The Positivity in Negative Results
Leonard J. Press, OD, FAAO, FCOVD, Editor-in-Chief

Theodore Dalrymple is the pseudonym under which a retired English psychiatrist, Anthony Malcolm Daniels, has written numerous articles and books. According to the website, The Skeptical Doctor (http://bit.ly/31gUyNP), Dalrymple is one of the most interesting people alive, having often been compared to George Orwell.

Dalrymple has a sparkling wit that sometimes hits close to home, as evidenced in his commentary at the 23:20 mark of this YouTube video (youtu.be/IAmJzc-lXFo) about the legitimacy of the deficiencies listed in the DSM, The Diagnostic and Statistical Manual of Mental Disorders. In his own case of bibliomania, he wonders if there should be an entry for a condition known as Book Purchasing Disorder. To merit this disorder, the individual must suffer from at least three of the following criteria:

1) He buys more books than 99% of the general population, making him statistically abnormal.
2) Such purchases amount to a significant proportion of his discretionary income.
3) He experiences difficulty in passing a bookstore without entering it.
4) He experiences a rising tension which can be alleviated only by purchasing another book.
5) He buys more books than he can possibly read.
6) He has either argued with his wife about the number of books in the house, or she has suggested a “one in one out” policy, or she has banned the presence of books from a number of the rooms in his house.

Bibliomania led me to a copy of Dalrymple’s latest book, False Positive: A Year of Error, Omission, and Political Correctness in the New England Journal of Medicine. In the introduction, Dalrymple notes that retirement from practice has given him time to read journals with much closer scrutiny. He used each weekly issue of the New England Journal of Medicine (NEJM) to study the extent to which doctors can rely on journals for guidance in clinical practice. And what he has come to realize is that a reader of journal articles must take responsibility for detecting error, keeping an open mind as much to what has been omitted as to what has been included. This critical reading of the literature was reflected in a Guest Editorial on Agenda Driven Research by Dominick Maino in the first issue of our journal (bit.ly/2NOZRA8), and in a reply in the second issue by Anna Horwood (bit.ly/2NKLLnw).

But what I wish to focus on here is publication bias of a different kind, which is the proclivity of all journals toward publishing positive results. Naturally this reflects the nature of manuscript submissions, in which most authors present articles detailing positive results of their research or interventions. Yet there is often as much that we can learn about what didn’t work in a particular experiment, or with a particular treatment, that can be as informative about what did work. In that regard,
Dalrymple writes: “There has been a tendency of late for the Journal to publish negative results, that is to say, results of experiments in which the treatment being tested has not worked. This trend toward more negativity is actually a positive development, a corrective to the publication bias following from a longstanding preference for positive results.”

This sentiment was echoed by Yilmaz et al in a paper recently published in the Canadian Journal of Ophthalmology titled Discontinuation and nonpublication of interventional clinical trials conducted in ophthalmology. (bit.ly/2NOGqY1)

The authors conducted a retrospective, cross-sectional study of ophthalmology-based interventional clinical trials reported in ClinicalTrials.gov from 1972 to 2019. During that time period, 81% of the completed trials were not published. They noted that the high non-publication rate in their analysis may reflect poor treatment outcomes with various treatment modalities over the decades, as researchers were less likely to report on studies with negative outcomes. Consider the cumulative effects: Investigator A performs a clinical trial on treatment X and finds equivocal evidence or evidence that contradicts the existing literature, and these results are not published or made easily available. Subsequent investigators go down the same path. Together their findings may have been significant, but because these investigators work in isolation and their work is never submitted, or is rejected due to editorial bias toward positive and conventional results, the nature of their work remains hidden or discounted. Yilmaz and colleagues also point out that discontinuation or non-publication of trials also undermines the confidence of volunteers who never learn of the results of their participation.

Recognition of these trends has contributed toward authors being critical of their own work when they submit a manuscript rather than putting an entirely positive spin on the data. This is evidenced by qualifying statements about the nature of the research, its statistical analyses, or potentially confounding factors that may have influenced the results. But as Dalrymple advocates, there is another level on which we can operate which is to welcome papers which produce negative rather than positive results. In that vein he writes: “Karl Popper, the philosopher of science stressed that what distinguishes science from non-science is the falsifiability of its hypotheses, and that no evidence in favor of such hypotheses can ever establish their truth once and for all, only their non-falsity so far. Therefore, scientific doctors have nothing to be ashamed of when they change their opinion about something, even if it is a diametrical change. Indeed, this is a strength, not a weakness: they are following the evidence rather than dogma.”

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