In this issue, Curtis and colleagues discuss the impact of guideline and policy changes which may affect clinical practice during the conduct of a pragmatic clinical trial. They go on to make recommendations based on their experience as to how to overcome challenges introduced by these changes. The potential impact of these changes is that the environment in which a trial is conducted mutates as the trial is underway. This may affect the way in which hospital or public health services are organised, the availability or licensing conditions of the study interventions, or may impact on the equipoise of the clinical community conducting the trial shifting community willingness to recruit to a study.

The paper has many strengths to commend it. This sort of meta-research – investigating the research process – is important in its own right. It’s essential to make the research process more robust and efficient 1. Getting the research process wrong contributes substantially to research waste 2. Here, Curtis has considered live issues, and real life external influences, and attempted to extract some general approaches to dealing with them.

However, there are two major challenges which make this paper less useful than it might be. One can only be addressed by the authors, but the other could be addressed by the wider research community.

Firstly, the process by which the recommendations have been generated is opaque. The best guidelines make their processes clear, so the potential user can understand how they are created and take a view on whether they trust that process, and hence whether or not to follow the guidelines. NICE, for example, publish their methods manuals and have a rigorous process of challenge should the agreed process not be followed 3. Even ad-hoc clinical groups working together to produce guidelines can be transparent about their processes 4. The recommendations presented here may be greatly strengthened if the method of production was clearer.

Secondly, the bigger issue is mentioned, but not thoroughly addressed, by the authors. This is very much the experience of a single group within an atypical context for pragmatic trials – the United States of America. Compared to other developed countries, the USA is late to the world of pragmatic trials – with pragmatic trials not taking off until well into the first decade of the 21st century, compared, for example, to a programme of pragmatic trials in the UK starting in the mid 1990s 5,6 . It is also unusual in that it has an atypical health system which relies almost entirely on private insurance companies as payers, alongside private health care provision. This makes findings from systems research like this challenging to generalise to systems using Beveridge, Bismark, or National Insurance models to provide health care 7,8. In addition, there appear to be legal and ethical differences between the way pragmatic trials are conducted in this environment compared to the rest of the world, for example six of the nine studies discussed in the paper had a waiver from the usual informed consent process. Deviations from standard consent processes would be much less common elsewhere.

The authors also edge towards but miss an opportunity in their recommendations. The existence of a trial, or other robust research, is an opportunity to influence guidelines or other elements of the environment that the trial is delivered in, even before the results are known. Trialist activity should go beyond asking guideline producers if changes are anticipated – getting a recommendation to recruit to a trial into widely accepted guidelines has the potential to drive research, and mitigate risks to accrual of guideline and other environmental change. As an example, recruitment to the FOXFIRE trial was recommended as part of NICE’s 2013 guidance on the use of selective internal radiotherapy 9,10.

Work such as that described by Curtis is essential and valuable, but would be so much more useful and generalizable drawn on experience of a wider set of health care and research systems. We have to start with stories like Curtis has told, drawing on a single health system; but with luck, these papers from single health systems will prompt comparisons across health systems - potentially driven by collaborations between research funders - improving health research to benefit everyone. Maybe these comparisons can lead to some robust recommendations for dealing with contextual changes which can be adopted across health research systems.

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