Bayes, Biosimilars and Sir Mick Jagger

Byron Jones, Senior Biometrical Fellow/Executive Director: Novartis Pharma AG

Most of you reading this will know whom the Reverend Thomas Bayes is, so I will not say any more about him here. Biosimilars may be less familiar and I will start by saying what these are. As for Sir Mick, you will have to wait to see the connection.

The US Food and Drug Administration (FDA) defines a biosimilar as "a biological product that is approved based on showing that it is highly similar to an FDA-approved biological product known as the reference product, and has no clinically meaningful differences in terms of safety and effectiveness from the reference product". Biologics are large-molecule drugs that have revolutionized the treatment and prevention of many disabling and life-threatening diseases like cancer, arthritis, psoriasis and growth disorders. Biosimilars are meant to be cheaper "copies" of the reference product that can be marketed once the patent on the reference product has expired. However, unlike generics, which are cheaper copies of small-molecule drugs, biosimilars are only "highly similar" to the original, whereas generics are equivalent to their original.

Because the development of a biosimilar takes place in anticipation of the expiry of the patent of the reference product, much is already known about the properties of the reference product, as it has been on the market for several years. It seems sensible therefore to distil this information into a prior distribution for a parameter of interest and to use Bayes theorem to integrate this with current data from the trial on the biosimilar to create a posterior distribution, from which conclusions can be drawn. Using informative priors on the reference product may reduce the sample sizes needed in the biosimilar trials and so help reduce development costs and make the studies more ethical. However, it is well known that the incorporation of historical information can lead to an inflation of the Type I error rate in situations in which the data from the historical studies do not match the data from the new trial. This is a big disadvantage, because as biosimilar trials are considered confirmatory, any inflation of the Type I error rate in situations that are realistic in practice will likely be unacceptable to regulators.

In a recent paper, Mielke at al. (2018), show how the Type I error rate can be controlled in the parameter space of most interest in a biosimilar trial while still providing an advantage in terms of power compared to an approach which uses the data of the biosimilar trial only. We describe a step-wise algorithm for implementing their methods and illustrate it using real data from historical studies on a biologic for the treatment of psoriasis.

Now for the connection to Sir Mick. One of the most well-known songs written by Sir Mick Jagger and Keith Richards has the lines “You can’t always get what you want. ... You get what you need”. This is exactly what you get from the proposed method. You would like to have control of the Type I error rate over the whole space of the parameter of interest: but you can only get partial control. However, this partial control is exactly what you need in practice!

Reference

Mielke, J., Schmidli, H. and Jones, B. (2018). Incorporating historical information in biosimilar trials: challenges and a hybrid Bayesian-frequentist approach. *Biometrical Journal*, Early View.

Acknowledgement

This work was supported by funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 633567 and by the Swiss State Secretariat for Education, Research and Innovation (SERI) under contract number 999754557.