Knowledge and Innovation Bulletin



A message from the Head of the Department of Psychiatry, Professor John Geddes

As a core part of the National Institute of Health Research (NIHR) Oxford Health Biomedical Research Centre (OH-BRC), the Oxford Brain Health Clinical Trials Unit (OBHCTU) is evolving into a really high quality outfit combining clinical and scientific expertise with robust operating procedures. In my view, a professional and expert CTU is an essential component of all high quality experimental medicine and clinical trials.

Welcome everyone to the first edition of the Knowledge and Innovations Bulletin from OBHCTU. We were established in 2019 to support the delivery of high quality clinical trials in psychiatry and cognitive sciences. In doing so, OBHCTU has become the only CTU dedicated to mental health and we have recently obtained ISO 9001;2015 and Royal Charter accreditation. Research in mental health and dementia can have specific challenges, particularly in terms of recruitment, the running of studies and interpreting the research data, so we hope we can help support all of our efforts in this complex field.

The scope of psychiatry therapeutic interventions have grown massively in the last few decades, thanks to clinical trials. Additionally, there is a greater understanding of the need for generalizability, as patients within clinical practice do not always mirror those enrolled in clinical trials. This emphasis has generated more large scale, stratified, sequential parallel, adaptive and innovative trial designs. As a CTU, we hope to support, collaborate and partner with researchers to mitigate the problems running and interpreting such complex mental health clinical trials, and so ultimately allowing more translation into our clinical services.

Vanessa Raymont
Director, OBHCTU

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A message from the BRC Manager, Marco Pontecorvi

The NIHR is the 'scientific arm' of the NHS. The NIHR invests in infrastructure and in health care professionals and scientists, who can work to translate their discoveries into better treatments, diagnostics and care. In collaboration with Trusts and Universities, the NIHR invests over £1 billion per year to improve the health and wealth of the nation by supporting high quality research. This collaboration is further developed into structures known as BRCs that encourage strong links with industry, patients and public involvement/engagement with the specific aim to develop a contemporary research landscape that is inclusive, transparent and effective. The NIHR OH-BRC is one of 20 BRCs in the UK and 1 of 2 centres completely dedicated to mental health. The OH-BRC collaboration structure includes the Department of Psychiatry, the Clinical Research Facility (CRF), Brain Health Centre and OBHCTU working to accelerate translational research using the 'bench to bedside' concept and implementation to clinical practice. Our BRC acts as a '*gateway to research*' driving innovation for disease prevention, diagnosis and treatment by way of research, thus, is a unique entity that oversee cross-sector research. The BRC has been able to support approximately 239 studies, 59 approved grants (excess of £11.6m) and leverage £32.1m of project funding in the last 2 years. The BRC is halfway through its 5 years funding period, thus, currently aiming to renew the bid for 2022-2027. We hope to replicate the successes and further research capability and capacity.

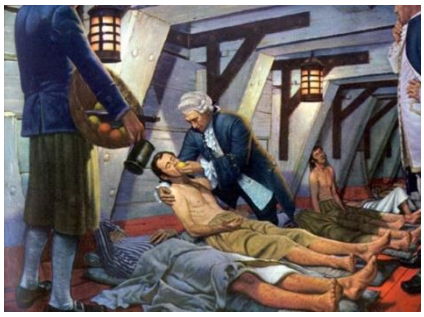
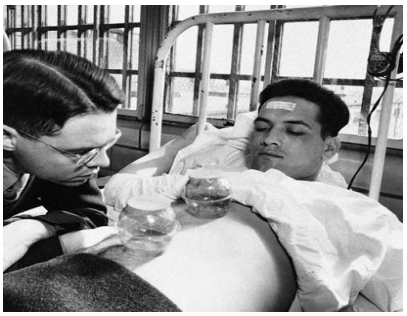
Where are we with Clinical Trials?

By Gayathri Delanerolle

The term "clinical trial" has evolved significantly over many years and it has an interesting history. If one casts their mind back to around 600 BC to Mesopotamia (present day Jordan), the world's first clinical trial was recorded in the "Book of Daniel" described within the Bible. King Nebu of Babylon conducted an experiment to compare 2 forms of interventions and then monitored the results. King Nebu instructed his soldiers to eat only meat and drink only wine in an effort to improve their cognition for battle readiness.

A few soldiers disagreed and informed the King that they would eat a diet consisting of primarily vegetables. Whilst the King allowed this, he restricted the test to 10 days and compared the results which showcased those who had consumed legume and water were fitter compared to the meat eaters. Fast forward from this event to around 2300 years later, Dr James Lind (1716-1794; World's first physician) conducted a controlled clinical trial during his tenure as a surgeon on a ship. He was intrigued by the health of the sailors on board the ship that showcased scurvy. Almost 100 years later, Dr Austin Flint planned and conducted a clinical trial within patients suffering from Rheumatism where he compared a placebo against a herbal remedy. Fast forward a further 100 years to 1943 and the UK Medical Research Council (MRC) conducted a trial to evaluate Patulin treatments for colds. As a result of this study, the first randomised controlled study of Streptomycine for pulmonary tuberculosis was carried out in 1946 by the MRC. This clinical trial showcased the first trial design and delivery aspects including a systematic enrolment criteria, data collection and recoding in comparison to contemporary clinical research controlled designs.

Unfortunately, clinical trials were criticised following a number of high profile public health disasters for researchers to fully comprehend to enforce ideas about implementing medical ethics, strict regulations and maintenance of compliance. A few tragedies were uncovered over the last few decades from the use of Adolf Hitler's concentration camp victims where testing of numerous drugs were made without participant consent, tragedies around the use of Thalidomide amongst pregnant women where misinformation led to still births and children with severe birth defects and Paraxel's TGN1312 first-in man immunotherapy clinical trial where participants were paid up to £2000 for taking part at Northwick Park Hospital (London) that almost cost them their lives due to the severity of adverse events. As a result of these disasters and many other findings by regulators in the UK, Europe and other parts of the world, global standards (e.g. ISO provisos etc.), regulations (e.g. ICH-GCP, IRMER, and MDR etc.), legislations (e.g. Clinical Trial Directive), policies (e.g. Health and Social Care Policy UK) and frameworks were developed. Patient safety is fundamental to managing clinical trials especially when a trial is used as part of a wider research project. As a result of these events, research studies/projects, whether they conduct a clinical trial or not, are audited and inspected by independent regulatory bodies.

Modern day clinical trials are not just for drugs, as there is a diverse array of interventions that are part of healthcare. As such, the use of the term of "clinical trial" has further evolved to remain fit for purpose when evaluating medical devices (including healthcare equipment), healthcare technologies (including software) and healthcare policy implementation. Since, the generation of new knowledge by way of research influences the manner in which clinical care is delivered, consequently, this will impact regulations, legislations and policies to maintain quality and safety for those using healthcare. Therefore, it is safe to say whilst there is a general definition for a clinical trial, it is our ability as researchers to keep up with the changing research and clinical landscape that will allow us to achieve research and clinical excellence.

Technology in Clinical Research

By Sophie Roberts

The use of technology in research has expanded significantly, featuring in areas such as participant randomisation, communication, data analysis, recruitment, and the study interventions themselves. In her keynote address at the recent MHRA Symposium, Sam Atkinson (Director of Inspections, Enforcement and Standards at the MHRA) highlighted the significance of 'Innovation' within the clinical trials landscape; specifically, advances in technology and electronic systems, and personalised medications. This particular focus is congruous with 2 studies recently adopted by the OBHCTU, namely PAX-D and PETRUSHKA.

PAX-D is a multisite, double-blind, placebo-controlled, randomised trial evaluating the effects of the addition of the medicine Pramipexole (a dopamine agonist) to regular antidepressant treatment in individuals with treatment resistant depression. Participation in the study lasts approximately one year, comprising clinic visits, mood monitoring via online questionnaires, a computerised decision-making task, and regular telephone contact. PETRUSHKA aims to evaluate the current evidence on antidepressant treatment of adults with major depressive disorder, and apply this knowledge, alongside individual choices and risks, to the development of an algorithm. This will be hosted within a web-based platform which will subsequently produce a personalised pharmacological treatment recommendation.

Both of these trials focus on improving the treatment of depression, with the aim to inform clinical practice, and offer more viable options for patients. Key data points for the analysis of these trials are informed by user interaction with electronic systems, thus reflecting the evolution of clinical research following advances in medicine and technology. Technology enhances clinical research by improving the efficiency of trial procedures and provide a financial benefit by reducing costs overall. Furthermore, electronic communication can occur instantly and provide opportunities to involve stakeholders who are further afield. However, such innovative research with technology at the centre is not without its challenges. For example, whilst technology is a common place in much of modern society, many individuals may still lack the necessary technical skills required to comply with trial procedures; therefore, investigators should consider the abilities of the participant and the complexity of the given task when designing the trial. In addition to this, software must be rigorously tested and validated to evidence the reliability of the data, and it is vital to carefully consider procedures for storing and transferring data to ensure participant privacy and compliance with data protection regulations. With all of this in mind, it is advisable to seek expert advice when designing a clinical trial, particularly one that involves complex technological systems. No matter the size or scope of the trial there will always be ethical considerations and strict regulatory requirements to adhere to. Technology continues to advance rapidly, and the evolution of clinical research methodology will need to incorporate such changes. This further reinforces the importance of a robust trial design and a clear, comprehensive trial protocol in order to protect the safety of trial participants and the integrity of research data. Overall, the increasing use of technology in research is exciting and largely beneficial, but investigators should also consider the risks involved and proceed with caution.

Women in Science

By Gayathri Delanerolle

Science is the basis to all other knowledge, and it shapes the world as we know it. However, science as a profession is still under-represented by women. Undoubtedly, we've had remarkable scientists that inspired generations, but mostly by bearded old men (sorry Einstein). There have been some extraordinary women who changed our understanding of the world making notable contributions but are often not perceived in the same light as their male counterparts. Women like Caroline Herschel (German Astronomer 1750-1848), Elizabeth Anderson (British Doctor 1836-1917), Valentina Tereshkova (Russian Cosmonaut 1937) and Marie Curie (Polish Physicist 1867-1934) broke the 'glass ceiling' in many ways. Marie Curie, the first woman to win the Nobel prize and the only woman to win this award twice in 2 different scientific fields, paved the way to a generation of young women to believe that hard work renders fruitful endeavours. She was also the first woman to hold a Professorship (Chair) at University of Paris, creating the laboratory that ultimately isolated radium that is fundamental to modern day diagnostic medicine.

"Nothing in life is to be feared; it is only to be understood."

Marie Curie

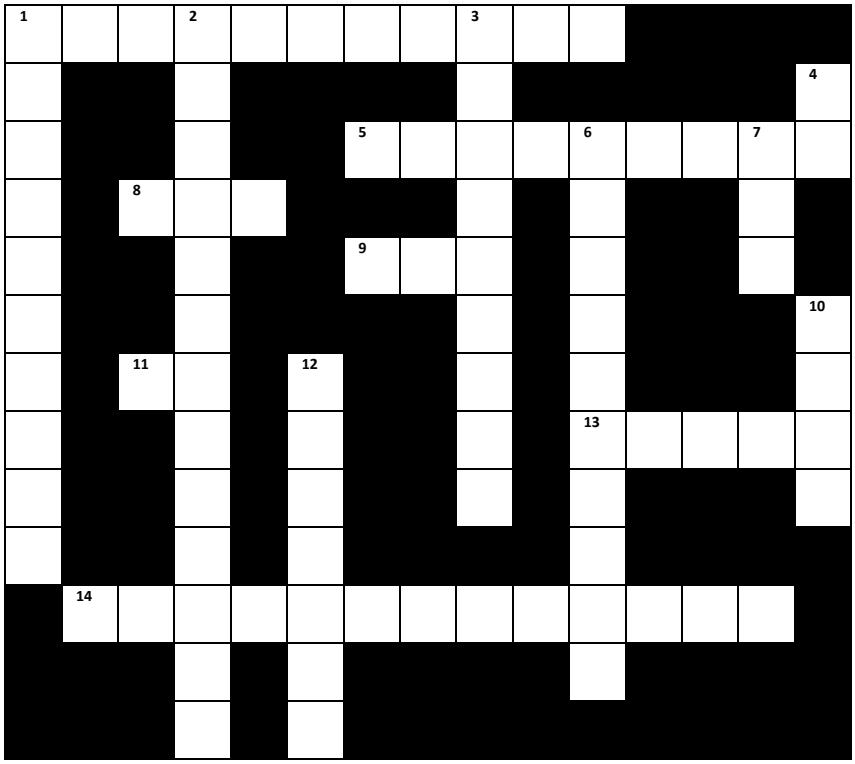
Despite these grand achievements over many centuries, women continue to be underrepresented in science and this is further purported with UNESCO's latest data that suggest, less than 30% of the world's researchers are women. In comparison, the UK, appears to have 38.6% whilst Latvia, Myanmar, Singapore, Bolivia, and New Zealand remain as the only countries that have a female science workforce exceeding 50%. In my own small way, I'd like to contribute to changing these figures and I hope young girls are inspired to pursue a career in science, especially in operational research which is based upon clinical, biomedical and applied sciences. This area of healthcare/medicine is collectively known as Clinical Trials. Clinical trial units or centres (known in some parts of the world) offer the opportunity to obtain a multitude of skills whilst working in different spectrums of science and directly influencing the health and wellbeing of the general public. Clinical trials have the ability to directly change clinical practice. Careers along this spectrum haven't always been clear as pathways to obtain positions were perceived to be restrictive. However, this has significantly changed within the last few years with a more versatile workforce being developed through various training schemes to ensure research undertaken can be delivered more effectively and efficiently whilst remaining more patient centric. As a result of this, there are more opportunities available for anyone interested in working within this domain.

My personal belief is that science has the ability to provide the understanding needed for the greater good of mankind. I'm grateful that I've had the opportunity to be part of such a valuable specialist area that has rapidly evolved especially over the last few decades to better clinical care.

Knowledge & Innovation Bulletin Crossword

Please submit your completed crossword to the email address at the bottom of this page to be entered into a prize draw!

The winner of the prize draw will receive the opportunity to collaborate on a paper and a gift bag.



Across

1. Something that enhances value or excellence. (11)
5. Facts, information, and skills acquired through experience or education; the theoretical or practical understanding of a subject. (9)
8. U.S. organisation responsible for protecting public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices. (3)
9. A taskforce that designs, conducts, analyses and publishes clinical research. (3)
11. The person who takes overall responsibility for the design, conduct and reporting of a study. (2)
13. A systematic, independent and documented process for obtaining evidence and evaluating it objectively to determine the extent to which certain criteria are fulfilled. (5)
14. Prospective biomedical research on human subjects that are conducted to allow safety and efficacy data to be collected for health interventions. (8, 5)

Down

1. The introduction of new ideas, methods, or devices. (10)
2. The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias. (13)
3. A gradual process of change and development. (9)
4. Any untoward medical occurrence in a participant or clinical trial subject administered a medicinal product, which does not necessarily have a causal relationship with this treatment. (2)
6. A facility that conducts manipulation, analysis or evaluation of samples collected as part of a clinical trial. (10)
7. A standard for clinical trials that provides assurance that the rights, integrity and confidentiality of the trial subjects are protected. (3)
10. A hospital, health centre, surgery or other establishment or facility in the UK at or from which a CTIMP, or any part of a CTIMP, is conducted. (4)
12. The absence of errors that matter. (7)

Get Involved!

If you would like to contribute to the Knowledge and Innovation Bulletin, or have any comments or questions for us, please get in touch via the contact details below.

Contact us by email: ga.brainhealth@psych.ox.ac.uk

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