

MATRIX V. SIRACUSANO AND STUDENT V. FISHER:



STATISTICAL SIGNIFICANCE ON TRIAL

By Stephen T. Ziliak



Matrixx v. Siracusano presented the Supreme Court of the United States with the question whether a plaintiff can file a claim of securities fraud against a company which failed to warn investors about adverse effects that are not statistically significant.

Matrixx Initiatives—the maker of Zicam—claimed not, arguing that a bright-line rule of statistical significance is necessary to establish causation.

The question was considered and decided by the Supreme Court in light of rule §10(b) of the Securities Exchange Act of 1934 as amended by §10b-5.



“Matrixx’s argument rests on the premise that statistical significance is the only reliable indication of causation. This premise is flawed.”

(Supreme Court Decision, Matrixx v. Siracusano, p. 11)



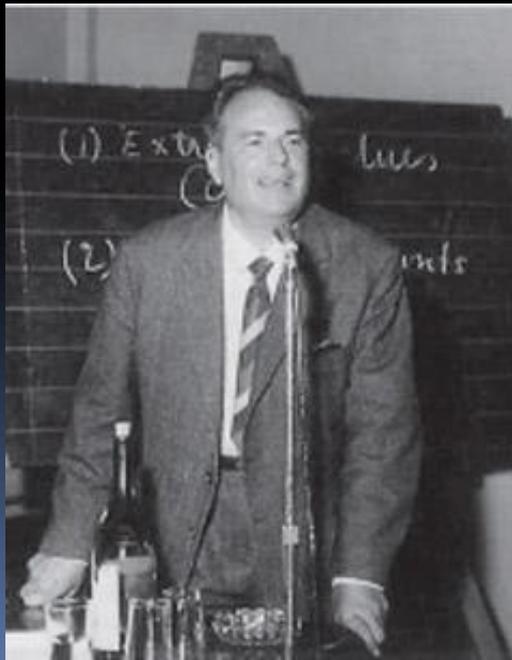
“We conclude that the materiality of adverse event reports cannot be reduced to a bright-line rule.

“Although in many cases reasonable investors would not consider reports of adverse events to be material information, respondents have alleged facts plausibly suggesting that reasonable investors would have viewed these particular reports as material”

(Ibid, March 22, 2011, pp. 1-2)

U.S. Supreme Court Unanimously Rejects Bright-Line Rule of Statistical Significance

**Promotes Contextual Inquiry,
Economic Approach to Logic of
Uncertainty**



“The economic approach seems (if not rejected owing to aristocratic or puritanic taboos) the only device apt to distinguish neatly what is or is not contradictory in the logic of uncertainty.”

Bruno de Finetti (1976)

The Significance Rule and Mistake Did Not Begin with Edgeworth (1885)

Edgeworth took an economic approach to estimation and testing, and nudged others to do the same.

“But for the purpose of science,” he told William Stanley Jevons, “the discovery of a difference in condition, a difference of 3 per cent and much less may well be important”

Francis Y. Edgeworth (1885)

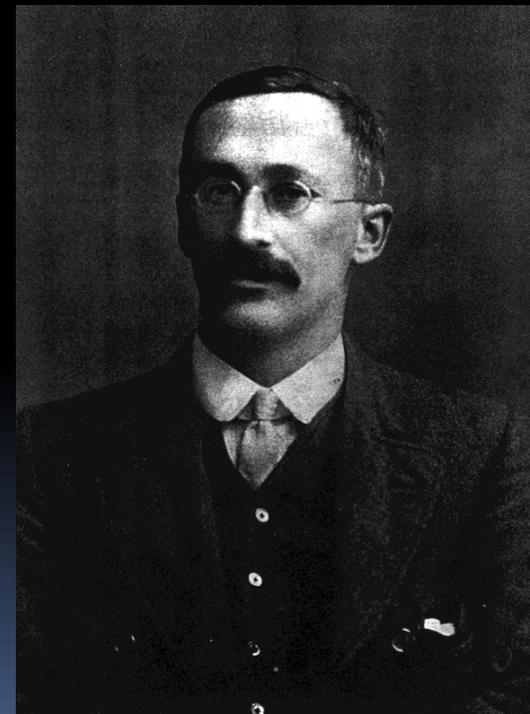


William S. Gosset aka "Student" —the Head Experimental Brewer of Guinness— theorized , practiced, and promoted the economic approach to uncertainty

Student (1876-1937) pioneered statistical and experimental methods to solve economic problems in the Main & Experimental divisions of **Guinness's Brewery, Dublin**

Student's methods were distorted, his warnings ignored, by Fisher and Fisherians

Copyright: The Galton Laboratory,
University College London



'Student' in 1908

Student rejected a bright-line rule of statistical significance . He told Karl Pearson in 1905:

“When I first reported on the subject [of "The Application of the 'Law of Error' to the Work of the Brewery" (Gosset, 1904)] I thought that perhaps there might be some degree of probability which is conventionally treated as sufficient in such work as ours and I advised that some outside authority in mathematics [such as Karl Pearson] should be consulted as to what certainty is required to aim at in large scale work.

However it would appear that in such work as ours the degree of certainty to be aimed at must depend on the *pecuniary advantage to be gained by following the result of the experiment, compared with the increased cost of the new method, if any, and the cost of each experiment.*”

Source: W. S. Gosset to Karl Pearson, c. April 1905, in E. S. Pearson 1939, pp. 215-216; Ziliak 2008; first italics in original

Fisher's Campaign for a Bright-Line Rule Has Caused More Than Headaches



Statistical Methods for Research Workers (1925)

"Arrangement of Field Experiments" (1926)

Design of Experiments (1935)

Statistical Methods and Scientific Inference (1955/1956)

Statistical Tables for Bio., Agri., and Medical Res. (with Yates, 1938)

And in scores of articles, letters, and speeches

R.A. Fisher 1925 [1941], *Statistical Methods for Research Workers*, p. 42:

“The value for which $P=.05$, or 1 in 20, is 1.96 or nearly 2; *it is convenient to take this point as a limit in judging* whether a deviation is to be considered significant or not. Deviations exceeding twice the standard deviation are thus formally regarded as significant.”

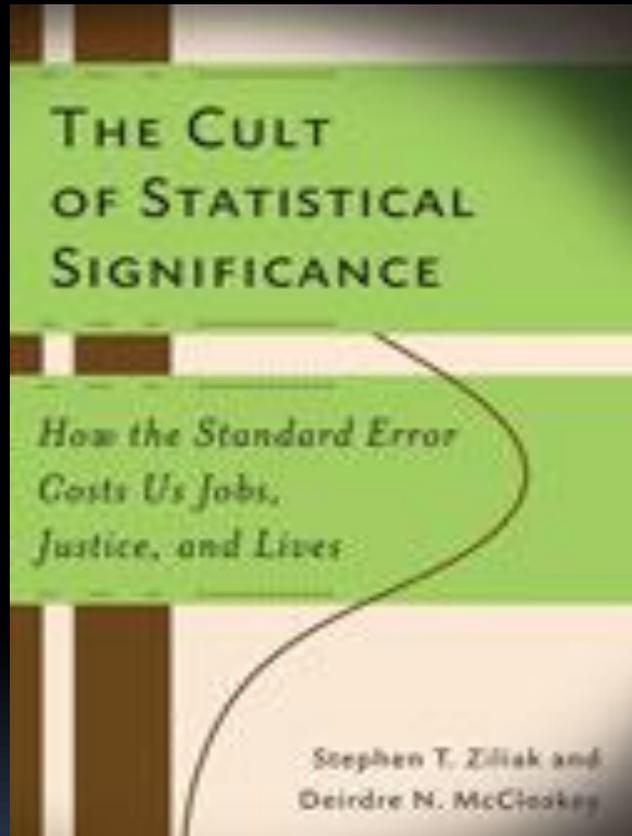


R.A. Fisher 1926, "Arrangement of Field Experiments," p. 504

“Personally, the writer prefers to set a low standard of significance at the 5 per cent point, and *ignore entirely all results which fail to reach this level.*”



Now the Cult of Statistical Significance Costs Us Jobs, Justice, & Lives



The test of statistical significance is the most important technique in the empirical branches of the life and human sciences, from economics to medicine - and it is broken

The main problem?

8 or 9 of every 10 articles published in leading journals fails to “test for” and “estimate” what we need, which is:

**Oomph and its odds
(but Oomph, especially)**

R.A. Fisher 1955, "Statistical Methods and Scientific Induction," p. 75

"Finally, in inductive inference we introduce no cost functions for faulty judgments . . . In fact, scientific research is not geared to maximize the profits of any particular organization . . . We make no attempt to evaluate these consequences, and do not assume that they are capable of evaluation in any currency."

The Court's rejection of a bright-line statistical significance standard (such as $p \leq .05$) will affect biomedical product supply and demand, securities regulation and liability, and the content and frequency of adverse effect reports to the S.E.C.

How will the Court's decision affect statistics education, if at all?

Consider, for example, the Reasoning of Justices During Oral Arguments

“Statistical importance [that is, statistical significance] can’t be a measure because it depends on the nature of the study”.



Justice Sotomayor, Oral Arguments, thanking *amici*, Matrixx v. Siracusano, Supreme Court of the United States, Jan. 2011.

“There are a lot of contact lens solutions in the world . . .

If I heard that, ten people went blind, three used it in one eye, [and] three went blind in that eye, I'd stop using the product; and if I were holding stock in that company, I would sell the stock.”



**Justice Kagan, Oral Arguments,
Matrixx v. Siracusano**

“This statistical significance always works and always doesn’t work”

- Justice Breyer, Oral Arguments, *Matrixx v. Siracusano*, Jan. 2011



**Chief Justice Roberts appealed to the
“total mix of information” required by the
“reasonable investor”, as in Basic v.
Levinson (1976)**



CHIEF JUSTICE ROBERTS:

“A reasonable investor is going to worry about the fact that thousands of unreasonable investors are going to dump their Matrixx stock. ”

**Justice Roberts, Oral Arguments,
Matrixx v. Siracusano**

JUSTICE SCALIA: “Mr. Shah, what do you think about Satan?”

MR. SHAH: “Let me try to unpack the satanic connection hypotheticals a little bit.”



Justice Scalia, opening question to U.S. Acting Solicitor General Pratik Shah, Oral Arguments, *Matrixx v. Siracusano*, Jan. 2011

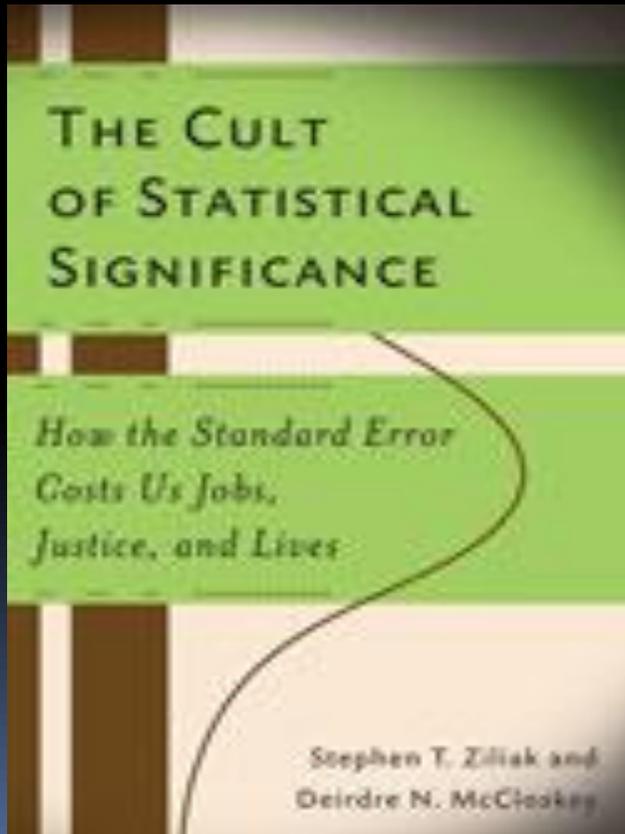
“Something more is needed”, Justice Sotomayor wrote—but what? And how can statisticians, editors, grantors, and policy makers help?



The Court asks for “something more” about the **“source, content, and context”** of information disclosed to investors and the S.E.C.

Justice Sotomayor, author, *Matrixx v. Siracusano*, Supreme Court of the United States, March, 2011, p. 15

What the Court did not say is that statistical significance gives us the wrong information—false hope and skepticism



The “Size Matters/How Much” Question cannot be answered by statistical significance—

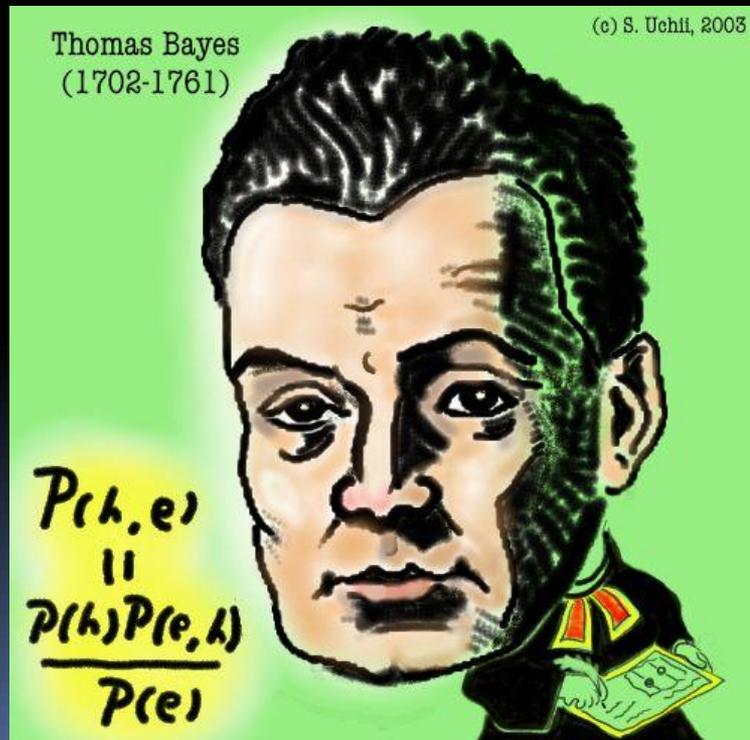
Ziliak and McCloskey find that evaluation of regression coefficients is eschewed in 8 or 9 of every 10 articles published in leading journals of science

The Probability of a Hypothesis (degree of belief) cannot be revealed by a Fisher test of significance

Teach the “How Much” Question

Teach “Oomph” Analysis

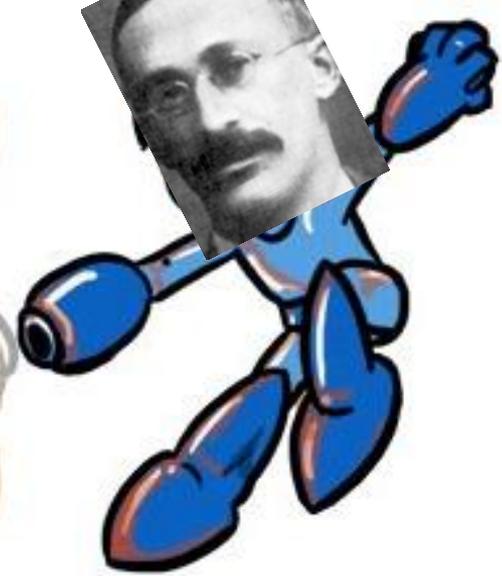
Teach the Fallacy of the Transposed Conditional (and How to Avoid It)



Student's economic approach was advanced by Harold Jeffreys, in *Theory of Probability* (1939) and by Egon Pearson, for example

Student's sampling distributions and tests of significance were based on actual repetitions, not imaginary

Student offers
a way forward



**We should teach less
Fisher, more Student**

**Most textbooks have to be
revised**

THE POWERS IN THE WORLD



Copyright and References

"Matrixx v. Siracusano and Student v. Fisher: Statistical Significance on Trial," was presented by Stephen T. Ziliak, in a Late-Breaking Session of the Joint Statistical Meetings (JSM), Aug. 3rd, 2011, in Miami, FL.

The contents of these slides are from Ziliak's article of the same title, *Significance* 8 (3, Sept. 2011); Ziliak's and D.N. McCloskey's *The Cult of Statistical Significance: How the Standard Error Costs Us Jobs, Justice, and Lives* (2008, University of Michigan Press); Ziliak's "Guinnessometrics: The Economic Foundation of 'Student's' t," *Jnl. of Economic Perspectives* (Fall 2008); and McCloskey's and Ziliak's Brief of *Amici Curiae* in support of Respondents (Siracusano et al.), U.S. Supreme Court, 2010. E. Labaton et al., eds.. Photo credits belong to others named here. Photos of Justices are from <http://www.SupremeCourt.gov>. I thank sponsors, participants, Milo Schield (the Late-Breaking Session Organizer, "Supreme Court finds statistical significance not necessary for causation," JSM 2011, Miami Beach), and panelists Joseph "Jay" Kadane, Danny Kaplan, and Donald Rubin. S.T.Z.

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SIGNIFICANCE, CAUSALITY, AND THE REASONABLE INVESTOR

THE COURT INVOKED THE EXPECTATIONS OF A REASONABLE INVESTOR. WOULD AN UNDISCLOSED ADVERSE EFFECT REPORT BE LIKELY TO NEGATIVELY AFFECT THE “TOTAL MIX” OF INFORMATION CONSIDERED BY A REASONABLE INVESTOR? IF YES, THEN THE REPORT MUST BE DISCLOSED, REGARDLESS OF STATISTICAL SIGNIFICANCE. THE COURT ARGUED, GIVEN THAT RESEARCHERS, THE FDA, AND MEDICAL EXPERTS DO NOT REQUIRE STATISTICAL SIGNIFICANCE, WHY WOULD A REASONABLE INVESTOR INSIST ON STATISTICAL SIGNIFICANCE?

ON PAGE 9 OF *MATRIX V. SIRACUSANO*, JUSTICE SONIA SOTOMAYOR, THE AUTHOR OF THE OPINION, SAID:

MEDICAL PROFESSIONALS AND RESEARCHERS DO NOT LIMIT THE DATA THEY CONSIDER TO THE RESULTS OF RANDOMIZED CLINICAL TRIALS OR TO STATISTICALLY SIGNIFICANT EVIDENCE. . . THE FDA SIMILARLY DOES NOT LIMIT THE EVIDENCE IT CONSIDERS FOR PURPOSES OF ASSESSING CAUSATION AND TAKING REGULATORY ACTION TO STATISTICALLY SIGNIFICANT DATA. IN ASSESSING THE SAFETY RISK POSED BY A PRODUCT, THE FDA CONSIDERS FACTORS SUCH AS “STRENGTH OF THE ASSOCIATION,” “TEMPORAL RELATIONSHIP OF PRODUCT USE AND THE EVENT,” “CONSISTENCY OF FINDINGS ACROSS AVAILABLE DATA SOURCES,” “EVIDENCE OF A DOSE-RESPONSE FOR THE EFFECT,” “BIOLOGIC PLAUSIBILITY,” “SERIOUSNESS OF THE EVENT RELATIVE TO THE DISEASE BEING TREATED,” “POTENTIAL TO MITIGATE THE RISK IN THE POPULATION,” “FEASIBILITY OF FURTHER STUDY USING OBSERVATIONAL OR CONTROLLED CLINICAL STUDY DESIGNS,” AND “DEGREE OF BENEFIT THE PRODUCT PROVIDES, INCLUDING AVAILABILITY OF OTHER THERAPIES.”. . . [THE FDA] “DOES NOT APPLY ANY SINGLE METRIC FOR DETERMINING WHEN ADDITIONAL INQUIRY OR ACTION IS NECESSARY”.

IBID, PP. 15-16

To **MATRIX** argument that a **fixed level of Type I error** ($p \leq .05$) determine the standard for disclosure over “background noise”
Justice Breyer (p. 22) replied:

“Oh, no, it can't be. I mean, all right -- I'm sorry. I don't mean to take a position yet. But-- (Laughter.):

JUSTICE BREYER: But, look -- I mean, Albert Einstein had the theory of relativity without any empirical evidence, okay? So we could get the greatest doctor in the world, and he has dozens of theories, and the theories are very sound, and all that fits in here is an allegation he now has learned that it's the free zinc ion that counts.

- **MR. HACKER (for Matrixx):** But -
- **JUSTICE BREYER:** And that could be devastating to a drug even though there isn't one person yet who has been hurt.



“Am I not right that all of these reports came from medical doctors, and in response to the very first one, the company representative said, yeah, we've been getting reports since 1999?”



Justice Ginsburg, Oral Arguments, *Matrixx v. Siracusano*, Jan. 2011