Making new drugs safer and faster to develop

Associate Professor of Statistics Wicher Bergsma helped pharmaceutical giant GlaxoSmithKline to develop a better way to analyse vaccine trials

What was the problem?

According to the Association of the British Pharmaceutical Industry (ABPI), on average it takes more than 12 years and £1 billion to research and develop a new medicine suitable for public use.

Perhaps the most critical phase of a drug's development is human clinical trials, which are used by pharmaceutical companies to assess the benefits and the safety of newly developed drugs. For every medicine that is successfully developed for use by the public, the ABPI says that 25,000 chemical compounds are tested, of which only 25 make it to the clinical trial stage and only five are ultimately approved for human use.

In every trial, researchers want to know two things. Is a drug bringing real benefits? And above all else, is it safe to use? Thus, to save money, time and potentially lives, pharmaceutical companies are constantly in search of the best way to conduct effective trials as rapidly and safely as possible.

What did we do?

Beginning in 2008, LSE Associate Professor of Statistics Wicher Bergsma led research with GlaxoSmithKline exploring how state-of-the-art statistical modelling techniques developed at LSE could improve the effectiveness of vaccine clinical trials. This research led to a book and the creation of a software package and website.

Bergsma's research centred on the novel use of a statistical methodology called marginal modeling, which fine-tunes data analysis by making frequent comparisons across a wide array of parameters in a testing process. He applied this research in a case study using data from a clinical trial of a new vaccine from GlaxoSmithKline Biologicals in Brussels. The GSK vaccine was

developed for paediatric meningococcal disease, which is a leading cause of meningitis among children and young people worldwide.

In particular, Bergsma and his colleagues sought to learn whether marginal modeling had more 'power' for clinical trials than traditional methods of data modeling. In other words, could Bergsma's methodology improve how much significant information researchers were able to glean from clinical trials? Doing so could mean potentially fewer patients involved in determining a vaccine's safety.

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The case study had two components. In the first component, a marginal modeling framework developed by Bergsma was applied to data from the meningococcal vaccine trial, which used an 'active' group – patients who received the trial vaccine – and a control group receiving standard treatment. The second component consisted of a simulation study that looked more broadly at the potential power of Bergsma's model in the context of other clinical testing.

What happened?

Applied to the meningococcal clinical trial data, Bergsma's novel use of marginal modeling revealed significantly more information for more trial symptoms, including pain, redness and irritability, than did traditional methods.

Importantly, Bergsma's model provided greater insight into adverse effects over a longer period and revealed how quickly the adverse effects of the trial vaccine diminished. For example, pain may take time to develop after taking a drug, something that traditional methods of assessing clinical trials often struggle to detect.

It was also possible to assess how differences in symptoms of active and control groups vary with time. Traditional methods of analysis allow the detection of adverse effects, but not a detailed assessment of how adverse effects change over time.

The results of Bergsma's research could allow pharmaceutical companies to develop a more accurate 'risk profile' for vaccines. This includes a better understanding of side effects which can lead to benefits for patients; in particular, drug prescription can be better tailored to patients' needs.

The methodology developed at LSE was generally found to have more power than traditional methods of data modeling for clinical trials, so that fewer patients are needed to detect whether a drug is safe or not. This could eventually allow for faster vaccine development cycles.

Bergsma gave a presentation of preliminary results to the Global Vaccine Development group in March 2009. Bergsma visited GlaxoSmithKline on several occasions, and numerous telephone conferences were held between Bergsma and researchers from GlaxoSmithKline. A presentation of the case study was given at the 33rd conference of the International Society for Clinical Biostatistics in 2012. A website for Categorical Marginal Modeling was set up by Bergsma in 2013.

The collaboration between GlaxoSmithKline and LSE is ongoing. GlaxoSmithKline plans to develop the methodology further in collaboration with LSE and to apply it in future trials.

Wicher Bergsma is Associate Professor (Reader) in Statistics at the London School of Economics and Political Science. His expertise is in statistics in general, with an emphasis on social statistics and with particular expertise in categorical data analysis, likelihood-based inference, measures of association and nonparametric regression.

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