

EDITOR'S PAGE

Dead Letter Office

The U.S. Postal Service started a Dead Letter Office in 1825 to handle undeliverable mail. By 2006, approximately 90 million undeliverable items ended up in the office. In the medical literature, the Dead Letter Office is a repository of clinical trials that have not been published. In this issue of *JACC: Heart Failure*, Dr. Milton Packer presents results of the REVIVE study—an important randomized controlled trial in acute heart failure, and at that time one of the largest clinical trials done in this population. I had the privilege of serving on the Data Safety Monitoring Board (DSMB) for this trial. At the conclusion of the study, there was a mixed clinical symptomatic benefit at the expense of increased arrhythmias and increased mortality. Dr. Packer presented these results at a national scientific meeting, and developed a manuscript that was ultimately never submitted.

What were the reasons, and how can we prevent multiple years of lapse in study completion to publication? We recognize as physicians and citizens in society that we are conducting clinical trials, obtaining knowledge based on experimentation, and that it is absolutely necessary to provide this information to the public domain. This indeed was done in a timely fashion as a Late-Breaking Clinical Trials presentation. However, the full report was not seen until today. Most senior leaders in heart failure have known the trial results, and we have kept the information in the back of our minds for decades. It is also clear that many clinicians in the trenches may not be acutely aware of the risks and benefits of the therapy that is available in many European countries. The reasons for delayed publication of neutral or negative trials are complex; clearly, positive trials have much enthusiasm behind them and have expedited reviews in the highest-impact journals. Negative or neutral trials require a deeper reflection on analyzing why the trial was negative, what could have gone wrong with the patient population, trial design, endpoints, and interpretation. After developing the manuscript, the varying opinions of interpretation on the results, the loss of funding from the sponsors to continue additional analyses, maintaining the database and statistical support all lead to an increased probability that the paper is not published. Yet, we all believe that the patients and the colleagues who care for these patients deserve better.

What can we do in the future? Dr. Califf, in his Editorial Comment, notes that “results must always be published,” but it is often not that easy. Some key steps could enhance this process. First, we can request that datasets be maintained outside the sponsoring institution to prevent database termination after a negative or neutral trial. Funding for additional analysis then becomes challenging, but at least the database can provide a protective environment for the academic milieu. Second, if there is no intent to publish after 1 year beyond study completion, the DSMB report could form the basis of the published trial results. This, I believe, falls in the realm of the DSMB whose role is to ensure the safety of the public, and that should include dissemination of information. Finally, it is imperative that journals keep an open mind for research results, even when they have been delayed for publication. Requesting a detailed reanalysis of primary and secondary endpoints can prohibit publication. Asking for additional phenotypic characterization is nearly impossible



**Christopher
O'Connor, MD, FACC**
*Editor-in-Chief,
JACC: Heart Failure*

in these situations when the database has long been dismantled and the original investigators are far removed from the project.

Thus, today, I am pleased to note that the Dead Letter Office at *JACC: Heart Failure* is open, and presenting as the first delivered "letter," the REVIVE study by Packer and colleagues. Our intention is to welcome trials such as these with an encouraging home, so that the many clinicians, care providers, and patients participating in trials can benefit from the results, at a much greater detail than seen before.

We hope you will enjoy this, and all our exciting research in this second issue of *JACC: Heart Failure*.

Address for correspondence:

Christopher O'Connor, MD, FACC
JACC: Heart Failure
3655 Nobel Drive, Suite 630
San Diego, California 92122
E-mail: coconnor@acc.org