Health & Science

Researchers: 2001 Paxil study seems to play down suicide risks to youths

By Lenny Bernstein and Ariana Eunjung Cha September 16
Follow @LennyMBernstein Follow @arianaeunjung

The study that paved the way for prescribing the antidepressant Paxil to millions of adolescents was seriously flawed, marked by what appear to be attempts to play down harms such as an increase in suicidal behavior by younger people who tested the drug, according to a reanalysis released Wednesday.

Using 77,000 pages of previously unavailable documents, a team of researchers concluded that paroxetine, marketed as Paxil by drugmaker GlaxoSmithKline, was no more effective than a placebo and considerably more dangerous than the original study indicated.

Similar criticism of what is known as “Study 329” began within a year of its publication in 2001, but Wednesday’s reappraisal in The BMJ, a medical journal, may be the most thorough yet.

In 2003 and 2004, the Food and Drug Administration issued warnings about an increase in suicidal thinking among some children and adolescents who took drugs in the class of antidepressants known as “selective serotonin reuptake inhibitors.” Those included Paxil and Zoloft.

Paxil still can be prescribed to young people, but in late 2004, the FDA ordered manufacturers to

include a “black box” warning on their labels about increased suicidal thinking among some youths who took the medication, and in 2007 the agency expanded the warning to include people under 25. In 2012, GlaxoSmithKline (formerly SmithKline Beecham) pleaded guilty and paid a $3 billion fine for illegally marketing Paxil and other drugs.

The team that published Wednesday’s study, led by Jon Jureidini, a professor at the University of Adelaide in Australia, went back to the raw data and found that Study 329 contained numerous transcription errors and other problems that violated the company’s own protocols for statistical analysis.

In some cases, the researchers said, it was difficult to tell what led to the mistakes.

But in one aspect — the coding of adverse events — they said the mistakes were so egregious it was difficult to see how they could have occurred unintentionally.

“It’s hard to think there wasn’t some mischief being done,” Jureidini said in a conference call with reporters Monday.

The lead author of Study 329, Martin Keller, retired from Brown University in 2012. He could not be reached for comment Wednesday.

[Government warnings about anti-depressants may have led to suicides]

The original study reported five instances of children becoming suicidal out of 93 in the study. Jureidini said a review found that the number was actually at least 12, a high rate. The discrepancy was caused by, among other things, the miscoding of a serious suicide attempt as “emotional lability,” a temporary condition that involves uncontrollable episodes of crying.

David Healy, a co-author of the new paper and a researcher at the School of Medical Sciences at Bangor University in Wales, said the suicide problem should have been obvious to anyone reviewing the data.

“It doesn’t take expertise to find these,” he said, adding, “It really takes extraordinary expertise to avoid being able to find them.”

GlaxoSmithKline issued a statement Wednesday saying the company was “able to help this team to carry out its reanalysis by providing access to the detailed data from the original trial. This reflects our commitment to data transparency — we publish the results of all our studies regardless of whether they are positive or negative.”

The company also said that “the findings from this team’s analysis appear to be in line with the longstanding view that there is an increased risk of suicidality in pediatric and adolescent patients given antidepressants like paroxetine. This is widely known and clear warnings have been in place on the product label for more than a decade. As such we don’t believe this reanalysis affects patient safety.”

The reanalysis was the first in a program by The BMJ to encourage a second look at abandoned or misreported studies to ensure that doctors have accurate information. In an article that accompanied the study, the journal again highlighted the American Academy of Child and Adolescent Psychiatry’s failure to retract the study, which it originally published in its journal. The article also noted Brown University’s public silence on the validity of the research.

Ivan Oransky, co-founder of Retraction Watch, said by e-mail that “although we don’t typically advocate for or against retraction, I’d say it would be consistent with how we’ve seen [guidelines from the Committee on Publication Ethics] interpreted in the past to retract this paper for unreliability.”

The child and adolescent psychiatry organization released a statement Wednesday saying that “the scientific process builds on itself over time through a cycle of new research, analysis, and dissemination. This process stimulates debate and moves the field forward toward a better understanding of critical issues.”

Brown released a previously issued statement saying that it could not comment on individual cases but has “procedures and policies in place that allow for a full and impartial review of

relevant information in response to any substantive concerns that are brought to its attention.”

Lenny Bernstein covers health and medicine. He started as an editor on the Post’s National Desk in 2000 and has worked in Metro and Sports.

Ariana Eunjung Cha is a national reporter. She has previously served as the Post's bureau chief in Shanghai and San Francisco, and as a correspondent in Baghdad.

Christian Science Monitor

Quantum teleportation record broken: Can life imitate Star Trek?

The Atlantic

The Black Family in the Age of Mass Incarceration

The Most Popular stories around the web