



Clinical Research

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Historical Perspective on Clinical Research.

In the nearly 12 years since I joined the Department, and 18 years since I formally transitioned from bench work to Clinical Research, I have enjoyed the work tremendously and am continuously grateful for the opportunity to be engaged in it. Strangely, fewer people than expected typically think of Human Subjects Research when they think of the broad topic of “science.” This could be in any context from a private conversation, to a scene from a movie, all the way through even to an academic setting. In fact, even in my own field, I have never heard a young person express the desire to grow up and become a “clinical researcher”. Until I was hired into my earliest role in this discipline, I too never knew it existed. At almost 2 decades, it is almost comical.

When the topic of Clinical Research does come up, sadly, the tragic failures of the past often drive the discussion and distract from the value of the bigger story. Undeniably, we all routinely purchase and use products that might or might not be safe or trustworthy if it were not for an unknown number of actual experiments performed with an uncountable number of participants over literally millennia. Millennia? Yes. It has been proposed, and I share with you, as a matter of interest, that the first true clinical research experiment was a nutrition study, performed, under conditions outside our current regulatory framework by the Prophet Daniel while captive in Babylon. The full story, interpreted as a research study is cited below.¹ Its impact was rather profound.

On more recent fronts, the National Institutes of Health (NIH) has defined as its own core mission as follows:

“NIH’s mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.”²

Similarly, the Food and Drug Administration (FDA) is similarly aligned in mission with NIH:

“The Food and Drug Administration is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices; and by ensuring the safety of our nation’s food supply, cosmetics, and products that emit radiation.”³

Independent of funding source, focus on living humans vs. large deidentified data sets, size of study, whether or not there

is publication potential or payment for services rendered, research involving human subjects or data from human subjects, clinical research is an intriguing and important part of the entire research world, a part of discovery itself. It is work which we do with pride and for which we should have some reverence to those who participate, usually with no benefit to themselves. For all the beautiful discoveries in all branches of science of which Clinical Research is one part, I am honored again to provide this year’s update.

Adult Reconstruction

Adult Reconstruction remains highly productive with 11 active funded studies. The myMobility study (NCT03737149) led by Dr. Israelite hit a significant milestone this year when we enrolled our 200th patient. The Medacta Masterloc study (NCT03168750), led by Dr. Sheth, reached its full enrollment goal of 50 patients and continues to follow-up with those enrolled. Dr. Nelson is having continued success with the PCORI funded PEPPER study with ongoing enrollment and about 50 Subjects in active follow up. Dr. Travers maintains his involvement in DePuy ACTIS and Biomet Perfuse and has taken on an important relationship with Drs. Michael Ashburn and John Farrar as a co-Investigator in the NIH funded EN20-01 Centrexion Knee OA Study. In this capacity, Dr. Travers plays a key role in strengthening Penn’s position as a both a HUB and an active study site in the UPENN HEAL- Pain Clinical Trial Network Specialized Clinical Center (U24NS115691-Farrar/Ashburn, NINDS). Dr. Hume continues his activity on two DePuy funded studies of Ceramic on Ceramic Hips one of which successfully closed and the other is fully enrolled and nearing the end of follow up. Lastly, we are very sad to recognize the pending departure of Dr. Lee who has been a tremendously active PI on many studies over the years with about a dozen different Sponsors. Dr. Lee has been extremely collegial and collaborative and has often been the first to step up to assist his partners with enrollment in their studies.¹ We will miss him and wish him well!

Staff in Adult Recon has undergone some growth. We acknowledge the steadfast dedication of Helena Moses who has been supporting Adult Recon since her first day in Orthopaedic Surgery. We welcome the arrival of Abigail Watson to the team. Abby has propelled the myMobility study enrollment forward and restored Penn’s standing among other sites. We also welcome back Warren Harding who has returned to our team. Warren is currently assisting with myMobility and PEPPER and has become our mobile CRC, traveling to our satellite sites to ensure enrollment and follow up activities are accomplished.

Foot & Ankle

Foot & Ankle has wrapped up industry funded studies recently, with Dr. Farber's Treace ALIGN3D study (NCT03740282) being the only active industry funded study currently in the follow-up stage. We look forward to continuing the successful partnership with Treace and initiating another study, MINI3D, in the coming year. We also look forward to additional projects in Foot & Ankle discussed elsewhere in this volume, led by Dr. Josh Baxter and others.

Fibrodysplasia Ossificans Progressiva (FOP)

The Penn FOP clinicians continue to advise industry sponsors on ongoing and upcoming clinical trial design, and their expertise shapes the direction of clinical research in this disease and prioritizes the safety of the FOP community they champion. Dr. Mona Al Mukaddam continues to serve as the PI on the ongoing multi-center industry sponsored clinical trials for FOP while Dr. Kaplan serves as a site sub-investigator and the global PI for these trials. Drs. Emily Chu (Dermatology) and Staci Kallish (Medicine) provide invaluable collaborative work as sub-investigators on FOP clinical trials. The FOP team completed a successful twelve-day FDA audit of 3 studies in their Palovarotene clinical trial program (NCT02322255, NCT02279095, and NCT03312634) over the summer of 2021. In addition to no inspection findings, the FDA auditor complimented the PI and her team on how well they executed the studies and on their thorough and complete record-keeping. Of important note, this FDA audit was the first performed in the Department in over 12 years. The success of this experience reflects very positively on the entire program and is testimony to the dedication and expertise of the FOP Team.

The ongoing Phase II and III clinical trials will come to an end in 2022 and active subjects will be given an opportunity to enter into a new Phase III roll-over study for continued IP access (NCT05027802). A new investigational product, IPN60130, will be studied in a Phase II study set to open at Penn in the spring of 2022 (NCT05039515). Study start-up is underway for a Phase II study of another new investigational product, INCB000928 (NCT05090891). The FOP Program is still supported by Katherine Toder, Project Manager, and Kamlesh Rai, Clinical Research Assistant. The team is excited to welcome two new Clinical Research Coordinators this year, Hongshik Park and Allison Bautista.

Hand Surgery

Hand Surgery has been successfully wrapping up groundbreaking and investigator-initiated studies. The results of Dr. Steinberg's Digital Tomosynthesis study (NCT03856450) are being prepared for presentations and publications. Dr. Levin's DOD-funded Hand Transplantation Qualitative Research Study (W81XWH1820067) has completed the critical milestone of 1st Manuscript submission. The impact and importance of this achievement cannot be understated. Dr. Levin and his co-PIs, Dr. Tulsky (University of Delaware)

and Dr. Tintle (Walter Reed National Military Medical Center) and the respective teams at each site have worked tirelessly to lead those involved in Composite Tissue Allotransplantation to a truer understanding of the entire patient population and patient experience. We look forward to the publication of this groundbreaking work that will assist all providers and patients in the future. The Hand Division welcomed Dr. Andrew Sobel as the Director of the Hand Surgery Clinical Research Program, and he is already making excellent contributions to the Division.

Shoulder & Elbow

Shoulder & Elbow continues its strong Clinical Research presence over the past 10 years with 5 industry funded studies ongoing. We welcomed Dr. John G. Horneff to the Shoulder & Elbow Division, and he brought multiple ASES studies to the Division. This Division has also diversified its energy and expertise by adding quality improvement initiatives to improve patient experience. We are also saddened by the departure of Dr. Huffman during this year but wish him the best in his new location. Dr. Huffman, like Dr. Lee, was very active in Clinical Research at Penn and will be missed. Dr. Tamara Rial has supported this Division successfully as CRC and we appreciate all her hard work, attention to detail, and diligence across this active and productive faculty.

Spine

Spine successfully initiated the new STRUCTURE study (NCT04294004). This project is a Phase II study enrolling patients undergoing single level transforaminal lumbar interbody fusion. This study is led by Drs. George Dodge and Harvey Smith. In the next year, we also look forward to beginning an investigator-initiated study led by Dr. Casper that has received a grant from Cerapedics focused on mindfulness techniques for residents. We welcomed Ellen Stinger as a CRC for this Division and she quickly adapted to not only assisting with Spine studies but also with ongoing projects in the Foot and Ankle and Hand Divisions. Ellen also has been serving as an asset to the entire Clinical Research Team in various capacities and always does so with an enthusiasm and a smile.

Sports Medicine

Sports Medicine continues to have a robust repertoire of active funded projects. Dr. Carey continues in his role as the Local and Global PI on the Vericel sponsored PEAK study (NCT03588975) and also participates in a Vericel sponsored retrospective study. Drs. Kelly and Dodge's study investigating the impact of Kenalog injections on metabolic syndrome biomarkers was also initiated. The recognition and regulation of the pre-diabetic state in the orthopaedic population is anticipated to be very impactful and we look forward to the success of this and similar projects. We recently welcomed a new CRC to this Division, Mounika Ponakala. We are happy to have her as part of the Team.

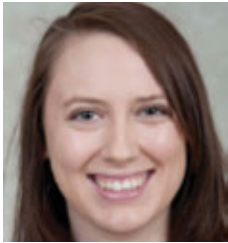
Ortho Trauma

Ortho Trauma is in a phase of expansion. One of Dr. Mehta’s grant funded projects, PREPARE, is wrapping up while another, investigating the relationship of infections, transcriptome, and microbiome in the trauma population, is quickly ramping up enrollment. We look forward to initiating 3 or more industry studies in this Division in the coming months. Linda To joined our team as the Trauma CRC and has swiftly adapted to the unique trauma environment. Linda had previously worked with us during two terms as a Drexel co-op student. We are glad to have her return to us! Dr. Mehta also serves as the

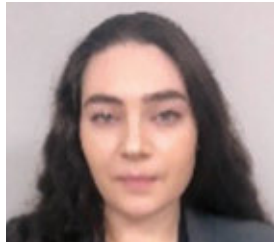
Medical Director of Clinical Research and we thank him for the outstanding job he does of supporting our Team.

Farewell

On a final note of both hearty congratulations, sincere thanks, and farewell, we say goodbye to Dr. Mary Dooley who is leaving our team to joyfully expand her family. We thank her from the bottom of our hearts for her outstanding work and wish her and her family health, prosperity, and success. Thank you.



Mary Dooley
Project Manager



Katherine Toder
Project Manager



Allison Bautista
FOP



Warren Harding
Adult Reconstruction



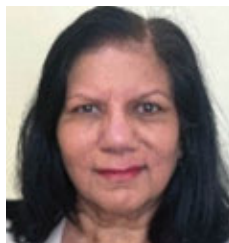
Helena Moses
Adult Reconstruction



Hongshik Park
FOP



Mounika Ponakala
Sports Medicine



Kamlesh Rai
FOP



Tamara Rial
Shoulder Elbow



Ellen Stinger
Spine, F&A, Hand



Linda To
Trauma



Abigail Watson
Adult Reconstruction



Samir Mehta, MD
Chief, Division of Orthopaedic Trauma, Medical Director of Clinical Research
Associate Professor of Orthopaedic Surgery



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Director of Clinical Research
Orthopaedic Surgery and Anesthesiology & Critical Care

1. Weingarten S. (2018). Food in Daniel 1:5-16: the first report of a controlled experiment? JLL Bulletin: Commentaries on the history of treatment evaluation.

2. National Institutes of Health (2017). Mission and Goals. National Institutes of Health Website.
3. U.S. Food & Drug Administration (2018). What We Do. Food and Drug Administration Website.