The Positives of Negative Data

APRIL STEMPIEN-OTERO, MD

Seattle, WA

In this issue of the Journal of Cardiac Failure, we issue an expression of concern regarding a review article published in 2002.[1] This article includes multiple citations of a primary paper by the authors[2] that was recently cited in an expression of concern by the New England Journal of Medicine. In addition, the review article in the JCF contains previously unpublished primary data including micrographs depicting proliferating cardiomyocytes. Similar micrographs are under investigation for image manipulation by both the NEJM and Brigham and Women's Hospital.[3]

As editors, our review of this publication made us pause to consider our culpability in propagating potentially fraudulent data. Like modern day social media, for years journals have been driven to publish the newest, most exciting data that will increase the number of "clicks" -measured in our world as citations in other articles. This bias results in the pre-ponderance of publications being of "positive" data that others will pick up and cite to justify their next round of studies. This positive feedback loop results in more and more positive studies justifying the previous ones. Researchers with contrary "negative results" are left out, and thus authors confronted with inconsistencies in their data can point to the existence of many "positive" studies and point out the absence of negative studies.

As scientists we scoff at the susceptibility of the public to the clickbait of sensational fake news stories. However, we appear to be no different in our desire to see what we want in the data presented. A parallel paper by the same group showing evidence that bone marrow cells can regenerate the heart[4] has received 3749 citations whereas two publications that presented negative data in the same model[5,6] have received only 1522 and 1230 citations respectively. More importantly, the Orlic paper led to aggressive propagation of human clinical trials in patients with heart failure despite continued evidence that these cells fail to induce regeneration in humans.[7]

The increasing use of preprint repositories such as *bioRxiv* may in part address this problem. Preprints allow rapid dissemination of data both positive and negative thus providing a mechanism by which investigators can quickly evaluate controversial results.[8] A majority of publishers, Elsevier included, do not consider data in pre-prints to be incompatible with publication in their journals. Indeed, as other scientists can comment on articles and suggest improvements to methods and experiments, pre-prints provide "pre-peer reviewing" and thus improve the quality of the final submitted publication. Critically, these services could provide documentation of the number of negative studies generated in response to a single positive study. Editors would do well to review these repositories prior to being entranced by the shiny new toy of a finding that seems too good to be true.

References

1. Leri A, Kajstura J, Anversa P. Myocyte proliferation and ventricular remodeling. J Card Fail 2002;8:S518–25.
2. Beltrami AP, et al. Evidence that human cardiac myocytes divide after myocardial infarction. N Engl J Med 2001;344:1750–7.
3. Drazen JM. Retraction: Kajstura J et al. Evidence for human lung stem cells. N Engl J Med 2011;364:1795-806. N Engl J Med 2018;379:1870.
4. Orlic D, et al. Bone marrow cells regenerate infarcted myocardium. Nature 2001;410:701–5.
5. Murry CE, et al. Haematopoietic stem cells do not transdifferentiate into cardiac myocytes in myocardial infarcts. Nature 2004;428:664–8.
6. Balsam LB, et al. Haematopoietic stem cells adopt mature haematopoietic fates in ischaemic myocardium. Nature 2004;428:668–73.
7. Stempien-Otero A, et al. Mechanisms of bone marrow-derived cell therapy in ischemic cardiomyopathy with left ventricular assist device bridge to transplant. J Am Coll Cardiol 2015;65:1424–34.
8. Bourne PE, et al. Ten simple rules to consider regarding preprint submission. PloS Comput Biol 2017;13:e1005473.

From the University of Washington, Department of Medicine, Box 358050, Seattle, WA 98109.
Tel: 206-616-9054. E-mail: april@u.washington.edu

1071-9164/$ - see front matter
© *2019 Published by Elsevier Inc.*
https://doi.org/10.1016/j.cardfail.2019.01.010