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# The BMJ
# Press Release

## Reanalysis of antidepressant trial finds popular drug ineffective and unsafe for adolescents

*Results contradict original findings and have important implications for research and practice*

The widely used antidepressant paroxetine is neither safe nor effective for adolescents with depression, concludes a reanalysis of an influential study originally published in 2001.

The new results, published by **The BMJ** today, contradict the original research findings that portrayed paroxetine as an effective and safe treatment for children and adolescents with major depression.

It is the first trial to be reanalysed and published by The BMJ under an initiative called RIAT (Restoring Invisible and Abandoned Trials), which encourages abandoned or misreported studies to be published or formally corrected to ensure doctors and patients have complete and accurate information to make treatment decisions.

In 2001 SmithKline Beecham, now GlaxoSmithKline (GSK), funded a study (known as Study 329) to compare the effectiveness and safety of the antidepressant drugs paroxetine and imipramine with placebo for adolescents diagnosed with major depression.

It reported that paroxetine was safe and effective for adolescents and was published in the Journal of the American Academy of Child and Adolescent Psychiatry (JAACAP) in 2001.

The study was criticised by the Food and Drug Administration (FDA) in 2002. Yet, that year, over two million prescriptions were written for children and adolescents in the United States.

In 2012 GSK was fined a record $3bn in part for fraudulently promoting paroxetine.

The RIAT team, led by Professor Jon Jureidini at the University of Adelaide, identified this study as an example of a misreported trial in need of restoration.

Using previously confidential trial documents, they reanalysed the original data and found that neither paroxetine nor high dose imipramine was more effective than placebo in the treatment of major depression in adolescents. The authors considered the increase in harms with both drugs to be clinically significant.

They conclude that “paroxetine was ineffective and unsafe in this study.”

The reanalysis of Study 329 “illustrates the necessity of making primary trial data and protocols available to increase the rigour of the evidence base,” say the authors.

In an accompanying article, Peter Doshi, Associate Editor for The BMJ says the new paper “has reignited calls for retraction of the original study and put additional pressure on academic and professional institutions to publicly address the many allegations of wrongdoing.”

He points out that the original manuscript was not written by any of the 22 named authors but by an outside medical writer hired by GSK. And that the paper’s lead author - Brown University’s chief of psychiatry, Martin Keller - had been the focus of a front page investigation in the Boston Globe in 1999 that documented his under-reporting of financial ties to drug companies.

Doshi also details the refusal of the American Academy of Child and Adolescent Psychiatry to intervene and retract the paper, and Brown University’s silence over its faculty’s involvement in Study 329.

“It is often said that science self corrects. But for those who have been calling for a retraction of the Keller paper for many years, the system has failed,” argues Doshi.

Dr Fiona Godlee, The BMJ Editor-in-Chief says publication of the reanalysed data from Study 329 "sets the record straight" and “shows the extent to which drug regulation is failing us.” It also shows that the public and clinicians do not have the unbiased information they need to make informed decisions.

She calls for independent clinical trials rather than trials funded and managed by industry, as well as legislation “to ensure that the results of all clinical trials are made fully available and the individual patient data are available for legitimate independent third party scrutiny.”

Liberating the data from clinical trials has the potential to benefit patients, prevent harm, and correct misleading research, writes Professor David Henry at the University of Toronto, in an accompanying editorial.

Data sharing is not without its risks, he says, but the pay-off from a systematic effort to reactivate important clinical trials will be high and will further justify the original huge investments of time and money, he concludes.

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## Notes to Editors:

Research: Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence
Feature: No correction, no retraction, no apology, no comment: paroxetine trial reanalysis raises questions about institutional responsibility
Editorial: Liberating the data from clinical trials

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