Irish Medical Journal
Established 1867

Issue: Ir Med J; Vol 113; No. 1; P1

Data Sharing Through the Lens of the New England Journal of Medicine

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Jeffrey Drazen, editor of the New England Journal Medicine (NEJM), in a recent address Oct '19 to the Charitable Infirmary Charitable Trust at the RCSI promoted the concept of data sharing in medical trials[1].

He showed a 1916 photo of patients with Polio. All parents at that time lived in fear of Polio. By 1929 one of the treatments for paralytic Polio was the use of negative pressure chambers. Drazen showed a sobering photograph of lines of patients in these chambers. The 1952 Polio epidemic was the worst in US history. There 58,000 cases, 3145 patients died and 21,269 were paralysed.

John Enders had previously successfully cultured the Polio virus in 1949. The big breakthrough was Jonas Salk's Polio vaccine in 1952.

The Salk Polio vaccine trials commenced in 1954. Nearly 2 million children were enrolled by their parents. Computers had just been introduced. The researchers succeeded in the immense task of tracking down the 2 million children after the vaccination. The trial reported in 1955. The rates of paralytic Polio was 16 per 100,000 in the vaccine group and 57 per 100,000 in the placebo group. The clinical trial and the subsequent universal introduction of the Polio vaccine was one of the greatest medical triumphs of the 20th century. And yet, nowadays, some sectors of the public think only about possible vaccine side-effects and the devastation caused by Polio has been forgotten.

In the early years, trials were frequently biased rather than being true randomised control trials. On Oct 12, 1962 John F. Kennedy signed into a law a directive compelling the FDA to do RCTs. Frances Kelsey a pharmacologist and physician, who was very suspicious of bias in drug trials had successfully prevented Thalidomide being introduced into the US. The narrative of Kelsey's persistence was subsequently used to help pass rigorous drug approval regulations in 1962.

Another example was a trial on the treatment of adolescent major depression. Depression was measured in 6 different ways. The medication appeared to benefit only 1 measure but the paper ignored the other 5 measures where it didn't work.

Drazen brought up the issue of changing the rules after the clinical trial has started. This is no longer permitted. Trial registration requirements since 2005 stipulate that trials must be registered. Furthermore the findings must be made available by 1 year after the last patient enrolment.

The process up to 15 years ago was different than now. A trial for example on blood pressure medication would involve the randomization of participants, data analysis, clear the data, and publish.

The current approach is different. The data scientists now have a role in the advancement of human health. The process is that once the RCT is completed and published, the trial data can be stored in a data warehouse. Authors

have the choice of open access, no access or partial access. The NEJM favours the sharing of data with the data scientists.

Drazen gave the example of the trial on the management of raised systolic blood pressure 130-180mmHg in patients over 55 years old. A total of 9361 patients were enrolled. They were divided into the intensive group with a treatment trigger BP>120mmHg and standard group with a treatment trigger BP>140mmHg. The lower target (SBP <120mm Hg) reduced cardiovascular events by 25% and the overall risk of death by 27%. The study underlined the importance of getting both the trialists and the data scientists to examine the data. It is the best way of avoiding delays in the transmission of a medical breakthrough. The NEJM used the SPRINT study for a data sharing challenge because of its importance. The trial had been stopped early because of the strength of the findings.

Furthermore 150 teams have submitted new scientific or clinical discoveries based on their analysis of the SPRINT data. The totality of information in an RCT can be analysed in a number of ways. There are the primary outcomes, the secondary outcomes, and the adverse events. It takes a number of groups to reap the full benefits from an RCT.

Some groups looked at the risk factors, while others examined the predictive elements and the patient variability. Drazen gives the example of a steam engine painting, up close it is difficult to recognize. Scientists removed from the initial study can identify items that were originally overlooked.

The BMJ points out that sharing of the full data sets of an article brings many benefits[2]. In particular it reduces research waste. Many researchers now require that data sets from the studies they fund be shared. The International Committee of Medical Journal Editors (ICMJE) initially stated that clinical trials must include a data sharing plan in the trial's registration. Subsequently, this has been watered because of the many voiced concerns about patient privacy, logistics, and the fostering of 'data parasites'.

The Lancet is somewhat more circumspect[3]. While supportive of the concept it emphasizes the importance of safeguarding the data and using it wisely. The identity of the patients must be protected. The process of data handover must be safe, regulated, and in line with current legislation. Researchers should not post their data openly in downloadable files as it a risk to the individual's privacy. It is pointed out that sophisticated web crawler software can find common numbers across domains. In Europe open data sharing may violate the EU general data protection regulation. There is a particular concern with pseudonymised data.

Randomised control trials guide medicine on the best treatment options in relation to both medication and surgical procedures. The trials, by their very nature, generate vast amounts of clinical information. Previously, much of this data went unanalyzed. Data sharing, undertaken within a regulated framework, has the potential to unlock additional, valuable clinical information.

References:

1. Drazen J. Data sharing in the context of medical journals, through the lens of the New England Medical Journal. The Charitable Infirmary Charitable Trust Tercentenary Medical Lectures. RCSI 24 October 2019.
2. https://authors.bmj.com/policies/data-sharing
3. Ursin G, Malila N, Chang-Claude J, Gunter M, Kaaks R, Kampman E et al. Sharing data safely while preserving privacy. Lancet 2019: 394; 1902.