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EDITOR'S CHOICE

Study 329

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This week we released our first "RIAT" reanalysis of a previously published randomised trial (doi:10.1136/bmj.h4320). Avid readers will remember that RIAT stands for "restoring invisible and abandoned trials." As described by its originators in 2013 (doi:10.1136/bmj.f2865), it provides a mechanism for researchers unaffiliated with the original trial to publish unpublished (or to republish misreported) clinical trials when sponsors and original investigators fail to do so.

Last year in *BMJ Open* Tom Treasure and colleagues reported a trial whose data had remained unpublished for 20 years (doi:10.1136/bmjopen-2013-004385). In a narrative article in *The BMJ* the restorative authors said that the data cast doubt on the now common practice of carcinoembryonic antigen testing and metastasectomy in people with colorectal cancer (doi:10.1136/bmj.g2085).

We expect many other trials to fall within RIAT's purview. However, when RIAT was first conceptualised, I and others had one specific trial in mind. Study 329 was a placebo controlled randomised trial of paroxetine and imipramine in adolescents with major depression. As originally reported in 2001, it concluded that paroxetine was "generally well tolerated and effective."

Paroxetine has never been approved for use in children, but as Peter Doshi reports this week (doi:10.1136/bmj.h4629), millions of off-label prescriptions later Study 329 has become infamous. Funded by the manufacturer of paroxetine, SmithKline Beecham, now GSK, it was quickly dubbed by the US Food and Drug Administration a "failed trial," as neither treatment was found to be better than placebo. We learnt that the paper was drafted not by any of the 22 listed authors but by a writer paid by the manufacturer. But most alarmingly, reports emerged of serious adverse effects of paroxetine in adolescents, including self harm and suicidal ideation. In 2012 the US Department of Justice, investigating a failure to report safety data and other misconduct by GSK, settled criminal and civil proceedings with a record $3bn fine. Efforts to get the authors, the journal that published the trial , the professional society that publishes the journal, and the authors' institutions to act or even respond to criticism have failed.

Given this history, there was little doubt that the study needed restoration. That the original authors chose not to do this came as little surprise. The restorative authors set to work accessing and analysing the clinical study report and patient level data. From this immense task they concluded that there is no advantage of paroxetine or imipramine over placebo. They also uncovered "serious, severe, and suicide related adverse events" that had been overlooked or hidden.

The RIAT re-analysis marks a new chapter in the story of Study 329, showing the remarkable power of open data. But it also shows how much our current systems are failing patients and the public. It should not have taken 14 years to get to this point. It shows that we need regulation, and perhaps legislation, to ensure that the results of all clinical trials are made publicly available and that individual patient data are available for legitimate independent third party scrutiny.

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