

First Rousseeuw Prize awarded to Causal Inference

The King Baudouin Foundation has chosen the recipients of the 2022 biennial Rousseeuw prize for Statistics. This new scientific prize of 1 million dollars was created by Peter Rousseeuw, professor of statistics at KU Leuven, Belgium. The goal of the prize is to reward excellent statistical research with an important impact. Half of the prize amount will go to James Robins (Harvard University), and the other half jointly to Miguel Hernán (Harvard University), Thomas Richardson (University of Washington), Andrea Rotnitzky (Universidad Torcuato di Tella, Argentina) and Eric Tchetgen Tchetgen (University of Pennsylvania), for their groundbreaking methodological contributions to Causal Inference with applications in Medicine and Public Health. The latter four laureates were either trained or deeply influenced by Robins. They remain his main collaborators to this day.

The work honored by this award has fundamentally transformed the way in which statisticians, epidemiologists, and other scientists infer the effects of exposures and treatments that vary over time using data from *observational studies*. As opposed to clinical trials, such studies contrast groups of people who received different treatments, without an experimenter's control over who receives which treatment. This absence of experimentation complicates the causal interpretation of observational study results. E.g., sicker people may be more likely to initiate treatment, thereby making a beneficial treatment appear harmful. However, it is often the case that experimentation is not feasible because of ethical reasons, e.g., when studying potentially toxic agents, or because of practical reasons, e.g., study cost or duration. Therefore, often one must rely on observational data to investigate the effects of certain treatments or exposures.

Specifically in Medicine and Public Health, the work of the laureates has drastically improved the methods for inferring the causal effects of medical treatments and interventions, thereby being of great benefit to individual patients and society. For instance, it has provided us with new insights and statistical methods for addressing central epidemiological questions, such as how harmful is a long-term radiation exposure in a nuclear facility, or what are the optimal strategies for treating persons with HIV.

These developments greatly improved on prior analytic methods. In 1986, Robins showed that the then state-of-the-art algorithms used to assess the causal effects on mortality of treatments or exposures that change over time could erroneously find a treatment effect even when no effect existed. This is because these methods ignored a feedback complication unique to studies of time-varying treatments. In persons with HIV, for instance, physicians initiate antiviral treatment in those whose immunity has been compromised by the virus. Therefore, patients who initiate antiretroviral treatment are sicker than patients who do not initiate treatment. However, the treatment itself improves a patient's immune response. This results in a complex feedback system, where immunity affects the treatment the patient receives, which in turn affects future immunity and survival, and thus future treatment. Prior to the work of Robins, this subtlety went unrecognized in the scientific literature. Robins solved this methodological problem in a series of ingenious papers, thereby laying the foundations for a long list of methodological innovations by the laureates that helped launch a revolution in the field of Statistics.

The laureates' novel methods have helped to resolve several high-profile disagreements between the results of earlier observational studies and subsequent clinical trials. Such disagreements have long been attributed to the absence of experimentation in the observational studies.

However, in studies of the effect of post-menopausal hormone therapy on coronary heart disease and of statin therapy on cancer, these disagreements largely disappeared after re-analysis using the laureates' methods, indicating that, in these cases, the prior use of older inappropriate statistical methods had likely been responsible. More recently, the new methods have been applied, prior to the availability of clinical trial evidence, to important observational studies of the timing of initiation of antiretroviral treatment in people with HIV, of the screening schedules for colorectal cancer, and of the benefits of anti-inflammatory therapy for Covid-19. In all three cases, the findings agreed with the results of later clinical trials.

The international jury appointed by the King Baudouin Foundation selected the winners from the nominations received after a widely advertised call earlier this year. The jury consisted of its chair David Hand (Imperial College), Lutgarde Buydens (Radboud University Nijmegen), Probal Chaudhuri (Indian Statistical Institute), Dianne Cook (Monash University), Roger Koenker (University of Illinois), Yanyuan Ma (Penn State), David Scott (Rice University), David Steinberg (Tel Aviv University), Jane-Ling Wang (UC Davis), and James Zidek (University of British Columbia). For more information on the prize see www.rousseeuwprize.org.

The prize will be awarded in a ceremony taking place at KU Leuven, Belgium on Wednesday October 12, 2022.