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A case for cautious optimism

To prevent false hopes and premature hype, public announcements of preliminary results from clinical trials should include access to the actual data to allow for scrutiny by experts.

On April 29th, the *New York Times* reported a promising outcome from a small-scale clinical trial of a drug for Fragile X syndrome (FXS) from the Swiss pharmaceutical company Novartis. For affected families, seeing this news in a well-respected newspaper is exciting, as it offers hope that the disease may be manageable in the near future. However, this announcement in the *New York Times* was quite unusual in that Novartis did not formally release any of the specific results of their clinical trial and they did not disclose many of the critical details. Although the article and the Novartis scientists interviewed in the piece made it clear that there were still many hurdles to be overcome before such a drug could be released and that the findings have not been peer-reviewed or published yet, this premature announcement could lead to disappointment if the drug does not work as well as it should in further tests. Announcing only the broad description of results without providing any supporting data does not allow the scientific community to independently examine the data and critically evaluate whether the preliminary results are indeed promising. This announcement and the accompanying article should have been made in a more cautious and timely manner after ensuring that the results were fully vetted by the scientific community.

Drug companies have traditionally kept their trial results confidential until the drug was approved. Nowadays, however, many companies, particularly the smaller ones, choose to announce their clinical trial results in scientific meetings or to submit their results for formal peer-review via journals so as to garner scientific and investor interest and feedback. At the same time, companies are also bound to hold on to proprietary information to prevent potential competitors from taking advantage of their preliminary findings. Novartis is not alone in the race to find a drug to help alleviate the behavioral impairments that characterize FXS. According to the US government's registry of clinical trials (http://www.clinicaltrials.gov/), Hoffmann–La Roche and Seaside Therapeutics have ongoing small-scale clinical trials to evaluate the safety and efficacy of compounds to alleviate FXS symptoms. However, all of these studies are in a preliminary phase and still have ways to go for the actual drug to be made available to patients, with the biggest hurdle being the large-scale validation in phase III clinical trials before drug approval.

Without a thorough scientific vetting of results, announcing reports of promising drugs in a highly visible forum such as a national newspaper gives premature credence to a drug and may falsely affect public awareness. Although the Novartis executive quoted in the *Times* article made clear the potential caveats of these findings and cautioned against premature optimism, these caveats are easy to ignore for families directly affected by the disease, and the news of a potential treatment on the horizon may be met with unabashed optimism. Moreover, the lack of specific information about the effectiveness of the drug may also be a source of confusion. For example, the *Times* article reported that the Novartis compound alleviated undisclosed behavioral impairments associated with FXS and that not all individuals responded well to the treatment itself. Readers may well wonder what these specific symptoms are and whether this new drug works better than existing ones to control them. In addition, the Novartis compound was tested on adult subjects for ethical reasons. However, FXS is a mental retardation that manifests in childhood, and whether the drug could be safely administered to children and mitigates the symptoms of FXS or whether it would have unwanted long-term consequences if administered too early remain unclear.

It is entirely appropriate for popular media such as the *New York Times* to cover success stories of drug research and to draw attention to promising new targets or research leads. To avoid raising false hopes and triggering the following backlash, however, responsible media coverage should wait for exciting results to be reviewed thoroughly and validated by scientists and physicians in the field. Promising results from small-scale clinical trials frequently evaporate in the large-scale trials that are necessary before the drug can be approved. For a recent example, the antihistamine drug dimebon was initially reported to confer substantial cognitive improvement in dozens of individuals with Alzheimer's disease[1], but failed to achieve similar results in two large-scale, multi-center phase III clinical studies (http://media.pfizer.com/files/news/press_releases/2010/connection_030310.pdf). For a disease such as Alzheimer's disease, which has seen numerous clinical trials fail, the field (and many individuals with Alzheimer's disease), are appropriately skeptical when hearing of new drugs in the pipeline. For a condition such as FXS, which hasn't seen as many therapeutic trials, a premature public announcement of this sort could cause huge disappointment if the ultimate outcome is not favorable.

Childhood disorders such as autism have already suffered as a result of now-discredited science; a 1998 study by Andrew Wakefield, linking autism to the MMR vaccine, was finally retracted earlier this year, but took its toll. Many parents shied away from vaccinating their children as a result of this study and valuable resources were diverted away from studying the real cause of autism. Given the immense public interest these childhood disorders garner, scientists (whether in academia or in the pharmaceutical industry) and journalists are well advised to be cautious in making claims of therapeutic progress to avoid public misunderstanding that any treatment is imminent. Any cautious optimism should be well-timed both for the patients' sake and to retain public trust. ■

1. Doody, R.S. *et al. Lancet* **372**, 207–215 (2008).