A Discovery of Significance
(With Apologies to Epidemiologists Everywhere)

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Almost 40 years ago, a satirical essay published in *The New England Journal of Medicine*1 gently teased oncologists and their preoccupation with creative acronyms for chemotherapy regimens. Now, bombarded with numerous studies reporting risk factors for cancer, consider the following…

A promising young epidemiologist, trained at an Ivy League school, committed his career to understanding the influence of environment on the risk of developing prostate cancer. Being skilled in multivariate analysis and questionnaire development, he designed a multicenter study examining diet, birth order, occupation, and many other potentially important factors. He also included the question, “What is your favorite baseball team?”

In a case-control study of patients with prostate cancer, he discovered the amazing fact that fans of the Boston Red Sox had an increased relative risk (RR) of developing the disease (RR, 1.9; 95% CI, 1.1–2.4). Prostate cancer was not associated with preference for any other baseball team.

He submitted his paper to *The New England Journal of Medicine* (NEJM), realizing they had once published an article noting an increased risk of pancreatic cancer in coffee drinkers who drank 3 or more cups per day (RR, 2.7; CI, 1.6–4.7).2 His article was rejected without review. It was later accepted by the *Journal of the National Cancer Institute* (JNCI), and many wondered whether the editorial staff of the NEJM had feared the economic repercussions to the New England region should this association become well-known.

The study created an immediate sensation. It was highlighted in *USA Today*, appeared on the CNN crawl, was discussed on Fox News, and was the subject of a 7-minute extended piece on NPR. The epidemiologist was circumspect about the conclusions but secure in his methodology. He noted that further studies would be required to validate these results.

The medical oncology community was besieged by patients seeking advice. They came with Internet printouts from the *Washington Post* and *The New York Times*. No one was armed with the original article. Many sought guidance. Should they switch deeply entrenched alliances? Should they seek diversion in the civilized sport of chess? Should they find new hobbies or horizons out of the realm of sport? Oncologists were at a loss. Even the conservative editorial accompanying the JNCI article, which advised caution in interpreting the findings, did not stop the frenzy.

Theories to explain the findings abounded. Was this association due to excess testosterone levels corresponding with the annual September angst surrounding the success or failure of the Sox? Perhaps those destined to get prostate cancer were genetically programmed to associate themselves with the unforeseen fortunes of Red Sox baseball. Other possible factors regarding this finding were proposed. It was noted that prostate cancer is more prevalent in the United States than in third world countries; baseball could be the difference. Some viewed this as further ammunition against the creeping threat of global Americanization.

The study was not without its critics. Questions abounded: “What is the definition of a Red Sox fan?” “Were the subjects fans at puberty?” “What was the duration of fandom measured in fan-years?” “Did this apply only to those who knew...
the significance (not in a statistical, but rather a philosophic sense) of Bucky Dent or Bill Buckner in Red Sox lore? “Was this finding restricted to fans of the team pre-2004, when, as one sage eloquently put it, the Red Sox were the ‘French existential baseball team; they teach us about the futility and meaninglessness of life’?”

The study had a dramatic effect on the fortunes of the Red Sox. Ticket sales plummeted and stores were left with huge stockpiles of Sox memorabilia and souvenirs. The restaurants and bars in Back Bay suffered, despite the recent decade of baseball success.

The NCI, realizing the potential importance of the finding, put out an RFA, with the intent of directing funds to further study this important question. Many investigators submitted detailed and well-referenced proposals. An ad hoc study section reviewed the proposals, and the priority scores were excellent. Only those with scores less than 1.8 received funding.

The epidemiologist received many requests for invited lectureships. He was proposed for promotion and tenure at his prominent Midwest medical school. His studies became widely available on the Web, and were furnished to many oncologists by patients, assuring rapid dissemination of the data.

At the peak of his popularity, a second study was published. This was the work of a large group from Harvard University, conducted in association with Tufts and Boston University. Their results were discordant with those of the original paper. They showed an increased risk of prostate cancer in fans of the New York Yankees (RR, 1.8; CI, 1.3–2.2), and surprisingly, the Kansas City Royals (RR, 1.6; CI, 1.1–2.4). Some thought these studies were tainted by bias, because of the potential conflict of interest of these Massachusetts authors. The Steinbrenner family was told about the association of testosterone with prostate cancer, and hailed the new study as clear proof of the manliness of Yankee fans.

A junior clerk on an internal medicine rotation asked her mentor about these studies. She wondered if these findings could have been caused by chance alone, the fallout from multiple comparisons. “After all, there are 30 major league baseball teams. Isn’t it possible this is just statistical artifact?” Her mentor pointed out that she didn’t understand the rigors of the peer-review process, and suggested that she devote her time to understanding the 3 (or was it 4) types of renal tubular acidosis.

With one problem solved, the now-famous epidemiologist planned his next studies, hoping to understand the influence of cinema on breast cancer risk.

References