JACC: BASIC TO TRANSLATIONAL SCIENCE VOL. 5, NO. 3, 2020

EDITOR'S PAGE

What I Learned From the Impeachment Process

Confessions of a Translationalist

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"If I had a world of my own, everything would be nonsense. Nothing would be what it is, because everything would be what it isn't. And contrary wise, what is, it wouldn't be. And what it wouldn't be, it would. You see?"
—Lewis Carroll, *Through the Looking-Glass and What Alice Found There* (1)

Regardless of whether one is political or apolitical, the spectacle that unfolded in Washington, D.C., beginning with the impeachment of President Donald J. Trump in the House of Representatives (largely along party lines) and ending up with his acquittal in the Senate (also largely along party lines), provided an opportunity to marvel at how tag teams of talented lawyers could interpret the same set of facts-only to arrive at 2 completely differently conclusions. There were a few moments when I thought I had fallen down a rabbit hole and entered an alternate universe where nothing was what it was, and everything was what it was not. The entire process brought to mind (remember I am a journal editor and cannot help it) the issue of how cognitive and confirmation biases influence everything that we do in life. Cognitive bias is a systematic pattern of deviation from norm or rationality in judgment, whereas confirmation bias is the interpretation of information in a way that confirms one's preconceptions (2). We, as humans, see our environment through the personal lens of how we have learned to adapt to the world we live in, which may explain how people are able to create their own personal realities that allow them to interpret the same set of facts and come to different conclusions. This reasoning, however biased, has allowed me to process everything that has happened.

As scientists we are taught to formulate a hypothesis and then design experiments that will test the hypothesis using a rigorous experimental design. Although this process has worked well for centuries, it is not immune from the influences of cognitive and conformation biases. For example, the steps of formulating a hypothesis, designing tests to prove the hypothesis, evaluating the results of the tests, and interpreting the results in the context of the hypothesis being tested, are subject to cognitive and confirmation biases at every step of the way. As I have noted in these pages before, translational science is inherently fragile because there are no firm guidelines for taking concepts from the bench to the bedside. Mouse models do not exactly phenocopy human disease, no matter how elegant. Yet mouse models are critical for identifying new drug targets and disease pathways. Large animal models are also critical for validating therapeutic agents before entering into Phase I and II clinical trials. However, large animal models are expensive, and therefore, are susceptible to confirmation bias, because the cost of the experiments often limits the scope of testing that can be performed. Moreover, there are no firm guidelines for how to design, conduct, and interpret Phase I and II clinical trials. Often, particularly in device trials, it is difficult to include proper control groups for ethical reasons. As a translational investigator, I have learned that the famous quote by W. Edwards Deming "In God we trust, all others (must) bring data" (3) needs to be expanded for early phase translational studies in humans to include: In God we trust, all others must bring randomized and properly controlled data. Small exploratory clinical trials are susceptible to asymmetric sampling errors that can seduce investigators into believing that effect sizes that are too good to be true are actually true. This, in turn, leads to advancing therapeutic agents into Phase III clinical trials, where the results of the Phase II trials are unlikely to be replicated.

ISSN 2452-302X https://doi.org/10.1016/j.jacbts.2020.02.005

Another lesson I have learned as a translational investigator is that you cannot fool Phase III (clinical trials). That is, errors in study design and data interpretation during the development process all become magnified in large clinical trials, in which heterogeneous patient populations are exposed to therapies that were previously studied in small, homogeneous patient populations.

The guiding principal that governs editorial decision-making at *JACC: Basic to Translational Science* is our focus on publishing scientific studies that we believe will lead to new therapies. As an Editorial Board, we are aware that translational science is at best an imperfect science, to which we assiduously attempt to apply a balanced and rigorous editorial process in an effort to advance new concepts and therapies. What I have learned from watching the proceedings in Washington, DC, is that cognitive and confirmation biases exist in all aspects of our lives, including how we interpret scientific data, and that, as Editor-in-Chief, I need to remain ever vigilant to ensure that these types of biases do not lead to publication bias in *JACC: Basic to Translational Science*. I am fortunate and grateful that I am supported by an Editorial Board that remains committed to the integrity of the scientific process, so that we do not publish papers that, with all due respect to Alice (1), would be nonsense in Phase III.

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