Clinical trial rules should protect patients and results not operational details

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Rules governing the conduct of clinical trials are failing to produce the intended benefits for patients and should be rewritten through a transparent process that involves academic clinical trialists and patient advocates as well as regulators and industry representatives, according to recommendations published today in *European Heart Journal*.

The call comes from the Cardiovascular Round Table (CRT), an independent forum of the European Society of Cardiology (ESC), which convened regulators, drug companies, academic clinical trialists and patients to discuss the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines.

"Well conducted randomised clinical trials are the bedrock of safe and effective, evidence-based treatment of cardiovascular disease. However, the cost and complexity of clinical trials has risen out of all proportion," said lead author Professor Martin Landray, Professor of Medicine and Epidemiology, Clinical Trial Service Unit, University of Oxford, UK. "It means that many potential new treatments are abandoned before their efficacy has been thoroughly assessed. Furthermore, some ineffective or harmful treatments may continue to be used widely because of a lack of robust clinical trial data."3

The paper argues that GCP requirements for randomised clinical trials should be based on the overarching principle of minimising issues that may materially impact the well-being of trial participants or the reliability of the results.

Professor Landray said: "The emphasis on reliable results is not just for academic reasons. It's the results that impact on the care of future patients. If a treatment really works but your trial fails to prove it then you've missed an opportunity. If a treatment is not safe and you miss that because your trial is too small or is badly conducted then that's also bad for patients."

"The rules should be based on the principles, not on the operational details which will, and should change over time," said Professor Barbara Casadei, ESC President-Elect and co-chair of the CRT. "We have no idea what technology and healthcare systems will look like in ten years. What we do know is that protecting patients and obtaining reliable results will remain a priority."

"Even today, innovative approaches to trial design, such as randomisation within the context of a large cardiovascular registry, are often thwarted by concerns about how to adhere to current GCP requirements that were written before the advent of smartphones or the widespread use of electronic healthcare records," said Professor Landray.

The current rules are determined by the ICH (www.ich.org) which includes a select group of regulators, for instance, the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA), and pharmaceutical companies. It does not involve patients, scientific organisations, or academic clinical trialists. The CRT asserts that these groups have a major role to play in improving clinical trial guidelines. Indeed, previous experience, particularly in the US but also in Europe, has demonstrated the importance of effective engagement of all those involved in clinical trials, including academic and patient communities.4

The CRT meeting was the catalyst for MoreTrials, a public campaign "for more, better, randomised trials", of which the ESC is an active

supporter. These efforts have had some success, including signs of positive engagement from the ICH. For example, ICH has already made some helpful changes to GCP. In June 2016, Professor Landray and colleagues were invited to present the CRT's concerns to the ICH meeting and as a result, in January 2017, the ICH launched a consultation on a proposal for more widespread revisions to its key guidelines.

Professor Landray said: "We are delighted that the ICH is starting to listen but there is still a way to go. The ICH has proposed only limited academic engagement in the development of new GCP guidelines (largely confining our input to studies that are observational or based on existing databases)."

Professor Casadei concluded: "The ESC will continue to campaign for much greater engagement between regulators, pharmaceutical companies, patients, scientific organisations and academic organisations in the development and application of clinical trials regulations. Such work is critical to advances in care and improvements in outcomes for patients with cardiovascular disease."

More information: undefined undefined. Effects of Extended-Release Niacin with Laropiprant in High-Risk Patients, *New England Journal of Medicine* (2014). DOI: 10.1056/NEJMoa1300955

Martin J. Landray et al. Improving public health by improving clinical trial guidelines and their application, *European Heart Journal* (2017). DOI: 10.1093/eurheartj/ehx086

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