Explaining the Bayesian Prior

Henry R. Black, MD: Hi. I am Dr. Henry Black, Adjunct Professor of Medicine at the New York University School of Medicine. I am here today with my friend and colleague, Dr. George Diamond.

George A. Diamond, MD: I am Professor of Medicine at the University of California in Los Angeles and Emeritus Senior Research Scientist at the Cedars-Sinai Medical Center.

Dr. Black: I always associate with you with Bayesian interpretation of clinical trials. I have heard you speak about this several times. Could you explain what a Bayesian interpretation is, starting with who Bayes was, what he said and did, and how you have applied that to clinical trials?

Dr. Diamond: I was introduced to Thomas Bayes of “Bayes’ theorem” fame back as an early postdoctoral student, when I was looking for ways to analyze cardiac stress test data. A seminal article was published in the New England Journal of Medicine back in 1975[1] that for the first time explained some of the paradoxes that we had been observing in stress test data.

Stress testing was extremely accurate in predicting coronary disease in patients with typical angina pectoris, but was very inaccurate in predicting the same coronary disease in asymptomatic individuals or those with very minimal symptoms. It turns out that Bayes’ theorem explains that paradox.

Dr. Black: How so?

Dr. Diamond: The paradox is founded on the differences in the prior probability of disease in those 2 populations. If you knew nothing else other than the fact that the patient was suffering from typical angina, about 90% of the time you would be correct if you predicted that the patient had coronary disease. But if it was an asymptomatic individual and you predicted that this person had coronary disease and referred the patient to a catheterization to prove it, you would be right only about 5% of the time.

Dr. Black: This is based on what the stress test showed, right?

Dr. Diamond: No, before the stress test. This represents the prior probability of disease, a concept that was introduced by Bayes and that is ignored by classical statisticians. I will make a little bit of a historical extrapolation.

Thomas Bayes came up with these ideas about the interpretation of probability as a belief rather than as a measureable frequency back in the mid-18th century. It was embraced by such luminaries as Laplace throughout the 19th century. But it was always controversial and was criticized by others, such as George Boole, who wrote the book on Boolean analysis and on the laws of thought.

Ronald Fisher picked up the critical ideas and developed a methodology that allowed us to analyze observational data without reference to prior probabilities. He wrote a book on this (several books, in fact), and it became a standard of analysis throughout the 20th century.

Only now are we beginning to question the assumptions under which Fisher’s classical school of analysis is based. We can’t ignore prior probabilities. We don’t ignore them in any other domain of our lives.

If you are sitting on an acceptance committee at a college, you would look at the transcripts of students who were applying for enrollment. That is prior information. If you are buying a new car, you might look at the frequency of repair records for that model before you made your decision -- prior information. If you are a judge sentencing someone in civil court, not in criminal court, you would look at the person’s rap sheet on his prior convictions. That’s relevant prior information.
information. In fact, in every walk of life we use prior information, save one: the analysis of clinical trials.

**Dr. Black:** One could ask, if you have a good history, why do the stress test at all?

**Dr. Diamond:** In many cases, that is absolutely true. You most often refer to testing to confirm a preconception that you have already made on the basis of prior information from the history and the physical examination. So when it comes to using sophisticated diagnostic tests, we naturally apply prior information to the interpretation. We frequently say that if we weren't suspecting a disease was present, that abnormal test result was likely to be a false-positive.

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**Bayesian Probability in the Clinical Setting**

**Dr. Black:** How does this work with the interpretation of a new clinical trial in light of former clinical trials?

**Dr. Diamond:** Suppose I had a new diagnostic test, and I came to you and I said, "Henry, I love this test. It's wonderful. It's got a specificity of 95%. It's highly, highly specific. Is that enough information for you to embrace that test? It is.

**Dr. Black:** I'd want to know the sensitivity too.

**Dr. Diamond:** Why? I gave you incomplete information, and yet that is the basis for the interpretation of clinical trials. The P value of < .05 is equivalent to a false-positive reading.

**Dr. Black:** Right.

**Dr. Diamond:** It's equivalent to my statement that there is a 95% chance that you wouldn't have made these observations if the null hypothesis was true. Therefore, you should reject the null hypothesis.

But that is only specificity. You need to know also how often it would be likely to make those observations in somebody where the hypothesis is true, and how likely that hypothesis was before you even engaged in performing the trial. Bayesian analysis incorporates that additional information. Instead of reporting the results as a false-positive reading, it reports the results as a posterior probability, as a predicted accuracy that the test hypothesis is true -- a much more natural piece of information for our interpretation.

**Dr. Black:** How does that affect what we recommend to doctors and patients for the interpretation of clinical trials? How do you see this evolving with time? Is this something we should be thinking about?

**Dr. Diamond:** I have no real faith that things are going to change overnight. We have been debating the use of Bayesian prior probability for 300 years now. But belief, which is the foundation of Bayesian analysis, is what we all reason with in our clinical decision-making. We don't have data to support every decision that we make. Most of our questions are analogous to what the likelihood is that there will be a hurricane tomorrow.

It has never occurred before. Tomorrow has never occurred before, so any statement we make is a belief. It can't be based on empirical evidence. Analysis of clinical trials is also a belief because we don't repeatedly analyze the same test hypothesis in multiple trials. We are lucky if we get a handful of trials and analyze them by meta-analysis. But most of the time, we are dealing with one publication, one hypothesis, and one study at a time.

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**A Blow to Evidence-Based Medicine?**

**Dr. Black:** Does this mean do you think that this worshipping of what has been called evidence-based medicine might be a little premature or maybe even incorrect?

**Dr. Diamond:** It is overly optimistic. There is no question that it is a desirable goal, but I would guess that 90% of our decisions are made in the absence of evidence. They are based on consensus opinion and on community standard, not on firm observational evidence.

Even when we have observational evidence, it's often biased. Observational registries are being used more often
because it costs so much to do a clinical trial. The observational registries come at much less cost, and much less in the way of invested resources. But the problem with them is that the observational registries are subject to verification bias.

If we believe that some new treatment works -- let's say a new stent for use in percutaneous coronary intervention procedures -- then we are going to refer most of our patients to treatment on the basis of that belief. If we always refer patients to the new treatment, then the observational registry would be grossly biased in favor of the stent. So you wouldn't learn anything from analyzing those data.

**Dr. Black:** I am seeing the use of the word "Bayesian" more and more in looking at large databases. I am very concerned about some of the conclusions that are made. Whether it is because they are Bayesian or non-Bayesian, they just don't make sense. They don't fit what a person who was part of a consensus might say, and it's very disturbing.

There were some recent attempts to look at a relationship in patients with kidney disease where yes, you can draw a nice graph. But the logic is incorrect. For example, in the recent study about mortality in people with chronic kidney disease, a systolic pressure of 120 mm Hg had the same risk as a systolic pressure of 180 mm Hg.[2] I don't think that's right, and I don't think anyone who has ever really dealt with those individuals would agree with that finding.

We have to be much more careful (and thanks to you, I feel justified in saying this) in accepting a lot of what people tell us is evidence. I think it's often incorrect.

**Dr. Diamond:** Your intuition is very correct on that point, and your statement that you "don't think that's right." As a Bayesian, I would simply ask you to quantify it. To what degree don't you think it's right? Is there only a 5% chance that you don't think it's right? Or is there a 45% chance you don't think it's right? Then incorporate that prior belief into the analysis of the same data.

If every one of the investigators or study groups that were reporting the clinical trials reported their prior beliefs, then we could interpret their analysis in light of that prior. If there are differences of opinion, it is very likely that those differences of opinion don't relate to an interpretation of the observations. They relate to differences in our beliefs as to what the prior likelihood of the hypothesis being true was.

**Dr. Black:** It sounds as if that kind of information should be collected before the trial starts.

George, I appreciate you sharing this information with us. I find it very persuasive. I am becoming concerned, even though I'm a trialist, about what is happening with so-called evidence-based medicine. To throw away expert consensus as not being important is a very serious mistake. Thank you very much.

References


Medscape Cardiology © 2013  WebMD, LLC

Cite this article: Clinical Trials: A 250-Year-Old Interpretation. Medscape. Nov 13, 2013.