Institute for Mathematical Innovation

UNIVERSITY OF BATH

Improving clinical trials

Clinical trials are a crucial step in translating fundamental medical research into improved healthcare. But they are expensive to conduct, and making changes to a trial while preserving statistical validity is difficult. Research carried out at Bath has developed methods to help make decisions on when to stop a study, and to allow a broader range of adaptations to be made during the course of a trial. The results of this research have made clinical trials faster and more efficient while maintaining safety.

IMI

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Improving clinical trials

Clinical trials are a crucial step in translating fundamental medical research into improved healthcare. Many hundreds of trials are conducted every year, each involving hundreds, sometimes thousands, of patients.

The challenge

Clinical trials are expensive to conduct, with costs as high as £30,000 per patient. Results can be slow to obtain, and it can be challenging to get large enough sample sizes. There can be good reasons to make changes to the trial once it is underway, or to stop a trial early with a positive result and so bring a new medicine to market sooner. However, it is essential to account for such adaptation properly so that the conclusions remain statistically valid.

The solution

Research carried out at Bath has developed sequential methods which are used to monitor trials and make decisions on when to stop it early, and designs for adaptive clinical trials which allow a broader range of decisions to be made during the course of a trial, such as treatment selection or a re-definition of the target population. These research insights are summarised in the book *Group Sequential Methods with Applications to Clinical Trials* by Christopher Jennison and Bruce Turnbull (Chapman and Hall / CRC Press, 1999), which has become the standard text on the topic and is widely used by medical statisticians.

The benefits

By establishing better 'stopping rules' for the termination of a clinical trial, research in Bath benefits huge numbers of future patients beyond the trial either by making effective new treatments available sooner, or by halting a poorly performing treatment early to release resources for studies of other promising therapies.

"Our flagship software package East© is used by almost all major pharmaceutical companies ... and governmental agencies (e.g., FDA, NIH). ... The statistical methodology that we have implemented in East for such trials relies on the theory that was published by Jennison and Turnbull. This seminal paper has had a huge impact on clinical trials and has facilitated the use of group sequential and adaptive methods that can save patient resources and bring new drugs to market faster. It is fair to say that many companies have purchased East© almost entirely because of its Survival Module. The reason that the methodology developed by Jennison and Turnbull ... has been so influential is that it provides a unified group sequential theory that covers normal, binomial and survival distributions, with or without covariates."

Dr Cyrus Mehta,
President, Cytel Inc.

"Jennison's work has been invaluable in providing benchmarks by which to judge group sequential designs, in appraising the benefits of novel proposals for adaptive designs, and in extending adaptive methods to overcome impediments to their application."

Dr Sue-Jane Wang,
Associate Director for Adaptive Design and Pharmacogenomics, Office of Biostatistics,
US Food and Drug Administration