Welcome to our special edition for International Clinical Trials Day! ICTD is an annual event when we raise awareness of clinical trials and celebrate their impact on our health and quality of life. We celebrate on the 20th May as this is believed to be the date of when the first controlled clinical trial was conducted by James Lind in 1747 into the causes of scurvy on board HMS Salisbury. His trial consisted of just 12 men, grouped into pairs and given a variety of dietary supplements from cider to oranges and lemons. The trial only lasted six days but, within that time, there was a noticeable improvement in the group eating the fruit, providing Lind with the evidence required of the link between citrus fruits and scurvy. The evolution of clinical research has been a long and fascinating journey with a wide variety of challenges - scientific, ethical and regulatory. James Lind's trial contained most elements of a controlled trial. The MRCs trial of patulin for the common cold in 1943 was the first double blind controlled trial. This paved the way for the first randomized control trial of streptomycin in pulmonary tuberculosis in 1946. This landmark trial was a model of meticulousness in design and implementation, with systematic enrolment criteria and data collection compared with the ad hoc nature of other contemporary research and continues to be referred to as ground breaking. The ethical advances in clinical trials include several milestones; the Nuremberg Code, Declaration of Helsinki, Belmont Report, and 1996, International Conference on Harmonization Good Clinical Practice guidance. In parallel to ethical guidelines, clinical trials started to become embodied in regulation as government authorities began recognizing a need for controlling medical therapies in the early 20th century. As the scientific advances continue to occur, there will be new ethical and regulatory challenges requiring dynamic updates in the ethical and legal framework of clinical trials, and I think we are all excited to just be a part of it.

The current COVID19 pandemic will no doubt have a lasting effect on all clinical trials - some good and some bad. This recent BMJ paper summarises this very well: BMJ 2020;369:m1744 doi: 10.1136/bmj.m1744. The development of non-COVID related treatments may well be delayed, but this just emphasises that engaging the wider public in our work will become even more vital.

Dr Vanessa Raymont  
Director, Oxford Brain Health Clinical Trials Unit
The NIHR Clinical Research Facility at the Warneford – part of the integrated neuroscience research community in Oxford.

The NIHR Oxford cognitive health Clinical Research Facility (CRF) based at the Warneford Hospital, Director Professor Andrea Cipriani, is funded by the NIHR for early translational (experimental medicine) research.

The CRF works in partnership with Oxford Health NHS Foundation Trust and the University of Oxford and is aligned with the strategies for both the Oxford Health and Oxford Biomedical Research Centers (BRCs). The CRF provides a flexible, integrated neuroscience resource that facilitates efficient, timely conduct of experimental neuroscience, including high intensity, early phase experimental medicine (EM) research and clinical trials.

Since opening in 2011 under the leadership of Professor John Geddes, we have responded to ever changing demands in order to deliver high intensity research by ensuring expert training of our specialist staff and acquiring additional equipment as needed. We work with the Oxford BRC PPI group to develop research delivery with those who have experience of participating in research.

The main research areas include dementia and adult mental health, with a focus on mood disorders. Examples of current studies include: the European Prevention of Alzheimer’s Dementia (EPAD), a research ready cohort study in preparation for an adaptive clinical trial for new treatments; RESTART/RESTAND, studies that use an experimental medicine model to investigate a potential new treatment for depression and SINAPPS2, a phase II clinical trial aiming to test the efficacy and safety of immunotherapy vs placebo treatment in people with acute symptoms of psychosis and anti-neuronal membrane antibodies.

An exciting new development is the integration of the CRF with the Oxford Health BRC ‘Brain Health Centre’ (based at the Oxford Centre for Human Brain Activity), a new integrated research and clinical environment providing high-quality assessments for patients. Patients who are referred will have a detailed brain scan and memory assessment and will hear about a number of opportunities to join in with research. The Centre integrates research into clinical services to improve the diagnosis and management of mental health disorders in a way that can rapidly be implemented to provide improved care for patients and is due to open in 2020.

The CRF is uniquely positioned to collaborate with the neuroscience community in Oxford and beyond, enabling high intensity experimental medicine research and we look forward to working with the Oxford Brain Health Clinical Trials Unit!

For further information, please use the following link;

https://oxfordhealthbrc.nihr.ac.uk/about-us/core-facilities/crf/

Dr Mary-Jane Attenborough
Deputy Director, Clinical Research Facility
The World Health Organisation (WHO) Report on Clinical Trials

By Gayathri Delanerolle

Whilst, it is important to understand that clinical trials grow differently across different parts of the world, gathering of this data is vital for continuous improvement which enhances quality assurance for current and future clinical trials conducted globally. The global clinical trials register is associated with the WHO that maintain these records to develop fit for purpose global healthcare initiatives and agendas by way of research. The WHO’s International Clinical Trials Registry Platform is used to ensure research transparently is achieved, thus, allowing healthcare policy makers to access relevant details. This further assists with strengthening the value and validity of the scientific evidence. One of the challenges many policy makers and researchers have highlighted is the lack of trial transparency and reporting of clinical trial findings. As such, the WHO published a new statement in regard to this in 2015 which showed acceptable timeframes for reporting, calls for reporting previously unpublished studies and to improve association between the trial registry entries and published results. Following on from this, in 2017, the largest funders that support medical research globally, agreed to provide new standards that are required as part of funding applications and subsequent registration of these in a public domain. Whilst these steps have been taken, around 50% of clinical trials remain unreported due to a variety of reasons including negative results, thus, could mislead the risks and benefits of the drug, medical device and/or vaccine that were tested. Therefore, this could lead to further use of suboptimal or even harmful products The WHO’s ICTRP statistics showcase the growth in clinical trials on a global scale. Globally, an excess of 60,000 studies were registered in 2018 alone, thus, this is likely to have increased even further.

“Clinical Trials Day is a well-deserved ‘time out’ to recognize the people who conduct clinical trials and to say thanks for what they do every day to improve public health”

ARCP 2020’

ICTRP Search Portal Statistics

Number of registered clinical trials per year
In 2019, the number of registered clinical trials globally was 2281. It is clear, USA and China appear to have registered the highest number of clinical trials in 2019. These results are quite interesting to see from a socio-economical perspective as well given that R&D investment to further medical research is an important facet to understand and predict continuous improvements healthcare systems could benefit from.

Furthermore, the number of participants globally is quite considerable with the highest number being reported in the US closely followed by Europe. This dataset is quite insightful to furthering capacity and capability aspects of organisations as well given the complex requirements needed to deliver modern day clinical trials.
Patient and Public Involvement: the journey so far

By Claire Murray

Clinical trials have come a long way since their initial conception many centuries ago. Patients and the general public are becoming increasingly involved in clinical trials and research in general. Most organisations that conduct research now insist upon having appropriate patient and public involvement to help design better research. It is a requirement of many research funders and PPI members sit on research approval bodies, such as research ethics committees. Patient and Public Involvement is the focus of Principle 4 of the UK Policy Framework for Health and Social Care Research, which specifies involvement in the design, management, conduct and dissemination of research. PPI has the potential to empower the general public providing democratic accountability which enhances the quality aspects of healthcare research and services.

Evidence associated with PPI itself has evolved quite rapidly over the last 10 years. However, there are challenges with conceptualization, substandard quality reporting and non-standardised definitions. Systematic reviews have identified benefits of PPI on research, researchers, patients and healthcare service communities. Patient-focus research topics are now prioritized by many funders and PPI has been found to contribute to the successful recruitment of clinical trial participants especially if it includes lived experience of people with the health condition under study.

Healthtalk.org researchers interviewed patient and public members who identified personal benefits to being involved, including helping others and making a difference, giving purpose after a serious illness, a route to developing new knowledge, skills and confidence, and satisfaction from being involved in an interesting project.

As we commemorate International Clinical Trials Day 2020, we wanted to take a closer look at how Patient and Public Involvement can inform clinical trials.

PPI plays a key role in the development of successful trials. It allows both patients and clinical researchers to understand the needs of one another and helps to ensure a clinical trial that is fit for purpose. Involvement activities can provide important contributions to:

- Helping define the most relevant research question and outcomes
- Designing a trial appropriate to the needs and lifestyle of the patient community it serves
- Developing accessible and useful participant materials
- Conducting the trial in a participant friendly and ethical way
- Disseminating trial results to maximise and awareness and ensure the adoption of trial results in clinical practice

We asked three senior clinical researchers working with the Oxford Brain Health Clinical Trials Unit to share their experiences of patient and public involvement.
John Geddes, Head of Department of Psychiatry, University of Oxford, Director of Research and Development for Oxford Health NHS Foundation Trust, Director NIHR Oxford Health Biomedical Research Centre

“Our clinical trials are very complex and usually begin with a high-quality stock taking of the existing evidence. Questions asked by my patients have led directly to specific pieces of research that reveal the state of the science and inform the design of our clinical trials. So, in this way PPI is an essential part of the process of how we develop questions for clinical trials.

It makes sure that the questions asked are right, the design is acceptable and robust, and massively helps with the impact and implementation. Only a very inexperienced – or foolhardy - researcher would fail to involve PPI in the conduct of a clinical trial.”

Michael Browning, MRC Clinician Scientist Fellow, Associate Professor, Honorary Consultant Psychiatrist

‘In my experience, the most useful aspect of PPI is that it improves studies in ways I hadn’t even considered beforehand.

During the recent set up of a trial of a medication which has quite a few side effects, the research team was focused on how to ensure the trial was safe. We had lots of rules in place along the lines of ‘ask the patient if they have side effect X, if they do reduce and stop the treatment’. We discussed the trial with our PPI group and got the feedback — ‘if I think this drug is helping me, and you tell me that you will stop it if I have side effect X, I am just not going to tell you that I had side effect X’.

It needed the patient perspective for us to see that our safety rules were in fact not very safe because they just stopped people being open with us.”

Vanessa Raymont, Senior Clinical Researcher, Director Oxford Brain Health Clinical Trials Unit

“From my perspective, PPI is vital to clinical trials.

I would say that especially within trials for dementia as we are moving towards earlier and earlier biomarkers, in order to identify those at risk, and most importantly track any response to new drugs, the need to include PPI is really important. Without knowing what people may want to engage with when they are still well, we cannot plan such studies.

Also, we need to know now more than ever what people feel about being given a preclinical diagnosis while no effective treatments exist. This has been a cornerstone of setting up the Deep and Frequent Phenotyping study in particular.

Understanding the perspective of patients and potential participants will also be key, to successful recruitment for example, as we move into a post COVID-19 world, with the ‘new normal’, when people may be much more cautious about travelling and taking part in research.”
With increasing pressure and health and social care challenges, the importance of diverse thinking in order to develop innovative and sustainable clinical care solutions is vital. Therefore, it is imperative to have the support and involvement of PPI groups to harness their experience, wisdom and energy to take clinical trials to the next level.
Coping mechanisms following the impact of COVID-19

By Sophie Roberts

As we commemorate International Clinical Trials Day (ICTD), we find ourselves in unprecedented circumstances due to the COVID-19 outbreak. Clinical trials have been adapted in different ways whilst many studies have halted their recruitment until further notice. However, novel pandemic-based research has been prioritized and rapidly initiated within academia, industry and healthcare. For those clinical trials that remain open, conducting these under trying times have resulted in many modes of innovative coordination.

In practice, this pandemic has introduced social distancing and isolation measures bringing about significant changes to daily life; many of us have now set up a new home office and have adjusted to working in an entirely different environment. Thus, clinical trials are now being delivered using this home-office method in some ways. Consequently, the clinical trial workforce is under increased pressure due to the high demand in workload, and those in redeployment are adapting to new work practices. These changes to our daily routine can be stressful and impact our physical and mental wellbeing. Now more than ever, it is vital that we consider our mental and physical health and methods to address any strenuous circumstance. Interesting research in relation to exercise and relaxation methods are being carried out globally by various research groups that may move on to become large scale multicenter clinical trials. Whilst new trials concerning the impact of COVID-19 on mental health will of course be a priority and will continue in the years to come, there are other ways the existing knowledge from previous pandemics such as SARS can be used in our daily lives to better cope.

Stress itself is a natural response to any unknown situation. However, chronic exposure to stress can have a negative impact and unmanaged stress may result in allostatic load. Surpassing the threshold where the body and mind are able to cope leads to allostatic overload. This can leave anyone feeling physically and emotionally exhausted, thus, affecting general well-being. To combat this, employing various coping mechanisms, which require both behavioural and cognitive action, could help. Some examples gathered from sources such as MIND, GOV.UK and Oxford University could be useful.

We can support the mental health of both ourselves and others by finding ways to continue to connect with each other despite the inherent difficulties of social distancing, perhaps through digital communication, listening to the radio or podcasts, or by putting up photos of those we care about. Concerning working life, it can be difficult to communicate effectively with colleagues as we are missing the visual behavioural cues that convey emotion and meaning in conversation. It takes time to adjust to new ways of working, but we need to make the best of alternative methods of communication, such as video calling, texting, phoning or emailing; the key thing is to maintain contact with others.

Helpful tasks at work for positive mental health include having a digital spring-clean: perhaps now is a good time to tidy up the inbox, better organise computer files and folders etc. In addition to this, several websites and universities around the world are offering training courses and other written material free of charge on a variety of topics.
Physical activity is highly beneficial to our mental and physical health, and this can be achieved even with seated exercises, workout videos, or household tasks such as cleaning. When working from home, it is beneficial to take breaks when possible, staying mobile is useful. It is very helpful to go out for a walk, run, or cycle in line with government guidelines.

Outside of work, it is important to draw the line between work and home life, especially if your home is now your office. Managing the hours can be challenging during these times as well. It may help to create a schedule for the day to better organize time and availability to conduct certain tasks. When the working day is done, build in time for activities you find enjoyable at home, such as arts and crafts, playing musical instruments, DIY projects, or yoga. You could also try breathing exercises, which can be found online, and keep your mind occupied with books, magazines, films, or puzzles. We all find different situations stressful, and similarly we each respond better to different methods of coping.

COVID-19 has caused feelings of fear, anger, confusion, sadness, and loneliness; it is important to recognize these negative emotions and address them. Be sure to eat and sleep well, perhaps talk to someone else about how you have been feeling, and if necessary, seek professional support. It is okay to worry sometimes; this is a normal part of life. Try to think rationally, objectively, and carefully about the situation, avoid catastrophising, and aim to problem solve.

Thinking of the bigger picture, it is reassuring to remember how social distancing and isolation measures are benefitting the wider population. Furthermore, when we show kindness to others not only does this make them feel better, but it boosts our mood too.

Comparable to clinical trials, coping mechanisms are beneficial to the health and wellbeing of the wider population. It is beneficial to our wellbeing to keep these approaches in mind, as such techniques can always be utilized in order to stay well generally. Looking ahead to the next ICTD, we may be in and out of lockdowns or find ourselves working in new ways following the impact of the pandemic. In fact, some of us may continue working from home even after restrictions are lifted, after finding successes or efficiencies whilst adapting to the pandemic. In an ideal world, life would be stable and predictable, yet we have to accept this may not always be the case. Either way, try to look after yourself and others as much as you feasibly can, be kind, and stay safe.
The father of scientific versatility; Nikola Tesla

By Gayathri Delanerolle

Many millennials know Nikola Tesla as a result of Elon Musk’s efforts to create eco-friendly industrial advancements. More so than ever, people have become interested in Nikola Tesla as Musk decided to name his fleet of electric cars, “Tesla” to honour the use of his concepts. This inspired generations of consumers and otherwise, to research start discussing about the somewhat forgotten investor, Tesla. Contrary to this notion, most clinicians know of Nikola Tesla for a variety of reasons as his patents resulted in the development of many different medical equipment and devices, especially in Clinical Radiology, Nuclear Medicine, Neurology, Oncology and Trauma Surgery. However, a relatively unknown fact is that Tesla’s patents and scientific reasoning is invaluable to the advancements in clinical trials and methodological designs to test technologies and devices. To explore this further, it is important to understand Tesla and his work.

Nikola Tesla was born on the 10th of July 1856 in Smiljan, Croatia. Tesla is undoubtedly one of the most understated inventors of modern times despite having 300 patents to his name and has made one of the most important contributions to the field of high frequency and voltage electrical currents. Also, Tesla was well known for his versatility as he focused on multiple areas of science. Whilst he was a great inventor, most of the academic community criticised him for completing 24 publications throughout his lifetime without realising, each had wider impact than any other published literature seen at the time and this misconception, prevented Tesla from receiving many academic honors. This is further evident, as Tesla’s contributions are not well discussed in academia compared to Albert Einstein or Thomas Edison, despite the impactfulness of his theories and applications across various genre. This is of course until the revival of his work by Elon Musk and the likes of Rohit Prasad, Steve Jobs and Steve Wozniak.

Some of Tesla’s interests were sparked as a result of random events. An example of this, which is also a fundamental discovery of diagnostic medicine, was ultrasound, that was first explored by Tesla due to the sound vibrations which hindered the use of arc lamps. Thus, Tesla built a high-frequency alternator to remove the sound vibrations. Furthermore, in 1891, Tesla showed that the rapid oscillation currents could cross the human body without the cause of any muscle spasms or tissue damage. This was a sensational discovery as it showed the possibility of therapeutic application and provided the basis to

"From time to time in the rare intervals, the great spirit of discovery finds itself on earth to communicate the mystery that will advance mankind. It selects the most able, the most deserving and whispers its secret into his ear. As a flash of light emerges valuable knowledge. While catching the hidden meaning the lucky one observes a magical change ... Miracles that he sees, although distant in time, will come to materialise. He knows it, there is no shred of doubt in his mind, in every fibre of his body he feels – it is a Great idea."

Nikola Tesla
modern day ultrasound. This methodology was further used by Tesla to create an oscillator to relieve fatigue from leg muscles that is used in the treatment of modern day musculoskeletal conditions. Following on from these discoveries, the Tesla coil and wireless remote controls were developed which is widely used within medical equipment in the modern day. Tesla’s theory and design of wireless streams is used in modern day technology which is applied to both diagnostic and therapeutic procedures such as HIFU which is innovating imaging methods within clinical trials. The same principles are also applicable in clinical trials used to test medical devices, technologies and equipment commonly seen in the 21st century. In 1896, Tesla also used high frequency currents to design an ozone generator to produce ozone with antiseptic and antibacterial properties. This concept was later used in bacteriology and vaccinology production as well as developing and designing aseptic pharmacy units required for clinical trials that comply to Good Manufacturer Production (GMP) standards.

The most useful discovery of all of course is, Tesla’s concepts in Artificial Intelligence (AI) that he demonstrated in 1898 at the Madison Square Garden Electrical Exhibition. At the time, his exhibit was the world’s first AI project which was a radio-controlled vessel and he described that the boat has a ‘borrowed mind’. His design and methods for this were patented (613:809) and he made it a point to generalize the knowledge as much as possible. Thus, Tesla’s device marks the birth of Robotics. Furthermore, an innovation within the circuity of the boat was referred to as “logic gate” became a vital steppingstone to semiconductors. This work resulted in the development of the first industrial robot in 1961 that led to the current theorems in medical technologies. Similarly, these methods were used to develop robots for surgical procedures that was pursued by the Interventional Clinical Trials Unit at UCL/UCLH that provided multiple inventions to the NHS for across specialties of urology, gynaecology, bariatics and general surgery in head and neck, colorectal and hepatobiliary. Furthermore, Tesla’s “logic gate” and primary patent influenced the modern day smart speakers like Amazon’s echo to missile-firing drone aircrafts and the rise to an entire section of applied sciences; referred to as operational research.

It is evident, Tesla’s gift was to explore science in the most intellectual way possible and in many ways, he was ahead of his time. His words often didn’t make sense to many listeners as his mind was a complex web of ideas. He could visualize highly complex systems in his mind with extreme precision and would often say that he can build anything that is in his mind. His presentations were often elaborate plans that were not well defined on paper and could only be executed by him; hence, it wasn’t a surprise that he didn’t work well with others. In many ways, Tesla’s situation itself was unique, since he worked without any affiliation with other academics, institutions or clinicians. He had investors that were interested in his ideas that supported his lifelong efforts to make scientific breakthroughs. Given his unique contributions to the world and the showcase of true human spirit in the form of courage, determination and drive as he didn’t allow his critics to prevail and went on to make his patented work freely available even today to anyone seeking applications using existing knowledge. He is also a great example of knowledge generation and synthesis with a translational focus that is the epitome of applied and biomedical engineering science. However, his work didn’t provide the business sense and financial profits his investors expected, therefore, some of his patents remained

“The day science begins to study non-physical phenomena; it will make more progress in 1 decade than in all the previous centuries of its existence”

*Nikola Tesla*
incomplete when he died. Thus, on this day, as we commemorate International Clinical Trials Day, let us remember, an unsung renaissance figure that showed us that various inventions can be made in one’s lifetime, by harnessing the power of the mind and its ability to innovate epochal discoveries.

“\textit{In 1909, Marconi received the Nobel Prize for the development of radio. In 1915, Tesla unsuccessfully sued Marconi, claiming infringement on his patents. That same year, it was rumoured that Edison and Tesla would share the Nobel Prize, but it didn’t happen. Unsubstantiated speculation suggested their mutual animosity was the cause}” Regardless of these issues, Tesla’s innovations support modern day healthcare and clinical trials. Tesla’s concepts have been instrumental with revolutionising clinical practice in the form of AI and AI based tools as well as medical devices.

\textit{Richard Gunderman}
Alzheimer's disease: The importance of characterising biomarker effects

By Nyla Haque

As we celebrate another International Clinical Trials Day, a key area of research to bear in mind is Alzheimer’s disease (AD). This neurodegenerative disorder can be defined by the presence of two main pathologies, amyloid plaques and neurofibrillary tangles (aggregates of tau protein). After years of extensive research, there are still many unknowns as to how the two pathologies are linked and unanswered questions remain.

In the field of AD and associated neurodegenerative disease, there is a great need for a robust disease-modifying therapy. In order to trial therapies in larger participant cohorts and evaluate efficacy, it is important to first assess the presence of biomarkers which are associated with drug activity. This is a fundamental step in guiding the study design of biomarker-led clinical trials and will allow for precise comparison at multiple time points.

In recent years, with the innovation of immunotherapies transforming other disease areas as a result of extensive clinical trials including several types of cancer and autoimmune diseases; a drive towards using similar concepts to treat AD has been utilized.

As animal model data and translational research has showcased, microglia, primary immune cells of the central nervous system, are thought to accelerate the production of amyloid and contribute towards tau pathology. Therefore, reducing the number of microglia may be beneficial in slowing the progression of AD. One of the key proteins responsible for regulating microglia is a protein called CSF-1R. CSF-1R is a known receptor for two ligands, CSF-1 and IL-34, both driving microglia proliferation. Therefore, inhibition of CSF-1R may be of key importance in the prevention or slowing of neural degeneration.

The MICAD study, being led by Dr Vanessa Raymont within the Department of Psychiatry, aims to investigate the effects of a novel drug which targets CSF-1R. The drug is a CSF-1R antagonist and has demonstrated inhibition of microglial production and a reduction of key brain cytokines (i.e. CSF-1, IL-34).

In this study, we want to evaluate how well this drug is able to block CSF-1R and in turn suppress microglial cells. One of the key aims of the study is to investigate whether or not it is possible to identify minimal changes in levels of proteins which interact with CSF-1R. This will be assessed by comparing change from baseline in levels of CSF protein markers including IL-34 and CSF-1.

Participants, aged 50-85 with mild cognitive impairment will be enrolled in the study and required to take the study drug (or a placebo) for a two-week period.
Throughout the study, participants will undergo assessments including blood tests, CSF collection and cognitive testing.

This study intends to identify biomarkers associated with microglial activity which can be used to measure the performance of the drug. Biomarkers which are identified in this study can then be used in further studies to more thoroughly measure the benefits of the drug and evaluate its ability to slow or prevent the progression of AD. The conceptualisation of biomarker identification is a vital one which has shown clinical value in many other diseases and AD is no different. The challenge here is ensuring the methodologies used for future clinical trials are rigorous enough to fully evaluate the impact a drug has on a multitude of outcomes including brain changes and cognitive decline. However, this hurdle is outweighed by the potential benefit to future populations of patients with AD.

“The neural networks that generate space and time are the very first cells that start to die, perhaps decades before we notice clear symptoms of Alzheimer’s Disease. The discoveries of how the brain encodes space, time and memory is crucial to understanding how higher mental function is generated and of great importance to clinical neuroscience and the global efforts to fight brain disease” Nobel Laureate Professor Edvard Moser
Coronaviruse-19; The Pandemic that will change the conduct of clinical trials forever

By Gayathri Delanerolle

Historical documents reveal, the first report of a coronavirus outbreak was recorded in 1889 in Central Asia. This ignited a global pandemic with the primary symptoms being fever and fatigue which resulted in an estimated death toll of 1 million. This was dubbed as the "Russian Flu" although there is no evidence to suggest this was an influenza as there were no tissue samples collected. Another possibility is that the first sample that was isolated in the 1960s showed there are serious aspects to influenzas than just a common cold. Furthermore, it was confirmed that there were 4 further viruses responsible for 20-30% of colds we often observe. It is only in the last decade or so, virologists have been researching further about these pathogens. As such, the current evidence suggests that viruses that infect human beings may have started a few centuries ago. Thus, it is logical to suggest, there may be commonalities shared between the viruses we have faced in the past and the current Covid-19. Insights into the origins, trajectories as well as features of these coronaviruses may provide researchers the information needed to develop, design and deploy better clinical trials to provide suitable vaccines. This would also provide valuable information to improve the manner in which clinical trials for disease areas other than infection is conducted during an outbreak.

Hence, there are a few more factors that needs to be considered for conducting clinical trials and the WHO’s Pandemic Preparedness whitepaper should be further developed to include contingency plans to effectively manage the global R&D front. A relatively clear fact the current covid-19 pandemic has showcased is that it has "short-circuited" existing clinical trials that were key to important disease groups such as Cancer, Diabetes, Psychiatry and Renal complications. Therefore, valuable resources required for researchers may not become available for a period of time, thereby, delaying the trial conduct and for patients, much needed access to research interventions that may have limited options where current gold standard treatments haven’t been much use to them. This if particularly true for cancer patients, where treatments such as immunotherapies which are otherwise not available within standard of care. In addition to these aspects, the research workforce that had previously worked in these projects may be furlough to other areas in a bid to save costs to funders and organisations, thereby, hindering the continuity and sustainability of the studies that may or may not recover as a result of the "break-in-service". Hence, there is an argument to be made here that patients and researchers from some
disease groups may be victims of the “by stander effect” created by the Covid-19 pandemic. Furthermore, the “by-stander” effect raises ethical and moral implications from a clinical, research and sociological standpoint. Anthropological reasoning would implicate some of Lewin’s social action research from the 1930s that prompted the 1950s cognitive revolution may influence the manner in which clinical trials will be accepted as a society. Whilst prosocial behaviors and engagements could very much increase the support for clinical research and the conduct of clinical trials in general, these short-term actions may still require nurturing and improve researcher-public interactions to sustain the same level of support long term.

As a result of the current pandemic, it is clear that the conduct of clinical trials will change globally and that we must better prepare ourselves to provide continuous delivery of the necessary research interventions to patients even during challenging times as oppose to, for example, stopping recruitment of trials or setting up of new trials. Furthermore, previously frowned upon remote methods may become utilised as standard practice such as e-consenting procedures or the preference for remote-monitoring or remote source data verification methods. Whilst, e-consent was favoured by many globally, there were those who were equally concerned about using this method to recruit patients to trials where studies were a drug or medical device study. In essence, many regulators, including those in the UK did not provide favourable opinions to use e-consenting tools as part of routine practice in clinical trials. Yet, this has somewhat changed during the current pandemic, where these methods are being approved for use to ensure there is continuity of research care where it is deemed appropriate.

Whilst we await for the end of the pandemic and life to reignite our social norms as we know it or perhaps new ‘norms’, it is imperative to expect, the conduct of clinical trials to undergo a revolution.
The Future of Alzheimer’s Disease treatment and The Deep and Frequent Phenotyping Study

By Tony Thayanandan

Alzheimer’s Disease is a complex disease area that requires greater emphasis both clinically and scientifically. Therefore, AD has always relied upon simultaneously gathering scientific and clinical evidence by way of conducting basic research and clinical trials together. Prevention of AD is the single most important need in medicine today; a common disorder with increasing prevalence in an ageing society that has enormous personal and financial bearing on individuals, families and societies. The estimated global prevalence of dementia in 2010 is estimated to be 34 million people, and is expected to double every 20 years (to approximately 66 million by 2030 and to 115 million by 2050) due to an ageing population worldwide and improved diagnosis. Direct and indirect costs for healthcare related to AD are estimated at nearly US$500 billion annually. Between 2002 and 2012, 99% of clinical trials into treatments for Alzheimer’s disease failed. A probable reason for the high failure rate is that treatments are being tested on those who already have irreparable damage to the brain. It is likely that treatments will be more effective in slowing or stopping further at onset of dementia at earlier stages of the disease. The absence of indicative outcome measures suitable for relatively short proof-of-concept trials is therefore an undoubted limitation in the field, and acts as an impediment on early phase drug development.

However, clinical trials for early disease state with either minimal or no symptoms have 2 critical challenges; firstly, identification of those with the disease prior to becoming symptomatic and secondly, measure precise outcomes of current interventions.

The Deep and Frequent Phenotyping study, led by Dr Vanessa Raymont, will recruit 250 volunteers from existing study cohorts led by the Dementias Platform UK (DPUK), and tests will be carried out over the course of 12 months. Together, the researchers will perform up to 50 tests on 250 volunteers from DPUK cohorts, including new tests that have never been used before to detect dementia. The tests will include wearable devices that will give researchers detailed information on people’s movement and gait, and sophisticated retinal imaging that will look at subtle changes affecting a person’s central and peripheral vision.

These potential new biomarkers will be used alone and alongside tests such as brain imaging and assessment of memory and other cognitive functions. They will allow the researchers to recognise the early stages of the disease and those who may be suitable for trials of possible treatments. Success of the DFP study would speed up trials, reduce costs, increase productivity and ultimately contribute to more effective pipelines for early clinical drug
development. The programme will also generate a rich dataset that we intended to make available for use by the scientific community.

“Between 2002 and 2012, 99% of clinical trials into treatments for Alzheimer’s disease failed. A probable reason for the high failure rate is that treatments are being tested on those who already have irreparable damage to the brain. It is likely that treatments will be more effective in slowing or stopping further at onset of dementia at earlier stages of the disease. Also, by targeting people in the earlier stages, it should be possible to design better clinical trials for treatments that make a real difference and improve people’s lives. This landmark £6.9million research project has been designed to identify measurable characteristics, known as biomarkers, which can detect the occurrence of Alzheimer’s disease very early on in the progression of the disease - when a person may have no obvious symptoms.” Adapted from the Medical Research Council Press Release

Editor: Gayathri Delanerolle

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