SCT Newsletter Vol. 11

May, 2017

New President's Welcome

Dear SCT members,

As your new President I want to say how excited I am to be able to lead the Society during the upcoming year. We have had a very busy and successful past year under the able leadership of Domenic Reda, who spearheaded several initiatives and who, together with our MRC Hubs colleagues, Scientific Program, and Education Committee chairs, worked tirelessly to ensure a successful meeting in Liverpool. I write this note on the eve of the Liverpool meeting, aware that over 1,000 individuals have registered and confident that all those who attend will find it to be a rich and rewarding experience!

As you all know, our mission is "to advance human health through advocating the use of clinical trials, leading the development and dissemination of optimal methods and practices in clinical trials, and educating and developing all clinical trial professionals." We do this not only through our annual meeting, but through our successful journal *Clinical Trials*, our ongoing webinar series, and our outreach activities, to name a few. Together with Domenic as Past-President and Sumithra Mandrekar as President-Elect, I hope to continue to advance our mission and, in particular, to attract individuals to the Society from all of the different professions engaged in the conduct of clinical trials. I am pleased to introduce our Program and Education Committee chairs for next year, Kaleab Abebe and Emily Van Meter Dressler, along with co-chairs Letitia Perdue and Lynda Constable. I look forward to working with them to develop another excellent program for our 2018 conference in Portland, and with our Board of Directors, Executive Committee, committee chairs, and Fernley & Fernley staff as we move ahead and address new challenges and opportunities. Please do not hesitate to contact me with your suggestions, ideas, and comments—it is vitally important that I hear from you. Also, if you have not served as a committee member previously and would like to do so, please let me know.

Regards,

Theodore Karrison
SCT President 2017-2018

2017 Election Results

By KyungMann, Chair, Nominating Committee

The Nominating Committee of the Society for Clinical Trials is charged with identifying candidates willing to stand for election to fill positions as President-elect of the Society and on the Board of Directors. Board members serve a four-year term; the President-elect serves one year in that role before becoming President and one additional year as Past President.

According to the Society's Bylaws (Article II, Section 4), the Nominating Committee includes the current SCT President and President-Elect, two (2) members from the Board of Directors; and three (3) from the membership of the Society at large.

This year the Committee comprised:

KyungMann Kim, Chair (Member at large)
Domenic Reda (President)
Theodore Karrison (President-Elect)
Elizabeth Wright (Board of Directors)
Li Chen (Board of Directors)
Dixie Ecklund (Member at large)
Jane Blazeby (Member at large)

The Nominating Committee was formed in December 2016 and began its work in January 2017 by identifying possible candidates. A call was also sent to all the membership in January, inviting nominations. A list was drawn up and then prioritized by the Committee members. Two for President-Elect and six candidates for the Board were identified. After ensuring that all the members of our short listwere eligible and willing to stand, the list was submitted to Fernley & Fernley in February for balloting.

The online election was held after that, with all current SCT members eligible to vote. The following individuals were successful in being elected:

President-Elect:	Sumithra Mandrekar, Mayo Clinic
Board of Directors:	Jim Dignam, University of Chicago
	Will Meurer, University of Michigan
	Liz Thom, George Washington University

Meet your newly elected President-Elect and Directors

President-Elect

Sumithra Mandrekaris Consultant and Professor of Biostatistics and Oncology at Mayo Clinic and serves as Section Head, Cancer Center Statistics, Mayo Clinic, Group Statistician for Alliance for Clinical Trials in Oncology, and Associate Director, Biostatistics Shared Resource, Mayo Clinic Cancer Center.
According to Sumithra, "I have benefitted greatly from being an active member of this society and participating in the annual meetings. I [am] deeply and humbly honored to serve as the president of the Society. A

few things I would like to explore as President in leading this prestigious society to grow the next generation of clinical trialists, and improve the visibility and membership to the society include:

- Expansion of the educational initiatives throughout the yearsuch as the webinars, satellite symposiums etc.
- Continued emphasis on mentoring and professional development of clinical trial professionals: one day training program in conjunction with the annual SCT meetings or in partnership with other societies
- Explore opportunities to expand international membership and collaborations since clinical trials are conducted globally
- Joint meetings with international societies such as the ICTMC, ISCB etc. every other year or so to strengthen and increase visibility of the Society.
- Thematic sessions for annual meeting focusing on areas of greatest need: big data – how to navigate it and its challenges; genetics, omics and clinical trials – PHI issues, statistical challenges, logistics; patient reported outcomes and comparative effectiveness research etc.
- Improve the financial stability and structure for the society
- Explore opportunities to have local or regional SCT chapters

Board of Directors

James J. Dignam is Professor of Biostatistics, Department of Public Health Sciences, University of Chicago.
His goals for the Society are as follows:

- This is a critical time to maintain and enhance advocacy for the role of clinical trials in preventative and therapeutic intervention development. There is ever-increasing support for broad data sharing followed by analyses using sophisticated tools, with the promise that credible data on interventions will emerge. While we cautiously consider these approaches that indeed may enhance evidence-based therapy development, the primacy of clinical trials should not be diminished. SCT should stand as the primary advocacy body for clinical trials as a proven and reliable approach to therapy development.
- In relation to maintaining the standing of clinical trials in the evidence-based paradigm, the SCT should continue to expand capacity to participate in the public discourse on medical research advances. Specifically, SCT should be better positioned to not only comment on results from high visibility clinical trials, but also results of other types of studies that achieve media coverage. We need to more proactively engage in this activity or else lose the opportunity to contribute to the discussion.
- Clinical trials are increasingly used in the social sciences, and it does not appear that SCT is capitalizing on this potential to expand its scope and membership. Such an initiative would also bring interesting new problems and contexts to our current membership, which is largely biomedical research oriented.

William J. Meurer is Associate Professor, Department of Emergency Medicine and Department of Neurology, University of Michigan.
His goals of the Society are as follows:

- Randomized trials are the best method for learning about the treatment effects of new interventions (drugs, devices, behavioral interventions). The Society should maintain and expand its position as the pre-eminent organization for the design and implementation of impactful and scientifically rigorous experiments. A growing set of distractors (“Big Data”, other

observational designs, genomics) have value, but cannot replace well-conceived, prospective research. My goal is to increase the profile of the clinical trial in the scientific community at large to ensure that randomized trials remain valued by the public, funders, and researchers.

- A practical goal will be to broaden and more deeply engage the membership in SCT. Trialists who practice clinically often are more focused on their subspecialty or specialty societies and their meetings. Statisticians are often more focused on ASA/JSM and ENAR meetings. That being said, science is done better when clinicians and biostatisticians and project managers and data managers and study coordinators collaborate early. As a group, we could be more forcefully illustrating the value of this collaboration and increasing the unique opportunities of the meeting as a gathering place to move the field forward and move forward individual projects. Stated simply, my goal would be to have more deliverables (new projects, guidelines, resources, collaborations) emanate from the annual meeting each year.
- A final goal would be to increasing the innovation in sessions. More audience engagement and interactivity would be welcomed. Some experimentation with alternate types of presentation (like TED talks perhaps) would be helpful. The board, program committee, and education committee should actually plan experiments to see what is attended and what leads to the desired deliverable (new trials, better research on research like experiments on how to do recruitment, and more collaborations.) Given the great thoughtfulness of our members, we need to make our meeting more experimental and quantitative. There is no reason there should not be 10 "trials" going on as part of the annual meeting of the Society for Clinical Trials that allow us to evolve and make the meeting better and more useful for the future.

Elizabeth Thom is Research Professor, Department of Epidemiology and Biostatistics, Milken Institute School of Public Health, George Washington University and serves as Director of the George Washington University Biostatistics Center.

Her goals for the Society are as follows:

- One of the unique features of SCT is its multidisciplinary nature. This aspect should be sustained and even strengthened. For example, there could be a targeted and sustained effort to increase the involvement of clinician investigators. Many are quite experienced in proposing and conducting trials, interested in trial methodology, are on data monitoring committees; yet do not think of SCT.
- Increased central support and perhaps oversight for invited sessions. The excellent diversity of the program is driven by the invited speakers, especially those from outside of the society. They have given up time and money to take part. We should make sure that they have a good experience to make it worth their while especially as they have demonstrated a commitment that we could tap into.
- I am looking forward to the joint meeting with the ICTMC. I thoroughly support the idea of collaboration among trialists globally, and in the process, building capacity in lower to middle resource countries.

This year, only 179 SCT members cast votes, a dismal number I might add. Please do take the time to vote in future elections. You saw what happened in the recent presidential election. There are consequences to abstaining from exercising your right and responsibility.

The 2016 David Sackett Trial of the Year Award – By Scott Evans

Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis (ORATORIO)

Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis (ORATORIO, NCT01194570), a randomized controlled trial, is the 2016 awardee for the prestigious David Sackett Trial of the Year Award, presented annually by the Society for Clinical Trials. Jerry S. Wolinsky, Emeritus Professor in Neurology, The University of Texas Health Science Center at Houston, and the senior investigator on the ORATORIO Trial accepted the award on behalf of the ORATORIO Trial team. Dr. Wolinsky presented the ORATORIO Trial on May 9, 2017 at the Society's 38th Annual Meeting in Liverpool, England.

Primary progressive multiple sclerosis,accounting for 10 to 15% of the overall population with multiple sclerosis, is a characterized by insidious progression of disability from disease onset. No disease-modifying treatments were approved for this form of multiple sclerosis until 28 March 2017 when the U.S. Food and drug administration approved ocrelizumab for this indication on the basis of the ORATORIO trial.

The ORATORIO trial had as its primary objective to determine if ocrelizumab, a humanized anti-CD20 monoclonal antibody directed against CD20-expressing B-cells, delays neurological worsening compared to placebo in patients with primary progressive multiple sclerosis. Ocrelizumab was superior to placebo with respect to the primary endpoint of 12-week confirmed disability progression (CDP) (HR 0.76, CI 0.58 to 0.98, p = 0.04). Using hierarchical testing, results on secondary outcomes including 24-week CDP, change in performance on a timed 25 foot walk, and changes in imaging markers, supported the primary outcome. Infusion-related reactions were more frequent on active treatment (39.9% versus 25.9% on placebo), highest at first infusion and diminished in frequency with subsequent dosing; in 1.2% these were severe, with none life-threatening.Infections and serious infections were similarly distributed and opportunistic infection were not seen during the controlled phase of the trial. Neoplasms were identified in 2.3% of actively treated patients and 0.8% of controls. The most recent safety profile updated in the ocrelizumab all-exposure population including open-label extensions remains consistent with the controlled treatment periods. As the first successful trialconducted in primary progressive multiple sclerosis, this is an important milestone, extending therapy to control worsening to our patients with what previously was a recalcitrant form of the disease.

Each year since 2008, the SCT Trial of the Year has been awarded to a randomized, controlled trial published (either electronically or in print) in the previous calendar year that best fulfills the following standards:

• It improves the lot of humankind.

• It provides the basis for a substantial, beneficial change in health care.

• It reflects expertise in subject matter, excellence in methodology, and concern for study participants.

• It overcomes obstacles in implementation.

• The presentation of its design, execution, and results is a model of clarity and intellectual soundness.

Nominations came from Society members, investigators, and interested scholars from around the world.

The 2016 Trial of the Year selection committee included Scott Evans (Chair), Kay Dickerson, Bob Dworkin, Dean Follmann, Toshimitsu Hamasaki, Frank Rockhold, Yves Rosenberg, Wendy Parulekar, and Janet Wittes.

The 2017 Trial of the Year Selection Committee will issue a call for nominations in fall, 2017. Visit www.sctweb.org for updates.

2017 Class of Fellows of the Society of Clinical Trials

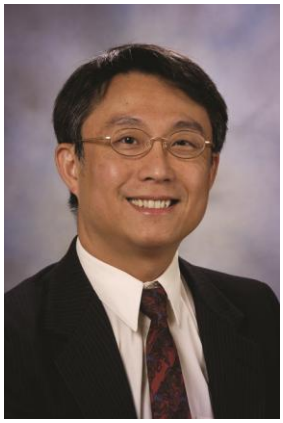
By Susan Halabi

The Society for Clinical Trials Board of Directors has unanimously approved the following candidates as Fellows of the SCT in 2017.On behalf of the SCT Board of Directors and members of the Fellows Committee, please join me in congratulating the class of 2017 fellows for their extraordinary professional achievements.Listed below are the elected fellows with a brief biography, and their citation in italics.

Daniel Heitjan, Ph.D. is a Professor of Statistical Science and the Director of Southern Methodist University, Dallas, TX, USA. He is a fellow of the American Statistical Association and is a fellow of the Institute of Mathematical Statistics.

For important contributions to statistical methods in clinical trials, particularly in real-time prediction, the design and analysis of phase II studies in cancer, economic analysis, and incomplete data and causal modeling; for leadership in the conduct of clinical trials; for contributions as a teacher and mentor; and for distinguished and sustained editorial service.

J. Jack Lee, PhD, MD,is a Professor, Kenedy Memorial Foundation Chair in Cancer Research and Associate Vice Provost for Quantitative Research at MD Anderson Cancer Center, Houston, TX. He is fellow of the American Statistical Association.



For seminal contribution to the development of Bayesian adaptive designs; for deriving innovative statistical methods in translational research; for leadership in the design and implementation of novel treatment and prevention trials in cancer; for dedicated education effort in developing software and organizing clinical trial method workshops; for training and mentoring the next generation clinical trial biostatisticians; and for service to the Society.

Kerry Lee, PhD, is Professor of Biostatistics and Bioinformatics,

School of Medicine at Duke University School of Medicine, Durham, NC, USA. He is fellow of the American Statistical Association and was the former biostatistics director of the Duke Clinical Research Institute.

For excellence in leading the statistical and data coordinating center for large multicenter clinical trials, including many important pivotal trials in cardiovascular disease; for excellence in teaching, mentoring, and advocating rigorous design, conduct, and analysis of clinical trials; for providing important clinical trials leadership at the Duke Clinical Research Institute; and for national leadership on NIH clinical trial review committees and active participation on many DSMBs.

Richard L. Schilsky, MD, Is a board-certified internist and medical oncologist. He is the Senior Vice President and Chief Medical Officer of the American Society of Clinical Oncology, Alexandria VA, the world's largest professional organization representing physicians who care for people with cancer. He is also fellow of the American Society of Clinical Oncology.

For exemplary leadership in the conduct of multi-center cancer clinical trials sponsored by the National Cancer Institute primarily through the Cancer and Leukemia Group B; for outstanding contributions to regulatory science and policy in support of efficient clinical trials through participation in numerous NCI and FDA advisory committees and policy boards; and for dedicated participation in clinical research training programs developed by the American Society of Clinical Oncology, the Cancer Education Consortium and the University of Chicago.

Yves Rosenberg, M.D., M.P.H., is Chief of the Atherothrombosis and Coronary Artery Disease Branch, Division of Cardiovascular Sciences at the National Heart, Lung, and Blood Institute, National Institutes of Health, in Bethesda, Maryland. He served as a member of the SCT Board of Directors.

For his contributions to the design, management, oversight and reporting of more than a dozen major, large, complex, multicenter international cardiovascular clinical trials supported by the National Heart, Lung, and Blood Institute, the results of which have been incorporated in clinical guidelines and are influencing today's practice of cardiovascular medicine in the United States and all over the world.

The SCT Fellows Committee is comprised of Drs. Gerry Beck, Ivan Chan, Simon Day, Marie Diener-West, Dennis Dixon, Ian Ford, Susan Halabi (Chair), Virginia Howard, Scott Rushing, Jay Siegal.

Sylvan Green Award Winner
By James Dignam

The 2017 Sylvan Green Award competition received a large number of excellent submissions. This year's awardee is Lawrence Richer, MD, MSc, Associate Professor of Medicine atthe University of Alberta. Dr. Richer is a pediatric neurologist with clinical and research interests in the treatment of headaches and disorders of the autonomic nervous system. He presented his work entitled "Placebo Response is Not Decreased by Enrichment Trial Designs in Randomized Controlled Trials of Triptan Medications in the Pediatric Age Group" in an oral session at the SCT/ICTMC meeting. Congratulations to Dr. Richer.

Thomas Chalmers Student Scholarship Program and Award

This year's Thomas Chalmers Student Scholarship Award competition again attracted a superb body of submissions spanning many important areas of clinical trials. The three Chalmers Award finalists, all of whom received travel support for an oral presentation at the Liverpool meeting were:Ting Wang from the Department of Biostatistics, University of North Carolina at Chapel Hill, presenting "Biomarker Stratified Design Enriched by Auxiliary Variables", Chi Kim Lam from the Department of Statistics and Actuarial Science, University of Hong Kong presenting "Nonparametric Overdose Control for Dose Finding in Drug-Combination Trials", and Yu Lan From the Department of Statistical Science at Southern Methodist University,presenting "Adaptive Prediction of Event Times in Clinical Trials".

Followingexcellentpresentations by all finalists in an invited session at the SCT/ICTMC meeting, the winner of the Chalmers award was Yu Lan. Congratulations to all.

June Issue of Clinical Trails
By Collin Begg

The June issue of Clinical Trials will as usual feature articles on a broad range of topics relevant to the practice of clinical trials of interest to the interdisciplinary spread of the Society's membership.

The lead article will be a report of a survey of clinical research staff and sponsors regarding the impact of the FDA's final rule on requirements for reporting serious and unexpected toxicities from investigational new drugs, conducted by Raymond Perez and colleagues from the Clinical Trials Transformation Initiative.

The report suggests widespread over-reporting with the vast majority of adverse event reports being uninformative. A thoughtful commentary on this work by Elad Sharon of the National Cancer Institute describes the various pressures and incentives that have led to this outcome, and outlines the challenges of creating a real-time reporting system that could be more effective in identifying important safety signals more effectively.

Professor Baron Peter Piot, Director of
The London School of Hygiene & Tropical Medicine
and
The Royal Statistical Society Medical Section

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University of Liverpool

On Monday, 12th June at 5:00pm
in the School's John Snow Lecture Theatre

Followed by a Reception

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38th Annual Meeting of the Society for Clinical Trials

Held Jointly With the International Clinical Trials Methodology Conference