Virtual Clinical Trials: Challenges and Opportunities – *A Workshop*

LANDSCAPE OF VIRTUAL CLINICAL TRIALS

Completed Trials

REMOTE (Pfizer) – 2011: https://bit.ly/2mIjhHb

- Disease: Overactive Bladder
- Intervention: Tolterodine ER vs. Placebo
- Mode: Web-based trial design
- Phase: Phase 4

Safety and efficacy of Detrol LA (tolterodine tartrate), a treatment for overactive bladder (OAB), the REMOTE trial was the first randomized clinical trial using web- and smartphone-based patient recruitment, enrollment and collection of study data without requiring patients to visit a physical study site. One of the main goals was to compare the virtual approach to a conventional Phase IV clinical study in order to determine if the virtual trial design would be a feasible way to conduct future trials. Unfortunately, Pfizer's REMOTE trial faced a host of challenges, not least of which was the issue of patient recruitment (most members of the target patient group were older, so the use of a technology-based trial was an unknown.) For more information on the trial, please view the study record: https://bit.ly/2Fvr3RV.

A Computerized Intervention for Depression (Beth Israel Deaconess Medical Center) – 2017

- Disease: Depression
- Intervention: Behavioral – interactive media based problem solving treatment
- Mode: Home-computer based
- Phase: Not Applicable

An interactive multimedia computer-based treatment program was developed to provide an electronic version of problem solving therapy for depression (imbPST). The program was entirely automated and did not require involvement of a live clinician. The imbPST program was built to help individuals who do not have access to traditional therapy due to living conditions or individual preferences. The computer based treatment offered several advantages, such as the ability to use it anywhere and its standardized and consistent approach. The aim of this study is to reduce symptoms of depression in subjects through use of an electronic format. For more information, please view the study record: https://bit.ly/2DzDKZm.

Exploratory Virtual Study in Migraineurs to Assess how Migraine Attacks Correlate with Activity Level Measured by Apple Watch and Migraine Tracker App (Amgen)

To leverage advances in consumer electronics, Amgen designed a virtual trial to understand the relationship between migraines and physical activity (as measured by an Apple Watch). Prospective participants registered and downloaded a Migraine Tracker App (developed by Amgen). After determining eligibility via a questionnaire, accepted participants are mailed an Apple Watch to monitor their activity level. Participants are also given instructions on documenting migraine episodes during a 90-day study period. This study tested the hypothesis that changes in activity will correlate with migraine occurrence. For more information, please visit: https://stanford.io/2FziDca.

Ongoing Trials

ALS AT HOME (Barrow Neurological Institute) – 2017

- Disease: Amyotrophic Lateral Sclerosis (ALS)
- Intervention: Other (data validation) – repirometer, handgrip meter, skulpt chisel, ActigraphyMeter
- Mode: Home-based data collection
- Phase: Information not available

A single-center study of up to 150 participants is being conducted to determine the extent to which frequent sampling can improve the qualities of outcome measures collected at home by study participants. The objectives are to 1) assess the extent to which frequent sampling can reduce variability of ALS outcome measures (ALSFRS-R, quantitative hand grip, pulmonary function, EIM in 4 extremities, and actigraphy and voice/speech tracking), 2) assess the compliance of ALS patients in obtained outcome measures at home over the course of 9 months, 3) directly compare outcome measures collected by patients with measurements obtained at study sites, and 4) more fully characterize patients in the Answer ALS study. The benefits of this study are 1) increasing data measurement frequency and thereby statistical strength of findings and 2) convenience for ALS patients who may have difficulty visiting a study center to part of the trial. For more information, please view the study record (https://bit.ly/2PFspOt) and profile at the Barrow Neurological Institute (https://bit.ly/2Q8cHLd).

Virtual-PND (Women's College Hospital) – 2017

- Disease: Perinatal Depression
- Intervention: Behavioral – virtual psychiatric care
- Mode: Video-based clinician visit
- Phase: Not Applicable

Perinatal depression (PND) occurs in 15% of pregnant women and new mothers. The Virtual-PND intervention consists of 12 weeks of the option of supplementing in-person psychiatric care with secure, in-home real-time video-visits through the Ontario Telemedicine Network. This pilot RCT will demonstrate the feasibility of proceeding to a future large-scale RCT evaluation of virtual psychiatric care of this population. Virtual-PND will compare virtual care to in-person care only, with patients being pregnant or postpartum women with a major depressive order. For more information, please view the study record: https://bit.ly/2KkuwBv.

Discussion Draft

ELECTOR Treat-to-target Via Home-based Disease Activity Monitoring of Patients With Rheumatoid Arthritis (Frederiksberg University Hospital) – 2018

- Disease: Rheumatoid Arthritis
- Intervention: Homebased diseased monitoring vs. standard clinical monitoring
- Mode: Telemonitoring tools
- Phase: Not Applicable

The aim of this study is to explore whether the effectiveness of home-based disease activity monitoring via an ehealth intervention is superior to standard clinical disease activity assessment in obtaining and maintaining lower disease activity in patients with rheumatoid arthritis. For more information, please view the study record: https://bit.ly/2BmyKFS.

Enhancing Quality of Life Through Exercise: A Tele-Rehabilitation Approach (McGill University, 2016)

- Disease: Spinal Chord Injury
- Intervention: Behavioral – Physical Activity Intervention
- Mode: Video-based tele-rehabilitation
- Phase: Not Applicable

A pilot RCT evaluating a video-based tele-rehabilitation physical activity intervention to enhance basic psychological needs, motivation, physical activity, and quality of life related outcomes for adults with spinal cord injury. This the first video-based physical activity tele-rehabilitation intervention and it is hypothesized that it will have moderate effects on self-determination theory variables, physical activity, life satisfaction, and depression. For more information, please view the study record: https://bit.ly/2BlR2XE.

Feasibility and Effect of a Follow up Tele-rehabilitation Program for Chronic Obstructive Lung Disease vs. Standard Follow up (University of Aarhus) – 2018

- Disease: Chronic Obstructive Pulmonary Disease (COPD)
- Intervention: Tele-rehabilitation
- Mode: Tele-rehabilitation
- Phase: Not Applicable

This study aims to assess and compare the feasibility of an innovative tele-rehabilitation platform to standard treatment with respect to exercise capacity, quality of life and activities of daily living in patients with COPD. For more information, please view the study record: https://bit.ly/2TvHqRw.

"Recovery 4 US" - A Photovoice-based Social Media Program (Boston University) – 2017

- Disease: Mental Illness, social isolation, and loneliness
- Intervention: Behavioral
- Mode: Social Media Program – "Recovery 4 US"
- Phase: Not Applicable

A randomized trial evaluating a social media program, "Recovery 4 US", aimed at the enhancement of community participation and overall recovery of individuals with psychiatric disabilities. This e-mental health program id designed to be a self-sustaining recovery-oriented virtual community for individuals living with mental disabilities – based on the principles of Photovoice. The "Recovery 4 US" platform includes a mobile phone application and a password protected website; it has three main components: 1)

receipt of a hope-inspiring message, paired with a corresponding visual image; 2) creation and viewing of Photovoice works; and 3) opportunity to attend community events initiated by members of the "Recovery 4 US" community. For more information, please view the study record: https://bit.ly/2zhZ1nu.

Maraviroc to Augment Rehabilitation Outcomes After Stroke (University of California, Los Angeles) – 2018

- Disease: Stroke
- Intervention: Maravirov v. Placebo (both arms receive tele-monitoring by mobile devices)
- Mode: Telephone based messaging
- Phase: Phase 2 and 3

This study will investigate a RCT of Maraviroc in patients with disabilities severe enough to have received inpatient stroke rehabilitation. The usual post-stroke care plus placebo v. Maraviroc (treatment for 8 weeks) will be investigated. Furthermore, all participants will be tele-monitored by mobile devices and be sent telephonic encouragement (based on device data) to walk, reduce sedentary time, and reach and grasp in the home between usual care therapies. For more information, please visit the study record: https://bit.ly/2Bmh3X5.

Announced/Planned

VERKKO (Sanofi) – 2016: https://bit.ly/2S7tStP

- Disease: Diabetes
- Intervention: Validation of remote platform (no investigational product)
- Mode: Online clinical trial platform supplemented with a 3G enabled wireless blood glucose meter (a complete remote clinical trial setting)
- Phase: Phase 4

Sanofi announced its intention to support a virtual diabetes trail (VERKKO) to be conducted remotely in Europe. This virtual clinical trial has one key difference compared to Pfizer's REMOTE study in that no drug is being tested. Instead, Sanofi has teamed up with three other organizations to test a 3G-capable, wireless glucose meter. This trial represents significant advancement in the clinical trial community, as it is the first clinical trial using an electronic informed consent approved by European regulatory agencies.

Virtual Diabetes Trial (Sanofi/Science 37) – 2017: https://bit.ly/2OWNcIa, https://bit.ly/2DO0rty
General Platform for Virtual Trials

Sanofi has partnered with Science 37, a remote research technology company to allow patients to participate from the comfort of their own homes – thereby speeding up the drug development timeline. The Sanofi/Science 37 partnership will enable patients to report data via an Apple iPhone, which are equipped with Science 37's Networked Oriented Research Assistant (NORA) technology – a cloud-based mobile research platform. Qualified participants are provided with a phone, other sensors needed for the trial, and medicines being researched. Study mobile devices allow participants to reach study staff at any time. Furthermore, patients' data are directly sent to researchers, who have ready access to data. This process can eliminate months of searching for participants and travel time to study sites.

Discussion Draft

The Sanofi/Science 37 partnership is the most recent development in a rapidly growing groundswell of interest in virtual clinical trials. Although totally remote research is still a relatively new concept, pharmaceutical sponsors stand to gain millions per trial if decentralization can indeed shorten duration and improve retention, as proponents argue.

Multiple Trials (Novartis/Science 37) – 2018-2020: https://bit.ly/2p0CAwO, https://bit.ly/2DO1wS8
General Platform for Virtual Trials

Novartis has partnered with Science 37 to boost its ability to run "site-less" trials. Its partnership is slated to launch up to 10 trials, with increasing decentralization over three years. Set to begin in late 2018 in the US, trials will focus on dermatology, neuroscience, and cancer. Novartis will leverage Science 37's NORA technology to facilitate remote collection of data. Novartis is no stranger to this approach and has used a "virtual approach" for cluster headaches, acne, and nonalcoholic steatohepatitis.

Neupro Path Pediatric Study (UCB/Science 37) – 2018: https://bit.ly/2wcPCyj
General Platform for Virtual Trials

UCB has announced a partnership with Science 37 to bring clinical trials into participants' homes. UCB plans to use Science 37's NORA platform to evaluate its Neupro® patch in pediatric restless leg syndrome (following its approval for adults). Participants will track their sleep, impact of the disease, and quality of life using the app.