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INTERVIEW

BETTER AND MORE EFFICIENT TRIALS FOR BETTER EVIDENCE

INTERVIEW with
Prof. SHAUN TREWEEK

-Professor of Health Services Research in the Health Services Research Unit at the University of Aberdeen, UK.

-Editor-in-Chief for Trials

-Leader of the Trial Forge initiative[1]

Education
1990 - 1994, PhD. Bioengineering, University of Strathclyde, UK
1986 - 1990, BSc. Applied Physics, Brunel University, UK

Current and previous positions
2013 - present: Professor, Health Services Research Unit, University of Aberdeen, UK
2005 - 2012: Senior Lecturer, Population Health Sciences, University of Dundee, Dundee, UK
1998 - 2005: Researcher, Norwegian Knowledge Centre for Health Services, Oslo, Norway
1994 - 1998: Research Fellow, University of Strathclyde, Glasgow, UK

Awards
Trial Forge won the 2019 international Cochrane-REWARD Prize for reducing research waste.

Reporter: *Professor Shaun Treweek, you are the initiator of Trial Forge, an initiative that aims to improve trial efficiency by increasing the evidence base for trial decision making. Could you say a few words about:*
- Why this is a very important topic,
- How does it relate to the evidence-based medicine current and also could you give us give us a brief overview of how the idea of Trial Forge developed?

Shaun Treweek (ST): Randomised trials are central to any health care system that considers itself to be evidence based. That means trials are important. But they can also be inefficient, by which I mean they can ask poor research questions, collect outcome data that are unimportant to patients, burden participants and staff with systems that eat up their time and goodwill. Unfortunately, despite trials being central to evidence-based healthcare we have remarkably little evidence to inform our own decisions about how we do things within those trials. Improving the situation is what we want to do with Trial Forge.

I got the idea for Trial Forge after hearing about ways of making marginal gains in performance in British Olympic cycling. The idea being that by making lots of small changes you could make an overall large change. I thought we could perhaps try to do that in trials by improving the evidence base behind our trial process decisions, e.g. how do we recruit, what's the best way of keeping people involved in trial, how should we collect our data. Each change might only lead to a small improvement but maybe by having evidence available to make those decisions, lots of small gains could add up.
We had our first meeting in Edinburgh, Scotland[2], in 2015 and things have progressed nicely since. We now have nine Trial Forge Centres across four countries.

R: *Based on your experience, which are some of the most important trial challenges and how could these be addressed? Which are the most important three issues that the international community of trialists should focus their effort on?*

ST: I think the top three problems in trials now are 1) not doing trials when they are needed 2) doing trials when they are not needed and 3) poor methodological design. The first is a belief that a trial is not necessary and it is considered fine to give patients a treatment for which we have little or no evidence regarding its effect. We see this right now in the COVID-19 pandemic. For example in the US President Trump recently authorized the use of convalescent plasma for COVID treatment despite it being unclear whether it is effective or not, or safe. There are ongoing trials but a decision has been made to just start using it.

These sorts of decision have the potential to do great harm; they have in the past. Similarly, not looking at the existing evidence before designing a trial means it is possible to run a large trial that is actually completely unnecessary because the question has been answered already. It is not difficult to find examples of trials answering questions that were answered many years earlier (there's a great example for tranexamic acid during surgery in the Lancet series on research waste[3].

The people taking part in those trials did not do so to make a modest improvement in the precision of a treatment effect estimate, they wanted to make a difference to the care of people like themselves. Let's not throw that goodwill away.

[1] http://www.trialforge.org
[2] https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-015-0776-0
[3] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)62229-1/fulltext

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And finally, poor methodological design is rife. Anyone who does systematic reviews will know that a depressingly large proportion of the studies included in our reviews are of poor, or very poor methodological quality. Why does this persist? If the methodological approach is poor, it means we can't trust the trial results and if we don't trust the results the whole trial is a waste of time. Once again, we are spilling the goodwill of those who took part. As Doug Altman , the great British medical statistician said 'We need less research, better research, and research done for the right reasons'[4]. There is no shortage of research; much of it is rubbish. This needs to change.

R: *In a recent editorial published in "Trials" you are arguing that research reporting should be clear, complete and easy to navigate. In the recent decades, efforts have been made to standardize the reporting of scientific literature as much as possible and journals are increasingly adopting specific reporting guidelines. In your role as editor-in-chief,*

- Have you observed a significant change in how authors report their results?
- Is there still room for improvement?
- What would you like to see change in the next five years in terms of reporting guidelines?

ST: There is evidence that reporting of trials has improved because of CONSORT (another Doug Altman initiative[5]). I think it is fair to say that reporting has improved. Reporting guidelines generally have helped. But reporting is still far from perfect, something else that is clear to anyone who does systematic reviews. The editorial you mentioned[6] in your question was about trial protocols and my key point was that scientific reporting is not meant to read like a novel but is meant to clearly present what was done and found. It frustrates me how much narrative goes into some articles when we just need to know what the authors did. I suggested in the editorial that those writing trial protocols should be highly structured in their writing so that it is not only clear what was done but it is also easy for a reader to find this information. Increasingly I'd like to see reporting guidance embedded into publication guidance. In other words, researchers follow guidance without having to think about it. There are a lot of reporting guidelines now and it is becoming a bit tricky to know which to use. Maybe more structured templates could help.

[4] https://www.bmj.com/content/361/bmj.k2588
[5] https://doi.org/10.1371/journal.pone.0235535
[6] https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-019-3865-7
[7] https://www.sciencedirect.com/science/article/pii/S0895435619304160

R: *Your focus for research has focused for years on identifying those interventions for trials that can improve recruitment and retention together with the design of complex interventions and the effective presentation of research evidence. Which are the most valuable lessons you appreciate to have learned in these areas?*

ST: For recruitment and retention the top lesson to me has been to think how a trial looks from the perspective of a potential, or actual participant. What may seem a simple recruitment strategy to a researcher may be fiendishly tiresome to a potential participant, or upsetting, or just irrelevant. More and more in trial design we need to talk and keep talking to the people who we hope to help with our trials. In other words, public, patients, health professionals and policymakers. The same is true of interventions. If the intervention is highly demanding of a participant then without a clear rationale for this demand we shouldn't be surprised if few people are interested and fewer still stay interested. Why would they?

For presenting research evidence my key insights came from project I co-led a few years ago on clinical guidelines. The first insight was to present information in layers, with the most important first. The second insight was that practically everybody has no interest in anything but the first layer. We as researchers might think it's important, some others do too. But most people just want the bottom line. I've mentioned systematic reviews a few times now and they are a good example of important work that needs to be repackaged for the information in them to be used by most people. Sometimes the key message from hundreds of pages can be written in one or two sentences. Writing those sentences well is something we should all work on. The GRADE approach to assessing the certainty of evidence has some fantastic resources[7] for linking those sentences to the size of effect and certainty of the evidence, as well as providing consistency in how we describe results.

R: *Would you like to add anything else, maybe an answer to a question unaddressed in this interview?*

ST: If anyone is interested in hearing more about Trial Forge, have a look at https://www.trialforge.org. The recruitment and retention literature is very UK-heavy so if you are outside the UK and would like to evaluate a trial recruitment or retention intervention (or any other trial process intervention for that matter), get in touch, we'd love to hear from you.

Thank you for your kindness to answer our questions

Interview conducted by Raluca SFETCU