of the current scientific and regulatory environments including pharmaceuticals, biologics and biosimilars, combination products and devices, and generics. DIA/FDA Biostatistics Industry and Regulator Forum will be entirely virtual from April 14 to 16, 2021. This meeting will include case studies that highlight particular issues of COVID-19 clinical development and how they were dealt with by sponsors and FDA. Speakers will also discuss the statistical issues and solutions to handle the unprecedented uncertainty and changing dynamics.

JSM 2020 BIOPHARMACEUTICAL SECTION CONTRIBUTED PAPER AWARD

Due to uneven votes through different voting platforms for 2020 JSM presentations, the contributed paper award could not be evaluated. The Biopharmaceutical Section Contributed Paper Award committee would like to express our gratitude and appreciation to all organizers, chairs, presenters and discussants of the sessions sponsored by the Biopharmaceutical section in 2020 JSM for the support.