Applied Bayesian Methods in the Rheumatic Diseases

Sindhu R. Johnson, MD, PhD[a,b,c,*], George A. Tomlinson, PhD[b,d,e], John T. Granton, MD[f,g], Gillian A. Hawker, MD, MSc[b,h], Brian M. Feldman, MD, MSc[i,j]

KEYWORDS

• Bayesian • Statistics • Scleroderma • Systemic sclerosis
• Juvenile inflammatory arthritis • Rheumatoid arthritis

KEY POINTS

- Bayesian methods permit simple, intuitive, and meaningful statements of statistical inference.
- They provide a transparent framework for combining new information with preexisting information and knowledge.
- Importantly, to the study of uncommon rheumatic diseases, the Bayesian paradigm allows for inferences to be made from a limited number of subjects.

Disclosure Statement: None of the authors have any commercial or financial conflicts of interest to disclose.
Dr S.R. Johnson has been awarded a Canadian Institutes of Health Research New Investigator Award. Dr G.A. Hawker is supported as the Sir John and Lady Eaton Chair of Medicine. Dr B.M. Feldman holds the Ho Family Chair in Autoimmune Diseases.
[a] Division of Rheumatology, Department of Medicine, Toronto Western Hospital, Mount Sinai Hospital, 155 College Street, Toronto, Ontario M5T 3M6, Canada; [b] Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada; [c] Toronto Western Hospital, 399 Bathurst Street, Toronto, Ontario M5T 2S8, Canada; [d] Dalla Lana School of Public Health, University of Toronto, 155 College Street, Toronto, Ontario M5T 3M7, Canada; [e] Department of Medicine, Division of Support Systems and Outcomes, Toronto General Hospital Research Institute, University Health Network, Mount Sinai Hospital, Eaton North, 13th Floor, Room 238, 200 Elizabeth Street, Toronto, Ontario M5G 2C4, Canada; [f] Division of Respirology, Department of Medicine, Toronto General Hospital, University Health Network, MUNK Building, 11-1170, 200 Elizabeth Avenue, Toronto, Ontario M5G 2C4, Canada; [g] Division of Critical Care Medicine, Department of Medicine, Toronto General Hospital, University Health Network, MUNK Building, 11-1170, 200 Elizabeth Avenue, Toronto, Ontario M5G 2C4, Canada; [h] Division of Rheumatology, Department of Medicine, Women's College Hospital, 76 Grenville Street, 8th Floor East, Room 815, Toronto, Ontario M5S 1B2, Canada; [i] Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada; [j] Division of Rheumatology, Department of Paediatrics, Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8, Canada
* Corresponding author. Division of Rheumatology, Toronto Western Hospital, Ground Floor, East Wing, 399 Bathurst Street, Toronto, Ontario M5T 2S8, Canada.
E-mail address: Sindhu.Johnson@uhn.ca

Rheum Dis Clin N Am 44 (2018) 361–370
https://doi.org/10.1016/j.rdc.2018.01.003
rheumatic.theclinics.com

INTRODUCTION

The ability to make precise estimates using observational data in uncommon diseases has historically faced several challenges. The first challenge relates to patient numbers. In the setting of uncommon diseases, small numbers of patients are available for study recruitment. The number of accrued patients (sample size) influences the amount of sampling error in a statistical test result. A low sample size will decrease the probability of concluding a treatment is effective when there is actually a treatment effect (referred to as the power of a statistical test).[1] As they often recruit relatively small numbers of patients, studies of uncommon diseases often have inadequate power to detect important effects.[2,3] One potential methodologic solution to the challenges of small sample sizes involves the use of the Bayesian statistical inference.

Science and Statistical Inference

According to some philosophers, science is based on forming models of the world from sensory input (or instrumentation). We use the models that are most successful at explaining events and assume that the models match reality.[4] The discipline of statistics, in part, describes the way people learn as they make observations.[5] Investigators try to understand the world by making mathematical models, say for example, the relationship between smoking and lung cancer. Each model represents our understanding of the process or phenomenon we are studying.[1] Statistical inferences are based on mathematical models.[1] In the long run, we retain models based on their validity, reliability, predictability, and perceived match to reality.[4] Statistics facilitate the description of the average person, ascertain how well the idealized model fits the sample on which it is based, and allow us to generalize from this sample to another group of people or the population.[6] Furthermore, statistics is a science of making inferences about unknown quantities. Unknown quantities can include important outcomes, such as measures of effectiveness, adverse events, and diagnostic test results.[7]

Models posit a relationship between observable data and some underlying set of mathematical functions and a set of constants in those functions that determine the values of the functions. A clinical example is the evaluation of the impact of male sex on survival in systemic sclerosis, whereby there is an exponential distribution for time to the event.[8] The true values of the constants in the model are referred to as parameters, inherent properties of nature. Because the complete population is usually not fully observable, the parameter is not known with certainty. Observations are most often restricted to a sample from the population.[1] Statistical inferences are based on observations and involve a description of uncertainty. There are philosophic differences in how uncertainty is conceptualized and handled that characterize the various schools of statistical inference.

Schools of statistical inference differ in their approach to truth and uncertainty. The frequentist statistical method (also referred to as classic statistics) is one method of making inferences from observations. Frequentist inference uses methods developed by Ronald A. Fisher, Egon Pearson, and Jerzy Neyman. Observations are treated as one of an infinite set of possible instances of data that could have come from a given probability distribution.[9] Hypothesis testing is based on the frequency of obtaining a result (data), as extreme or more extreme, if the experiment was repeated many times, under certain fixed conditions.[10] In fact, all inferential probability statements (*P* values, coverage percentages of confidence intervals) refer to these hypothetical replications of the data collection and analysis. Under the frequentist approach, it is not possible to