wcg™

CLINICAL RESEARCH TRENDS & INSIGHTS FOR 2021

2020 has been a remarkable year for clinical research in many ways. The COVID-19 pandemic disrupted our usual practices and created chaos for sponsors, regulators, researchers and research participants.

But our adjustments and movement toward recovery also brought us new flexibility, new collaborations and a focus on the importance of both patient-centric research practices and diversity. There have also been incredible achievements by the teams moving forward vaccines, potential therapies and new diagnostics for COVID. As we look back at 2020, the team at WCG is also looking ahead. Our subject matter experts talk about what they see as significant issues and trends in the clinical research world; what they are looking at and looking forward to, for 2021.

LINDSAY MCNAIR, MD, MPH, MSB
Chief Medical Officer
WCG

Regulatory and Ethical Considerations

DAVID FORSTER, JD, MA, CIP
Chief Compliance Officer
WCG

The evolution of privacy regulations will continue and will need to be balanced with the requirement to maintain appropriate documentation of clinical trials. In particular, the ability to transfer personal data among countries to conduct global studies and create submissions appropriate for drug regulatory agencies around the world can be impeded by privacy regulations and court decisions. On July 16, 2020, the Court of Justice of the European Union issued its opinion in Data Protection Commission v. Facebook Ireland, Schrems (commonly known as Schrems II). The decision invalidated the EU-U.S. Privacy Shield Framework, which was used by more than 5,000 U.S. companies to receive personal information regarding data subjects in the EU. Those companies are now transitioning to alternate methods to provide appropriate safeguards. Additionally, there is a small possibility that the U.S. will enact a privacy regulation at the federal level. In 2021 we are likely to see additional developments in the privacy sphere, and with each change there will need to be consideration of clinical trial recordkeeping, as both privacy and access to improved medical interventions are good for individuals in every country.

David Forster joined Western IRB (WIRB) in 1996 and is currently the Chief Compliance Officer for WCG. Mr. Forster co-chairs the Secretary's Advisory Committee on Human Research Protections (SACHRP) Subcommittee on Harmonization (SOH). He previously served a four-year term as a member of SACHRP and was a member of the SACHRP Subcommittee on Inclusion of Individuals with Impaired Decisionmaking in Research (SIIIDR). Mr. Forster also serves on the Certified IRB Professional (CIP) Council.

DAVID BORASKY, MPH, CIP
Vice President, IRB Compliance
WCG

The events of 2020 caused research sponsors and sites to quickly adapt to the reality that physical access to potential research subjects would be limited due to concerns about COVID-19 infection and public health measures put in place to reduce transmission. That had a significant impact on the informed consent process, which presumes that a potential subject will meet in person with the research team to have a consent discussion and, if interested, sign the informed consent document. Access to telemedicine platforms, electronic informed consent applications, and e-signature software allowed informed consent activities, including obtaining consent for changes in research, to continue even when researchers and participants could not be in the same room. Sponsors, sites and IRBs rapidly adapted to this new norm, and regulators provided assurance that the process was acceptable. From my perspective, the successful implementation of remote informed consent processes during the pandemic will have a lasting impact. It will motivate sponsors and sites to continue using that approach. Remote informed consent reduces the research burden on potential participants without compromising the integrity of the consent process while maintaining compliance with all regulatory and ethical requirements.

David Borasky is responsible for leading the quality and compliance activities for all WCG institutional review boards (IRBs). He has 20 years of experience managing IRBs in global public health organizations, large academic medical centers, and independent institutions. In addition to his compliance oversight responsibilities at WCG, Mr. Borasky also serves as co-chair of the Subpart A Subcommittee of the Secretary's Advisory Committee on Human Research Protections (SACHRP) and previously sat on the board of Public Responsibility in Medicine and Research (PRIM&R).

Scientific and Therapeutic Progress

CHRISTOHER DOYLE, PHD
Director, IBC Services
WCG IBC Services

Nucleic acid vaccines rely on intrinsic cellular processes to produce immunogenic proteins from DNA or mRNA molecules. Despite decades of research on these types of vaccines for prevention of infectious diseases, none have been approved by the FDA for use in humans prior to 2020. But that is changing this year with the FDA issuing Emergency Use Authorizations for at least two vaccines with eight more similar vaccines in late-stage clinical trials. In 2021, I look forward to more of these vaccines being fully approved by the FDA. Of note, the magnitude, duration, and nature of vaccine-elicited immune responses will likely differ for each vaccine, and the degree of protection conferred by each may be similarly different. With that in mind, one of the most interesting things to watch for during the upcoming year will be the emergence of "second generation" COVID-19 vaccines that build upon the knowledge gained from those currently being tested.

Christopher Doyle currently serves as an Institutional Biosafety Committee (IBC) Chair and Director of IBC Services at WCG IRB, working with research sites and sponsors to ensure human gene transfer clinical trials are conducted safely. Prior to joining WCG IRB, Dr. Doyle was a research fellow at the Albert Einstein College of Medicine, where he explored mechanisms of antibody activity against Streptococcus pneumoniae. He has authored a number of peer-reviewed publications describing his past research, has served as an ad-hoc reviewer for Infection and Immunity, and is a member of the American Society for Microbiology (ASM) and the American Biological Safety Association (ABSA).

DANIEL KAVANAGH, PHD, RAC
Senior Scientific Advisor, Gene Therapy
WCG IBC Services

Using the U.S. statutory definition, there are more than 6,000 identified rare diseases, with a large proportion attributable to inherited genetic mutations. That means that perhaps thousands of rare diseases could be potentially treatable with gene therapy. However, there are significant logistical barriers to launching bench-to-bedside gene therapy development programs for rare disease. Some of those challenges are disease-specific, but many involve solving platform, vector, and CMC issues that are very similar from program to program. That creates the risk that scarce resources will be used in parallel, redundant programs as each team needs to "reinvent the wheel."

In recognition of these issues, NIH and FDA are developing a public/private partnership, The Bespoke Gene Therapy Consortium (BGTC), building on the existing Accelerating Medicines Partnership model. Major goals of the consortium include making vector technology more accessible and streamlining preclinical and product testing. In the coming year I will be looking for signs that BGTC and similar public and private efforts can significantly reduce the time from discovery to approved treatment for rare disease, especially for pediatric populations with inherited congenital conditions.

Daniel Kavanagh was a principal investigator and assistant professor at the Ragon Institute of Massachusetts General Hospital, MIT, and Harvard prior to joining WCG. He was also vice-chair of the Partners Institutional Biosafety Committee, and a member of the executive committee of the Harvard Center for AIDS Research. Dr. Kavanagh has chaired clinical trials of an investigational human gene transfer vaccine in HIV-infected subjects and is the author of more than 35 peer-reviewed publications in microbiology and immunology.

MARK OPLER, PHD, MPH
Chief Research Officer
WCG MedAvante-ProPhase

2021 promises to be a monumental year for psychiatry clinical trials and other areas of neuroscience, regaining momentum after slowdowns and pauses related to the COVID pandemic. The broad themes of 2021 will be 'from crisis to critical mass' and 'realizing potential.' Significant improvements in characterization of molecular targets and a wealth of new mechanisms will continue to realize significant impact while the technologies and systems adopted to "pandemic-proof" trials become permanent fixtures of the landscape. FDA fast-tracked programs, long running studies reading out, and other narratives will come to some exciting conclusions in the next 12 months. It is interesting to note that some of the new study paradigms that have surfaced in the last few years are demonstrating durability, particularly the adoption of remote assessment as a modality and the blurring of lines between brick-and-mortar (traditional) and virtual trials.

Studies in negative symptoms and treatment resistant depression stand to gain significantly from new methods and the continued success of new mechanisms, such as TAAR1 and targeted NMDA-acting agents. However, it is critical to remember that many exciting advances have floundered in the face of high placebo response, the recurrent anti-climax of our field. Some important evidence continues to illuminate the root causes of trial failure, highlighting the vital need for better study designs to promote smaller, high-powered trials, careful endpoint selection to ensure validity and reliability, and bolder strategies to promote data quality. The promise of 2021 lies in our ability to capitalize on lessons learned during a crisis, our determination to integrate both traditional and novel approaches to research problems, and our willingness to invest in making clinical trials better, rather than just bigger.

Mark Opler was the founder of ProPhase and served as its CEO and chief scientific officer among other positions. He holds the titles of adjunct assistant professor of psychiatry at New York University and assistant professor of clinical neuroscience at Columbia University's College of Physicians and Surgeons. His academic research focuses on the etiology, phenomenology, and treatment of serious and persistent mental disorders. Dr. Opler is also leading the development of the new upcoming edition of the PANSS Manual.

"…some of the new study paradigms that have surfaced in the last few years are demonstrating durability, particularly the adoption of remote assessment as a modality and the blurring of lines between brick-and-mortar (traditional) and virtual trials."

—MARK OPLER

SANDRA SMITH, RN, MSN, AOCN
Senior Vice President, Clinical Solutions and Strategic Partnerships
WCG

Oncology will be a predominant therapeutic area in clinical trials in 2021 as the quest to transform cancer care via 'precision oncology' unfolds. Forty-nine percent of ongoing industry-sponsored clinical trials in 2020 were in oncology and led all therapeutic areas by trial starts at 33 percent. Ongoing interest in biomarkers and the increase in immuno-oncology targets are keeping the pipeline filled with hundreds of therapies in development across all phases. The success of gene modulation therapies in B-cell cancers continues to ignite progress in other hematologic malignancies and greater expansion in solid tumors. Combination options will continue to be explored, combining therapeutic agents as well as multi-modality therapies including novel surgical and radiotherapy approaches.

The abundance of new agents led to innovative trial designs, adding complexity in oncology trials with a resultant increase in patient and site burden. Sponsors are increasingly aware and are actively seeking the patient voice in every aspect of the clinical trial design process. Frequency of visits, use of digital health, patient concierge services, less invasive procedures (e.g. liquid biopsies), support a focus on patient-centered trials. The tumult of 2020 mandated new priorities and workflows at research sites. Financial pressures, staffing challenges, and the continual redesign of delivery pathways encourage review of technology and partnership models to sustain and elevate research programs.[1]

[1] Source: WCG Knowledge Base™

PETER DIBIASO
Senior Vice President, Clinical Solutions & Strategic Partnerships
WCG

Looking ahead to 2021 there continues to be significant interest and scientific advancement in the use of genetic profiling to better understand the biology of disease. Leading the charge with genetic biomarkers in clinical research is Parkinson's disease (PD). Prior research has demonstrated the linkages between certain genetic mutations in patients, which is viewed as another step closer to better understanding the disease, for which there is no cure. With this increased focus on drug treatment approaches, researchers are incorporating genetic counseling as part of study design with hopes for future precision therapy options for patients. Access to genetic screening can also be appealing to prospective study volunteers and as such leveraged as part of an integrated patient recruitment strategy. There has been early success with understanding the linkages of the GBA and LRRK2 genes in PD and I believe many more are expected to surface given the heightened awareness from the research community.

Sandra Smith is an oncology-focused healthcare leader who has held diverse roles in corporate, community-based practice and hospital settings. She has spent her career partnering with physicians and other healthcare stakeholders to drive customer value and clinical excellence in patient-centric oncology services. Prior to WCG, she was vice president of US Oncology Research, where she was responsible for developing strategic partnerships with sponsors and sites to expand clinical trial services in early and late phase trials and launched a gene and cell therapy program. She worked with more than 1,000 investigators and their site staff to redesign clinical trial workflows for operational efficiency, reduced study start-up times, and data integrity.

Peter DiBiaso has a diverse background that includes experience in healthcare management, technology and communications, Mr. DiBiaso has broad experience in portfolio planning, clinical site services, clinical technologies, and strategic outsourcing, most recently at IQVIA as managing director for customer alliances, and at Vertex Pharmaceuticals as a senior operations head. He is also a frequent contributor to trade journals and a featured speaker at international conferences and industry association events. Mr. DiBiaso advocates for the public education of a positive perception of clinical research and is a legislative policy advocate on behalf of the Michael J. Fox Foundation (MJFF).

Shifting to Data-Driven Decisionmaking

JONATHAN ZUNG, PHD
President, Sponsor & CRO Programs
WCG

COVID-19 has impacted our lives and clinical research on many fronts. In 2021 we will see the continued adoption of e-solutions and decentralized clinical trials, along with the need to be flexible given the likely spikes in the virus. For sponsors it will be increasingly important to understand research site constraints, patient concerns, retention in trials and enhancing the diversity of participants within trials. That means sponsors will need to be agile, but more importantly, able to leverage, aggregate and incorporate the insights from within their respective organizations and from their strategic clinical solution providers. Clinical service providers such as WCG touch thousands of institutions and independent sites on a regular basis, allowing us to see early trends and understand what is happening in real time. These insights will allow sponsors to develop plans and provide tailored resources that are aligned with the needs of the clinical program and study participants.

Jonathan Zung has more than 25 years of pharmaceutical development experience in oncology, immunology, cardiovascular disease and other major therapeutic areas. He has held executive leadership positions in the pharmaceutical and pharmaceutical services industries, most recently as group president, clinical development & commercialization services for Covance, where he led a global organization of more than 8,000 employees in 60 countries spanning all phases of development (Phase I- IV), along with global market access services. Prior to Covance, Dr. Zung was vice president and head of global clinical sciences and operations at UCB, with responsibility for clinical operations, data management, sciences, contracting, medical writing and operational excellence.

LINDA SULLIVAN, MBA
Executive Director
WCG Metrics Champion Consortium

I predict accelerated adoption of quality by design (QbD), risk-based quality management (RBQM) and centralized monitoring (CM) approaches detailed in the ICH-E8(R1) draft and ICH-E6(R2) addendums. Sponsors have implemented those approaches during the COVID pandemic out of necessity. Protocols were streamlined, remote and centralized monitoring programs were adopted and reduced/targeted SDV approaches were embraced. Looking ahead to 2021, organizations will implement those approaches across their portfolio of studies as non-COVID clinical trials are restarted. To support successful implementation of these programs across larger portfolios of studies, organizations will need to address two important areas: lack of data needed to support RBQM and CM data analytics and a shortage of staff trained to interpret and act on the data. Those challenges can be addressed through the adoption of industry-based performance and quality metric standards that improve the quality and consistency of the data available to data analytic programs. Additionally, risk management and root cause analysis training programs—developed specifically for clinical research staff—can be deployed to close the workforce skills gap. I believe that 2021 will be the year that the industry embraces QbD, RBQM and CM approaches

Linda Sullivan has more than 30 years of experience working in the healthcare and clinical research industries, helping organizations improve processes to improve financial and quality outcomes. She was a founder of Metrics Champion Consortium, an industry association dedicated to the adoption and utilization of standardized metrics and benchmarks to drive performance improvement. Ms. Sullivan has been a featured speaker at performance metrics, risk-based monitoring, quality management and clinical trial oversight industry meetings, and served on industry advisory boards such as the NIHNCATS Methods and Process Domain Task Force and the ACRP CRA Competency Steering Committee.

by designing less burdensome trials and using data to identify when human intervention is needed to determine whether patient safety and/or data integrity issues are occurring and to take timely action before they impact the integrity of the research.

"...we no longer must wait until the trial is completed to identify problems, and we have a chance to intervene early and minimize their impact."

—ARTURO MORALES

ARTURO MORALES, PHD
Vice President, Data and Technology Solutions
WCG Analgesic Solutions

One of the most exciting trends I see in the clinical trial space is the real-time review and assessment of clinical data, with the aim of correcting issues that may negatively affect their outcome. In the past, trials were treated like black boxes and interventions at the patient or site level were avoided for fear of affecting/biasing the results.

Recent breakthroughs in data analytics have shown that it is possible to identify data quality issues in blinded trials that may cause them to fail, and that it is possible to deploy mitigating interventions that can correct these issues without introducing bias. That means that we no longer must wait until the trial is completed to identify problems, and we have a chance to intervene early and minimize their impact.

The key is to identify data quality biomarkers that can be used as surrogates of underlying data quality issues that may make it difficult (or impossible) to separate drug from placebo (or other comparators) due to factors unrelated to the drug's effects. One can then use those digital biomarkers to monitor blinded trials and systematically deploy clinically informed interventions where applicable, to address issues as soon as they are detected, thereby protecting the trial's outcomes.

Arturo Morales leads the ongoing development and commercialization of the company's proprietary Quantitative Data Surveillance System (QDSS). Dr. Morales started his industry career with Genome Therapeutics as a senior computational biologist. He subsequently led a variety of teams at various companies including the Novartis Institutes for Biomedical Research, where he was global lead for biology platform informatics. Dr. Morales is also the founder of a digital health company that integrates traditional health metrics with a variety of data feeds in order to better identify trends and improve health outcomes.

Technology and Decentralized Clinical Trials

EMMANUEL OLART, MS
Chief Technology Officer
WCG

The rapid evolution of COVID-19 in 2020 accelerated many initiatives in the industry to conduct trials in remote settings. Service providers in the industry had to adapt quickly via both process and technology to prevent compromising study data or losing patient participation.

Now looking at 2021, it is becoming clear that the industry will not go back to where it was at the end of 2019 and that the use of remote visits in clinical trials will be common. Most studies will likely accommodate both in person and remote settings and service providers will have to support this hybrid model moving forward. Many solutions implemented in 2020 were put in place rapidly and were not meant to be used long term; the need for investment to implement permanent solutions will likely drive the agenda of CIOs and CTOs for the upcoming year.

Emmanuel Olart has more than 18 years of experience in the clinical research and technology space leading global software engineering and IT teams and architecting solutions serving the pharmaceutical industry. Before joining WCG, Mr. Olart worked for BioClinica in increasingly senior positions leading to vice president, systems architecture.

"Many solutions implemented in 2020 were put in place rapidly and were not meant to be used long term; the need for investment to implement permanent solutions will likely drive the agenda of CIOs and CTOs for the upcoming year."

—EMMANUEL OLART, MS

JONATHAN SELTZER, MD, MBA, MA
Chief Scientific Officer
WCG

The COVID-19 crisis accelerated the implementation of remote clinical trial methodologies. Recent advances in technology have demonstrated the possibility that remote clinical trials (also referred to as 'virtual' or 'decentralized') can provide increased cost efficiencies. That trend toward efficiency was buttressed by the COVID pandemic as in-person clinical trials became impossible. Regulators concurred, as the FDA and European regulatory agencies released COVID guidances that endorsed remote clinical trial visits. That endorsement by regulators likely was responsible for the ability of many clinical trials to endure throughout the pandemic. It is likely that trend will not end with the pandemic— in fact, most feel it will continue to accelerate. We can expect increasing regulatory attention on data integrity as well as demonstrating that patient safety can be preserved using remote visits.

Academic and industry clinical investigators should begin to work more closely with regulators to develop best practices to detect potential safety issues in a remote setting.

Jonathan Seltzer is a recognized leader in cardiac safety, endpoint adjudication committees and data and safety monitoring committees. He has chaired and served as a committee member for scores of protocols and has functioned as an advisor for dozens more. Currently Dr. Seltzer is on the scientific programs committee for the Cardiac Safety Research Consortium (CSRC) and the steering committee for the Clinical Trials Transformation Initiative (CTTI). Previously, he served as the president and chair of trustees for the Academy of Physicians in Clinical Research.

"Academic and industry clinical investigators should begin to work more closely with regulators to develop best practices to detect potential safety issues in a remote setting."

—JONATHAN SELTZER, MD, MBA, MA

The Business of Clinical Research

MELISSA BOMBEN
Senior VP, Clinical Solutions & Strategic Partnerships
WCG

The talent needs of specialist versus generalist skillsets is accelerating in response to the increasing complexity of clinical research. Today, the talent available to fulfill traditional clinical trial roles (PI, CRC, CRN, CRA, etc.) is anemic, highly competitive, and not scalable at a pace to meet demand. One of the early lessons we are learning in adjusting clinical trial conduct via pandemic-induced transformation are the benefits of talent specialization. Augmentation of clinical trial site resources with specialists has alleviated burden on clinicians, increased access to clinical trials for patients, and improved site performance. That increases our collective confidence that talent specialization is the right direction to increase capacity and efficiency.

ROS CHEETHAM
Senior Vice President, Clinical Solutions & Strategic Partnerships
WCG

I believe that in 2021 the biotech sector of the market will continue to drive growth in both the number of clinical trials and drug approvals. One projection shows that biotech will reach more than $775 billion in value within the next four years. So what's driving this? The current COVID-19 situation is certainly driving some of the growth as companies seek to develop vaccines and treatments for this devastating disease. There are already more than 250 vaccines in development for COVID-19, which is resulting in the need to recruit an unprecedented number of investigational sites and subjects for these trials. However, I also see other areas of exponential growth for the biotech sector. Personalized medicine due to advances in genetics means that other exciting areas of medicine are opening up like never before. Some of those areas are neurology, cardiology, oncology, ophthalmology and rare diseases, because of the advances in genetic determinants of diseases in those areas.

Melissa Bomben is responsible for increasing collaboration across the WCG enterprise to bring best-in-class solutions to our clients. She functions as a subject matter expert for all aspects of clinical operations, providing key strategic input to clients and internal teams. With more than 20 years in clinical research, most recently at Syneos Health, Ms. Bomben translates her vast experience and mastery of clinical trial management into developing evidence-based clinical trial strategies. She is an approachable and decisive executive leader with experience in clinical, academic, and service provider settings. As a highly respected business partner, skilled communicator and facilitator, Ms. Bomben uses a strategic consultancy mindset to partner with clients.

Ros Cheetham has more than 25 years of experience, primarily in clinical and global clinical operations within multiple therapeutic areas, she has successfully led global clinical trials from first-in-human to phase IV, holding such senior positions as Head of Global Clinical Operations at Allergan and vice president and medicines development leader at GlaxoSmithKline in neurology and rare diseases. Ms. Cheetham has an outstanding record of process improvement and change management and has led initiatives within clinical operations, and the wider company ecosystem, that have netted multimillion-dollar savings. She has led teams in the early adoption of eCRF and ePRO tools as well as the adoption of risk-based monitoring.

DAVID B. RUSSELL, CRCP
Director, Site Strategies
WCG

In today's unstable environment due to the COVID-19 pandemic, clinical research has changed dramatically. What was originally seen as a short-term issue in March 2020 has turned into a long-term dilemma with no current end in sight. It has taken some time for sponsors and CROs to formulate remote functions where they were absent before.

I've worked with many research sites that unfortunately had to implement layoffs and hiring freezes shortly after the beginning of the pandemic. For those lucky enough to keep their employment, they were asked to augment other areas of the institution such as the emergency room or care being performed on other floors. Due to these changes, we saw a tremendous decline in enrollment for numerous trials-and the ability to start new studies diminished.

Currently, due to reduced revenue and profits of many healthcare institutions, those research positions have yet to be considered for redeployment. What I've seen is that many of the positions not being brought back are administrative in nature, whether it be data entry, legal CTA review, coverage analysis, budget and contract negotiations, or billing sponsors for the dollars they are owed for the work performed. That is beginning to put research sites in danger of non-compliance, not collecting the funds they are owed- and not negotiating for all the funds needed to be properly reimbursed for the expenses involved in a study.

GEOFF SCHICK, MBA, CHRC
Senior Consultant, Site Strategy
WCG

With the continued economic downturn from the pandemic, research sites in healthcare systems and academic medical center settings will be increasingly challenged to prove the business case for clinical trials research. Sites will have increased pressure to perform cost-effectively and to develop revenue streams beyond enrollments into clinical trials research.

David B. Russell oversees institutional consulting, assists with the institutional sales process, and works with accounts utilizing multiple administrative services that WCG Clinical offers. David Russell has more than 26 years of experience in the healthcare industry, the last 15 of which have been focused on clinical research. David has extensive experience in study start-up, financial reporting, budget/contract negotiations, investigator compensation, revenue cycle management, coverage analysis, research billing adjudication, and process improvement. He has been instrumental in the building, restructuring, and turnaround of numerous research sites, both large and small, throughout the country.

Geoff Schick has extensive experience leading teams through all aspects of complex assignments, customer service initiatives, patient relations, financial management, resource allocation and change management in a variety of large health care groups, including Catholic Health Initiatives, Tenet Healthcare, and Aurora Healthcare. Mr. Schick excels at designing and implementing changes for the benefit of health care companies engaged in clinical research -- creating system solutions, streamlining processes, and engaging external partners to conduct efficient, compliant, and profitable clinical research programs.

Clinical Trial Conduct

BINDI SHAH-JOHNSON, MD
Chief Medical Officer
WCG ACI Clinical

In 2020 we have been forced into a new era of safety in clinical trials. The sense of urgency that we have felt—all parties involved in clinical trials, including sponsors, investigators, participants and supporting vendors—is unprecedented during the COVID pandemic. We are learning to find the perfect balance between "warp speed" development without compromising quality and safety.

In my opinion, one of the most interesting advances we will see is the evolution of trial management and development to optimize efficiency without compromising quality. We have shifted to remote monitoring with limited in-person visits that will be a trend I believe will continue beyond the pandemic. That shift of focus from travel and process to efficiency will cause a shift in clinical trials that may shoot us forward in our ability to develop therapies and bring them to market in a novel way in 2021 and beyond.

MIKE CIOFFI
Senior VP, Clinical Solutions & Strategic Partnerships
WCG MedAvante-ProPhase

The year 2020 has been a year that will be remembered for a lifetime. The challenges during the year have affected our way of life as a society, including the conduct of clinical trials. The COVID-19 pandemic halted economies, lives and clinical trials.

Sponsor companies, sites, and patients have had to adapt to this new environment and have turned to technology to help do that. We have seen a surge in remote visits being supported by telemedicine allowing for patients and sites to safely conduct clinical trial visits during the pandemic. The next year will bring much-needed change to our industry. Hybrid trial designs will dominate the landscape to reduce patient and site burden. Instead of depending solely on in-person visits, hybrid trials use telemedicine, wearables, mobile apps, and other technology to aid patient participation. If as an industry we truly want to make our trials more patient centric, we must improve the patient experience by being flexible, listening to our patients and embracing technology to support our goal of delivering new medicines to patients.

Bindi Shah is an accomplished cardiac electrophysiologist and served as associate professor at Temple University and assistant professor at Weill Cornell Medical College. She was the chair of the ACC scientific sessions planning committee. Dr. Shah is board certified in internal medicine, cardiovascular diseases and cardiac electrophysiology.

Mike Cioffi brings more than 20 years of pharmaceutical industry experience to his role leading MedAvante-ProPhase's operational business units in support of project delivery and implementing global enterprise solutions that drive continuous improvements in efficiency, output, and quality. Before joining MedAvante-ProPhase he was the external clinical innovation leader at Roche, where he was responsible for developing, integrating and operationalizing strategic innovations throughout drug development. Prior to that, Mr. Cioffi was vice president, project management, Americas for PRA International, leading a team of more than 200 clinical research professionals covering all therapeutic areas.

Endpoint Assessment and Interpretation

NATHANIEL KATZ, MD, MS
Chief Science Officer
WCG Analgesic Solutions

One of the most interesting directions I see in clinical research is integrated endpoint protection. We know that for a clinical trial to be successful, much depends on patient performance. Some expectations are obvious, like adhering to medications or to entering data in electronic diaries, although even for those obvious expectations it is appalling how little effort is expended to optimize these tasks. Other expectations are at least as important, but far less obvious, such as reporting symptoms accurately or keeping expectations of personal benefit neutral (the main driver of the placebo response). We have recently launched an integrated endpoint approach, which is the culmination of years of research and development of the original components, and includes validated patient training, handheld e-diaries that recognize when patients are entering "implausible" data and provide training tips so patients can correct those entries before they become part of the clinical database, and central statistical monitoring that detects aberrant patterns in the clinical data and presents automated, customized retraining to patients without any human intervention. Our expectation is that this automated and integrated approach to improving clinical data quality will improve the reliability of clinical trials, and we look forward to proving it!

Dr. Nathaniel Katz is a leading expert in treatment and study design of pain clinical trials. A neurologist and pain management specialist at Harvard Medical School, Brigham & Women's Hospital, and Dana-Farber Cancer Institute, Dr. Katz founded Analgesic Solutions to modernize the design, conduct, and "scientific quality" of pain clinical research, and empower effective treatments for patients. He has completed numerous clinical trials for treatments of pain involving pharmaceuticals, non-pharmaceutical analgesics and devices, and has also conducted studies related to opioids, pain, addiction, and other issues related to opioid therapy.

BOB DAGHER, MD
Chief Medical Officer
WCG MedAvante-ProPhase

To assert that the year 2020 had an unprecedented impact on the clinical trials industry is an understatement; the challenges have been of great magnitude and the changes to protocol design and study conduct have cut across many barriers and boundaries.

As we look toward steering clinical trials strategy to succeed in 2021 and beyond, industry leaders are urged to adapt existing processes and study procedures at the core of any given trial. That pertains to the selection, administration and interpretation of study endpoints. When it comes to the interpretability of any given study results, one must consider the contextual environment for the design of the assay: how homogeneous is the chosen study population, not only with regards to intrinsic patient and disease characteristics; but also with regard- to the possible impact of environmental factors and exacerbation of comorbid conditions on surrogate measures of disease activity. Consequently, the choice and mode of administration of the study endpoints, whether in-person or via remote assessments, become even more important when considering all possible study design options.

Bob Dagher is a seasoned executive leader with diverse biopharmaceutical roles in clinical development and medical affairs. Prior to joining WCG MedAvante-ProPhase, Bob was the Chief Medical Officer of Cadent Therapeutics in Cambridge, MA. Preceding that, he had occupied multiple leadership roles at small and large biopharmaceutical and clinical research organizations, including GlaxoSmithKline, Genzyme, Sanofi and Covance. Bob has fostered the development of multiple products in different indications and development platforms and advanced several small molecules and biologics across all stages of clinical development.

Certain types of clinical outcome assessments are more easily amenable to remote administration than others. When conducting remote assessment, the ability to maintain a high level of engagement and sustained effort on the part of the subject and/or informant is a critical determining factor for standardizing and validating a new mode of administration. In order to maintain consistency across assessments, especially relevant for neurologic evaluations of motor or cognitive impairment, it becomes critical to be able to adapt the technology equipment and tools to the use-case, devise item-level guidance for various scales and allocate training and dedicated support towards the participant and their supportive environment. For presentation of balance abnormalities, it is important to extract out what may not be feasible, despite all concerted efforts and deployment of all available technologies.

With the end in mind, where quality data and interpretability of results are the guide for any informed decisionmaking, expertise is required to de-risk the clinical trial from the added dangers the current pandemic has brought upon us. This new era is foreseen to be especially prone for a spike of new confounders and factors that can negatively impact study integrity. Ensuring additional layers of protection of study endpoints, by reducing the level of "noise" in the signal, is an especially important step in 2021 that can impact the detectability of a therapeutic signal.

"This new era is foreseen to be especially prone for a spike of new confounders and factors that can negatively impact study integrity. Ensuring additional layers of protection of study endpoints, by reducing the level of "noise" in the signal, is an especially important step..."
—BOB DAGHER, MD

JANET WITTES, PHD
Founder & President
WCG Statistics Collaborative

At the end of 2019, had someone asked me to predict the direction medical research would take in 2020, I probably would have looked to more successful immunotherapies in oncology, better understanding of the variety of forms that heart failure would take, increasing focus on rare diseases, and, in light of some disappointing studies of vaccines, less interest in development of vaccines. How wrong I would have been! I never would have guessed that clinical research in 2020 would be dominated by a pandemic caused by a newly emerging coronavirus. Thus I am tiptoeing with humility into guessing what will happen in 2021.

The pandemic has dominated clinical trials in 2020. Efforts to pull old drugs off

Janet Wittes founded Statistics Collaborative in 1990. She is a Fellow of the American Statistical Association, the Society for Clinical Trials (SCT), and the American Association for the Advancement of Science, and an elected member of the International Statistical Institute. Formerly editor-in-chief of Controlled Clinical Trials, she is an associate editor of SCT's current journal, Clinical Trials. Her co-authored monograph on group sequential trials, Statistical Monitoring of Clinical Trials: A Unified Approach, is widely used by students and researchers in biostatistics. Dr. Wittes was honored with the W.J. Dixon Award for Excellence in Statistical Consulting and with the Janet L. Norwood Award for outstanding achievement by a woman in the statistical sciences.

the shelf to test them in COVID-19 patients, a rush to develop at least one effective vaccine, and innovative approaches to operational aspects of trials have characterized clinical trials in 2020. Next year, 2021, is likely to see an explosion of vaccine development for viral diseases given the new understanding that mRNA vaccines are likely to be highly effective. The dramatic success of immunotherapies in cancer will probably encourage the development of molecularly targeted treatments for other diseases with an emphasis on patient-specific interventions. The knowledge the clinical trial community has gained in learning how to implement operationally efficient trials leads to the promise of concerted efforts to design trials that are less burdensome on participants and clinical staff. The community of trialists has learned how to collect data without requiring as many clinic visits and as much data as we have demanded in the past. While many trials, especially of diseases of the cardiovascular system and conditions like diabetes, will likely continue to study a large number of participants, 2021 may well see many more very small trials of rare diseases with mature approaches to utilization of historical controls. At the FDA, the Center for Devices and Radiological Health has accepted Bayesian approaches for approvals of devices. Those methods may become used more often for drugs and biologics as well. Perhaps most importantly, the promise of effective COVID-19 vaccines and treatments may lead to the public's understanding that each of us has a vital role in development of products to benefit the public health.

"The dramatic success of immunotherapies in cancer will probably encourage the development of molecularly targeted treatments for other diseases with an emphasis on patient-specific interventions."

—JANET WITTES, PHD

Patient Advocacy and Diversity

LORI ABRAMS
Executive Director, Patient Advocacy & Diversity
WCG

Over the past decade sponsors and regulators of clinical trials have understood the importance of designing and developing clinical trials with diverse patient populations in mind. Despite this intention, there has been minimal improvement in diverse representation among clinical trial participants. Without diverse input into the design and operationalization of a protocol or program, a study team lacks insights that remove barriers to enrollment; miss cultural and or community concerns that require mitigation; lose opportunities to increase community ambassadors; and may fail to enroll patients that reflect the population of the disease. While many sponsors create recruitment and patient engagement strategies, they fail to develop diversity strategies, which can be incorporated into the engagement plans or stand-alone. Approaches may include partnering with the community and patient advocacy groups to bring awareness of the clinical trial; convening focus groups or community advisory boards; conducting surveys; and partnering with local minority businesses. Successful diversity-related activities engage diverse patients, care providers and communities early in the clinical trial process, thus sending a message that their voice is important and that they have a seat at the table.

Lori Abrams has a long history of improving clinical drug development by including patients, caregivers and advocacy groups into every aspect of the development continuum. In her last corporate role, Lori was the director of diversity and patient engagement in R&D at Bristol-Myers Squibb (BMS). Ms Abrams built one of the first clinical trial advocacy groups in pharma.

STEVE SMITH
President, Patient Advocacy
WCG

Patient advocacy becomes transformational for a disease, a community and a society if those advocating for patients are no longer only the patients themselves, but also those with resources from across all stakeholders. Patient advocacy starts with awareness of obstacles. Multiple crises in 2020 brought awareness of obstacles to accessing health care and clinical trials. Some obstacles the public faced got addressed with home health technologies and methods. Minority patients are also in the spotlight, as long underserved by the medical system and from clinical trials. Impactful advocacy for them would channel awareness into long-term, sustained commitments at high levels of clinical trial organizations to fund and staff community engagement. Relationships based on kept promises builds trust that is sorely missing. Actions to address the well-known list of social determinants of health, and other obstacles to participation in health care and clinical research would be at the core of transformation. Transformation will come from a type of patient advocacy in which all stakeholders passionately collaborate.

Steve Smith is a seasoned patient advocate with an extensive career in software, consulting, process transformation, health care systems and patient-focused drug development. His strong sense of mission to increase the rate at which new treatments for disease can be developed to address unmet medical need is complemented by his conviction that we can develop drugs faster, while remaining safe.

wcgclinical.com