YALANCININ MUMU YATSIYA KADAR… SENELERCE YAZDIK AMA ANLATAMADIK… PAROKSETİN GENÇLERDE EMNİYETSİZ VE ETKİSİZ

Yaygın kullanılan SSRI grubu antidepressanlardan Paroksetin (Paxil, Seroxat, Aropax ve diğerleri) 2001 yılında ‘’Journal of the American Academy of Child and Adolescent Psychiatry de’’ study 329 olarak yayınlanan sahtekar bir makalede *(*[*Martin Keller*](https://en.wikipedia.org/wiki/Martin_Keller_%28psychiatrist%29)*, et al,* [*"Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial"*](http://www.justice.gov/sites/default/files/opa/legacy/2012/07/02/complaint-ex2.pdf)*, Journal of the American Academy of Child and Adolescent Psychiatry, 40(7), July 2001, pp. 762–772)* paroksetin gençlerde çok emniyetli ve çok etkili bir antidepressan olarak lanse edilen, daha sonra yazarının gerçekte bilim adamları olmadığı, hayalet yazar ‘’Sally Laden’’ yazıldığı ortaya çıkan Paroksetin skandalı nihayet tüm gerçekleri ile ortaya çıktı (*Le Noury ve ark., Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence, BMJ, 351, 2015*).

# Antidepressant Paxil Is Unsafe, Ineffective for Teens, Reanalysis Finds

(AP / Kirsty Wigglesworth)The widely prescribed antidepressant paroxetine — branded as Paxil, Aropax and Seroxat — isn’t a safe or effective treatment for depression in teens, finds a reanalysis of a 2001 study published Wednesday in *[The BMJ](http://press.psprings.co.uk/bmj/september/paroxetine.pdf?" \t "_blank)*.

The original study, published in Journal of the American Academy of Child and Adolescent Psychiatry — known as [study 329](http://study329.org/?" \t "_blank) — helped propel the popularity of prescribing the drug. Yet, over the years, it’s faced much controversy, with researchers calling for the retraction of the 2001 paper due to data analysis misrepresentations, among others.

The BMJ study is the first published reanalysis of a drug trial by a group of researchers collaborating on an initiative called RIAT (Restoring Invisible and Abandoned Trials), aimed at correcting abandoned or misreported studies. The original study was funded by SmithKline Beecham, now called GlaxoSmithKline (GSK), who despite the controversy, has stood by its findings.

“This paper is alarming, but its existence is a good thing,” Brian Nosek, a professor of psychology at the University of Virginia, who was not involved in either the original study or the reanalysis, said in*[The New York Times](http://www.nytimes.com/2015/09/17/health/antidepressant-paxil-is-unsafe-for-teenagers-new-analysis-says.html?smid=tw-nytimes&smtyp=cur&_r=0&" \t "_blank)*. “It signals that the community is waking up, checking its work and doing what science is supposed to do — self-correct.”

Jon Jureidini, a professor at the University of Adelaide in Australia, who led the reanalysis, received access to previously confidential documents, such as “about 77,000 pages of de-identified individual case report forms” posted by GSK “after negotiation.” What they found was the following:

* Paroxetine was no more effective at treating major depression in adolescents aged 12 to 18 than a placebo.
* Serious side effects associated with the antidepressant were underreported. Five of six adverse events labeled “emotional lability” in the original study involved suicidal thinking or behavior but were not presented as such, reports The New York Times.

In a statement sent to BMJ editors by Dr. Martin Keller of Brown University who led the original study, nine of the 22 authors voice “strong disagreement” with the reanalysis. They take issue with critiques of the analysis of side effects, and the charge that it was ghostwritten (the “report was authored mainly by the academic investigators with industry collaboration,” they wrote.)

“In summary, to describe our trial as ‘misreported’ is pejorative and wrong,” they wrote.

GSK said in a statement the new results “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.”

BMJ Publishes Study Revealing How Flawed Drug Research Fails a Trusting Public

**Band of Intrepid Researchers "Sets the Record Straight" on Ghostwritten Study**

**Toronto (September 16, 2015) —** Today the [BMJ published Restoring Study 329](http://study329.org/bmj-press-release-and-materials/), a decade-long effort by researchers to uncover the truth about the safety of an antidepressant approved for use by adolescents. Restoring Study 329 is a reanalysis and rebuttal of the original Study 329 ... [more](http://study329.org/bmj-publishes-study-revealing-how-flawed-drug-research-fails-a-trusting-public-2/)

[See news coverage](http://study329.org/in-the-news/)

Medicine’s Most Infamous Clinical Trial

[Study 329](http://study329.org/wp-content/uploads/2015/02/Keller-et-al-329.pdf%22%20%5Co%20%22Keller%20et.%20al.%20329%20%282001%29%22%20%5Ct%20%22blank) had all the makings of a scandal.

Thousands of North American children and adolescents were seriously harmed by taking SSRIs like Paxil. Many died. Neither doctors nor parents had the information they needed, and the FDA only reluctantly issued the appropriate warnings, as might be expected from a regulator that has “corporate partnership” in its mandate.

So why aren’t we all scandalized?

The impact of the 2001 study stayed under the radar for many reasons. People trusted the integrity of scientists at major universities. They believed that drug regulators’ top priority was public safety, not really understanding that their mandates were more complex than that. Journalists, doctors, and the public were captured by effective marketing of the drugs.

**Evidence Without Data Is Not Evidence**

[Restoring Study 329](http://study329.org/wp-content/uploads/2015/09/Study-329-Final.pdf%22%20%5Ct%20%22blank) is a decade-long effort by researchers to uncover the truth.

Using the same data (obtained through an arduous process), it is a reanalysis and rebuttal of the original Study 329, coming to exactly the opposite conclusion — namely that, “Neither paroxetine nor high-dose imipramine demonstrated efficacy for major depression in adolescents, and there was an increase in harms with both drugs.”

This website is aimed at identifying needed changes to restore scientific integrity to the clinical drug trial process. It is intended to inform and educate by offering the facts for all to see. We hope to inspire you to [demand better medicine](http://study329.org/what-can-i-do) — for yourself, for your family, for everyone.

“In Restoring Study 329, our authors present a significantly different version to the original Keller article — one that raises many questions about drug safety, the limitations of randomized controlled trials, the need for access to individual patient level data, and the question of how to reduce harms from misleading health information.”

**What Happened?**

In the early 2000s, based on Study 329, GlaxoSmithKline (GSK) marketed Paxil (paroxetine) as safe and effective for children and adolescents when company executives were aware that a number of studies (all but Study 329 unpublished) had shown that the drug was no better than placebo and caused thought disturbance and suicidal behavior in some youngsters.

Paroxetine brand names around the world

Study 329 was a randomized, controlled trial of the efficacy and harms of paroxetine and imipramine in the treatment of adolescent major depression published in the journal with the highest impact factor in the field, the *Journal of the American Academy of Child and Adolescent Psychiatry* (JAACAP), in July 2001.



Ghost writer Sally Laden

After Study 329 was published, Paxil rose to be GSK’s bestselling drug and became the #1 antidepressant in the United States with sales of $340 million by the end of 2001. It was one of a number of drugs in the SSRI class, and prescriptions of these drugs to children and adolescents continued to increase throughout the decade.

Notionally authored by Dr. Martin Keller, et. al., but actually ghostwritten by Sally Laden, Study 329 concluded that, “Paroxetine is generally well tolerated and effective for major depression in adolescents.”

**Legal Settlements Merely a Marketing Cost?**

Study 329’s conclusions were not compatible with the data.

In 2004 New York Attorney General Elliot Spitzer filed a consumer fraud action against GSK for mismatches between their marketing claims and the data. This lawsuit was settled the same year for $2.5 million. The terms of the settlement included a requirement for GSK to post study results on the company website, including those for Study 329. Access to data was difficult, however, due to different interpretations of what should be included in “data” and what constituted “access.”

In November 2012 GSK pleaded guilty and agreed to pay $3 billion, the biggest fine in corporate history. The next year, the number of prescriptions for paroxetine in the United States increased by 3%.

In 2012 the US Department of Justice brought an action against GSK in US District Court to recover damages and civil penalties under the False Claims Act, and damages and other monetary relief under common law for causing the submission of false of fraudulent claims to federal health care programs (Medicare and Medicaid). In November 2012 the company pleaded guilty and agreed to pay $3 billion, the biggest fine in corporate history.

In 2013, the year following the settlement, the number of prescriptions for paroxetine in the United States increased by 3%.

**Data Transparency Critical for Drug Studies**

Beginning soon after its 2001 publication, a number of journalists and researchers spotted the anomalies in Study 329’s data classification and interpretation and raised concerns with the authors, their institutions, and the JAACAP. Despite this, the 329 trial continued to be presented as a “landmark” study demonstrating the drug’s efficacy and safety.

Despite requests from concerned scientists, the Study 329 article [has never been retracted](http://study329.org/request-to-retract-study-329/).

Drug studies have been seriously flawed for a long time. Study 329 is typical of all drug trials, for patients of all ages, for patented drugs. The lack of access to its data, and the fact that it was“ghost-written” by a writer hired by GSK, and not by the nominal Study author, reflect standard practice.

The core problem is that the process for safety and effectiveness testing is left to drug manufacturers, who have a vested interest in seeing positive results, without the medical and scientific community being able to scrutinize what they are doing.

Currently, there is no requirement that complete drug trial data (excluding personal identifiers) be made available to all interested parties in the name of good science. Without complete transparency, the tendency for drug companies to manipulate and interpret data in an unduly favourable light is impossible to avoid.

In Restoring Study 329, our authors present a significantly different version to the original Keller article — one that raises many questions about drug safety, the limitations of randomized controlled trials, the need for access to individual patient level data, and the question of how to reduce harms from misleading health information.

**Restoring Invisible and Abandoned Trials (RIAT)**

RIAT stands for Restoring Invisible and Abandoned Trials and is the brainchild of Peter Doshi. Its purpose is to improve the integrity of the process to determine drug efficacy and safety.

Restoring Study 329 is the first example of the RIAT process applied to a company trial. The RIAT protocol enables teams to re-author studies that have not been published or that have been misleadingly published. Its purpose is to put pressure on drug companies to make good on their stated commitment to data access.

**Same Data, Opposite Conclusions**

Restoring Study 329 is based on an assessment of as much of the original data as the researchers could get through in nine months. After much wrangling, they finally gained access to scanned copies of redacted patient data through a remote access portal, which they could not print or download. The information was not organized in a way that they could clearly see how the original conclusions had been reached, and more than personal identifiers had been redacted.

Still, the researchers were able to determine from a detailed review of 77,000 pages of patient records that suicide attempts were significantly higher than what the original study had reported, and that there were many other unreported serious adverse events in the Paxil group. They noted that the drug was no more effective than placebo for alleviating depression in young people.

Restoring Study 329 asserts that paroxetine (known as Paxil in North America, Seroxat in the UK, and Aropax in Australia and New Zealand) is ineffective and causes thought disturbance and other serious adverse effects, including suicidal behaviour in a significant number of young people.

**Marketing Harmful Drugs to a Trusting Public**

The issues are bigger that what happened with Study 329. This was not simply one anomalous series of randomized, controlled trials, but rather what has become standard industry practice for branded medicines.

The FDA decision in 1997 to allow direct-to-consumer advertising of medications may have led to the overuse of drugs, and a false sense in the general public that drugs must be safe or their use would not be openly promoted.

**Setting the Record Straight…**

This is the first case of two radically different versions of the same article in print. Our version, Restoring Study 329, comes with the data.

How will the scientific and medical community respond?

How will [you respond](http://study329.org/what-can-i-do)?

**Same Data, Opposite Conclusions**

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| --- | --- | --- |
|  | **Original Study 329(2001)**[Click here](http://study329.org/wp-content/uploads/2015/02/Keller-et-al-329.pdf%22%20%5Co%20%22Keller%20et.%20al.%20%282001%29%22%20%5Ct%20%22_blank) | **Restoring Study 329(2015)**[Click here](http://study329.org/wp-content/uploads/2015/09/Study-329-Final.pdf%22%20%5Ct%20%22_blank) |
| **Conclusion** | Paxil was effective. | Paxil was not effective. |
| Paxil was well tolerated. | Paxil caused serious side effects, including hostility, insomnia, and akathisia. |
| **Adverse Events** | Did not include all | Included all adverse events, including in taper phase |
| **Suicidal behavior** | 6 adolescents experienced “emotionally lability” | 13 adolescents became suicidal |
| **Implications** | Misled doctors into prescribing a drug that is ineffective, unsafe for adolescents | Corrects the record, reveals that the data did not support the conclusion of the original study |

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| **Table 1:  Adverse events (AE) for paroxetine and placebo groups in Study 329 according to clinical study report (CSR), paper by Keller and colleagues (ADECS coded), and RIAT reanalysis (MedDRA coded)** |
|  | **Paroxetine (n=93)** | **Placebo (n=87)** | **AE ratio paroxetine:placebo****RIAT reanalysis** |
|  | **CSR** | **Keller** | **RIAT** | **CSR** | **Keller** | **RIAT** |  |
| Total AEs | 338 | 265 | 481 | 277 | 207 | 330 | 1.4 |
| Severe AEs | 70 | — | 70 | 25 | — | 25 | 2.6 |
| Psychiatric AEs | — | — | 103 | — | — | 24 | 4.0 |
| AEs in taper phase\* | 45 | — | 47 | 10 | — | 10 | 2.2 |
| Severe AEs in taper phase\* | 13 | — | 13 | 1 | — | 1 | 6.2 |
| Suicidal and self injurious patients (acute/taper) | 7 | 5 | 11 | 1 | 1 | 1 | 10.3 |
| \*Paroxetine n=19, placebo n=9 |

16 September 2015 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.

RESEARCH CONDUCT No correction, no retraction, no apology, no comment: paroxetine trial reanalysis raises questions about institutional responsibility As a new data analysis adds weight to calls for retraction of a paper on paroxetine in adolescents,

Peter Doshi examines the resistance to action of a professional society, its journal, and an Ivy League university

Peter Doshi associate editor, The BMJ s: BMJ 2015;351:h4629

A major reanalysis just published in The BMJ of tens of thousands of pages of original trial documents from GlaxoSmithKline’sinfamous Study 329, has concluded that the antidepressant paroxetine is neither safe nor effective in adolescents with depression.1 This conclusion, drawn by independent researchers, is in direct contrast to that of the trial’s original journal publication in 2001, which had proclaimed paroxetine “generally well tolerated and effective.”2 The new paper, published under the restoring invisible and abandoned trials (RIAT) initiative,3 has reignited calls for retraction of the original study, putting additional pressure on academic and professional institutionsto publicly addressthe many allegations of wrongdoing.

A major reanalysis just published in The BMJ of tens of thousands of pages of original trial documents from GlaxoSmithKline’sinfamous Study 329, has concluded that the antidepressant paroxetine is neither safe nor effective in adolescents with depression.1 This conclusion, drawn by independent researchers, is in direct contrast to that of the trial’s original journal publication in 2001, which had proclaimed paroxetine “generally well tolerated and effective.”2 The new paper, published under the restoring invisible and abandoned trials (RIAT) initiative,3 has reignited calls for retraction of the original study, putting additional pressure on academic and professional institutionsto publicly addressthe many allegations of wrongdoing. Troubled from the start Few studies have sustained as much criticism as Study 329, a placebo controlled, randomized trial of paroxetine and imipramine carried out by SmithKline Beecham (which became GlaxoSmithKline (GSK) in 2000). In 2002, a US Food and Drug Administration officer who formally reviewed the trial reported that “on balance, this trial should be considered as a failed trial, in that neither active treatment group showed superiority over placebo by a statistically significant margin.”4 Yet this same year, according to the New York State Attorney General’s office, which sued GSK, over two million prescriptions were written for children and adolescents in the United States, all off-label, after a marketing campaign that characterized Study 329 as demonstrating “REMARKABLE Efficacy and Safety.” The disparity between what the manufacturer and study authors claim the trial found and what other parties say the data show was an important element in the US Department of Justice’s criminal charges against GSK. In 2012, GSK wasfined a record $3bn (£2bn; €2.7bn), in part for fraudulently promoting paroxetine.

Then there are the matters of “editorial assistance” and undisclosed financial conflicts of interests of one of the paper’s authors. The first draft of the manuscript ultimately published in the Journal of the American Academy of Child and Adolescent Psychiatry (JAACAP) was not written by any of the 22 named authors but by an outside medical writer hired by GSK. And the paper’slead 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. Senator Charles Grassley, who led a congressional investigation and published a report on ghostwriting in the medical literature, reportedly wrote to Brown University about Keller. 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. None of the paper’s 22 mostly academic university authors, nor the journal’s editors, nor the academic and professional institutions they belong to, have intervened to correct the record. The paper remains without so much as an erratum, and none of its authors—many of whom are educators and prominent members of their respective professional societies—have been disciplined. This propelled University of Adelaide child psychiatrist Jon Jureidini, who led the reanalysis team, and his colleagues into action. “The RIAT initiative offered us a chance to report Study 329 ourselves, so as to correct the record, and perhaps finally embarrass the authors, institutions and the journal into taking the actions they have so far resisted.” Journal’s response Disputesin science are often put down to differences of opinion. But in the case of Study 329 no epistemological acrobatics would seem able to reconcile the differences between the 2001 JAACAP paper and the RIAT republication. They cannot both be right. Take, for example, the straightforward issue of reporting the trial’s primary outcome. In the JAACAP paper, Keller and colleagues describe “response” as a “primary outcome measure” and says it “separated statistically from placebo.” But according to the RIAT team, the effect of paroxetine was not significantly different from placebo for any prespecified primary or secondary outcome measure. Such stark differences between the original paper and the rewrite are bound to put particular pressure on Andrés Martin, Yale University professor and current editor in chief of JAACAP. Martin has been under pressure to retract the paper for years, including from within his own society. Last October, Martin was compelled to address the academy’s assembly about Study 329. According to the minutes, members heard how Martin had investigated the matter thoroughly by consultation with the authors, the Committee on Publication Ethics (COPE), clinical experts, “a whole range of attorneys, and more.” Martin’s assessment, completed in July 2010, concluded that no further action was necessary. A follow-up inquiry, again by Martin, in 2012, after GSK was fined $3bn, similarly concluded “no basis found for editorial action against the article.” No specific findings from Martin’s investigation are recorded in the minutes, and Martin did not respond to multiple requests for comment from The BMJ. Ivan Oransky, cofounder of the Retraction Watch blog, says that transparency is vital. “GSK agreed to pay a $3bn fine and you’re [Martin] saying you had completely different results? Great. Show me.” Oransky described Martin’s silence as part of the “typical scientific playbook.” “It has certainly been our experience that journals and researchers and institutions can be incredibly stubborn about failing to retract a paper, about ignoring calls, or not responding favourably to calls to retract.” The academy It has proved no easier to get the professional society to talk. Several of the authors of the JAACAP paper are members of the American Academy of Child and Adolescent Psychiatry (AACAP). The BMJ sent four requests for comment to the academy’s president, Paramjit Joshi, and past president Martin Drell, but received no response. Others have had better luck. In 2012, Mickey Nardo, a retired psychiatrist who subsequently joined the RIAT team, wrote to the AACAP ethics committee with a plea to retract the Keller paper. “It’s the right thing to do and a right time to do it.” “The letter wasreceived warmly by the president of the AACAP, the president elect, and the chair of the ethics committee, who assigned a member of the committee to work with me . . . We had several amicable exchanges,” Nardo later commented in his blog.5 Then, silence. Behind the scenes, Nardo’s letter had impact. Minutes of an AACAP Council teleconference obtained by The BMJ confirm that the topic was formally discussed in a call that included JAACAP’s editor in chief. Martin said, “that while the [Keller et al] article is not perfect, the ethical concerns raised by the GSK lawsuit are not substantiated,” according to the minutes. Furthermore, the journal editors “believe that there is little to gain in responding and that doing so would simply ‘fuel the fire.’” The agenda item ends: “Action: if council members receive any inquiries about Study 329, please direct these to Andrés Martin.”

What does not appear in the minutes is any mention of AACAP’s ethics committee and its role in handling complaints about members. “The AACAP leadership has asked us to defer any comments representing the organization on this matter to them so we have forwarded your request to the current president and CEO,” AACAP ethics committee cochairs, Arden Dingle and Gail Edelsohn, told The BMJ in an email. They added that their committee has never had an “investigatory role” within the academy, leaving unclear how—and indeed if—the academy investigates allegations of misconduct against its members. The AACAP ethics committee’s lack of an investigatory role seems to be unusual. Related professional organizations, including the American Psychiatric Organization, American Psychological Association, and the American Psychoanalytic Association all have ethics committees charged with responding to allegations of ethical misconduct within their respective societies. Discontent within the academy The refusal of AACAP’s leadership to call for retraction of the Keller paper has become a rallying point for some in the academy who view Study 329 as symbolic of fundamental ethical problems within the profession. One regional chapter, the Northern California Regional Organization of Child and Adolescent Psychiatry (NCROCAP), features the Study 329 story on its homepage. Ed Levin, a Bay Area based child psychiatrist who has held many offices in the chapter, including that of president, has led the charge. Warning for more than two yearsthat a RIAT rewrite of Study 329 could be expected, he has urged the academy leadership to take action on Study 329 and to review its policies on relationships with the drug industry. Financial reports that AACAP makes available show the organization has received between $500 000 and $1m from the drug industry each year since 2003, roughly 5-20% of its annual revenue.6 7 But after successfully bringing the topic to the national agenda at last October’s annual meeting, Levin describes an “increasing defensiveness of the leadership.” He and former NCROCAP president George Stewart increasingly think that going public may be the only route forward. As an example, Levin says the academy began advance screening of emails to be submitted to the assembly listserv. Following that, the chair of the assembly “would not allow me to post on the assembly listserv my thoughts about how s329 was handled at the last assembly meeting.” And he added, “AACAP leadership also set up first time ever rules controlling communication between different regional organizations—just after we requested, and were denied, the email addresses of the presidents of the other ROs.” Distress over Study 329 has caused at least one person to resign from the academy. Mary Olowin, former president, secretary and treasurer of the Northern California regional group, told The BMJ that she first withheld her academy dues in 2014. “When the journal did not retract the article and AACAP leadership did not press for the editor to do this by the time the annual meeting ended in October, Isent in a letter of resignation, explaining why I was leaving.” The academy did not acknowledge her letter. “We’re not out here to destroy the academy; we’re trying to protect it before it hits the mainstream media because it’s going to make us look like fools,” Levin said. One topic the media may soon pick up on is that the incoming president elect of AACAP, Karen Wagner, is a coauthor of the JAACAP paper. Wagner, a psychiatrist at the University of Texas, is also named eight times in the 2011 US Department of Justice complaint against GSK. According to the complaint, Wagner promoted paroxetine at a 1999 GSK sales force event. A GSK newsletter cited in the complaint quotes Wagner as telling the sales force that major depression was “a lethal disorder and it requirestreatment.” Based on the results of Study 329, which were at the time still unpublished, “Dr Wagnersaid: ‘We can say that paroxetine has both efficacy and safety data for treating depression in adolescents.’” The newsletter also states that the “clinical study demonstrating the success of Paxil in treating depression among adolescents will be published in a peer reviewed journal during first quarter 2000.” The manuscript, however, was rejected by JAMA in late 1999 before JAACAP ultimately published it in 2001.8 Wagner did not respond to The BMJ’s requests for comment. University keeps silent It’s often argued that fairness in journalism requires getting “both sides” of the story, but in the story of Study 329, the “other side” does not seem interested in talking. “I would caution you not to confuse the University’s policy of confidentiality with inactivity,” wrote Edward Wing, former Brown University dean of medicine and biological sciences. Wing was responding to Jureidini, who had written to the university’s president, Ruth Simmons, requesting retraction of the Keller paper. Simmons gained national attention asthe first African American president of an Ivy League university and had appointed a steering committee to examine how the school benefited from slavery in the 18th century. But on Study 329, the university did not take such a transparent course of action. “The University takes seriously any questions about the soundness of faculty-conducted research. While we cannot comment on individual personnel cases, we do take appropriate actions whenever we receive substantive concerns about the conduct of research. The University gathers relevant information, conductsinternal reviewsif appropriate, and makes any adjustments or corrections that may be warranted,” read Wing’s letter to Jureidini in late 2011. The BMJ has been unable to determine whether Brown ever investigated the university’s or faculty’s involvement in Study 329. Mark Nickel, interim director of the news and communications office, said that such matters are considered confidential. “I’m not confirming or denying anything regarding what the university may or may not have done.” David Savitz, Brown’s vice president for research, said: “I appreciate your interest, but having been in my position for only the last 1.5 years, I have no personal insights into this case. While there are issuesin what can be disclosed, in my case there is simply the absence of knowledge of the case other than through the media.” Savitz is the integrity officer for the university, and in this role helps assess allegations of research misconduct at Brown. However, he explained that “these matters have to be handled with complete confidentiality regarding particular allegations and individuals.” The university also said it does not report aggregate data regarding how many such allegations it investigates or their outcome. Roy Poses, president of the Foundation for Integrity and Responsibility in Medicine and clinical associate professor of medicine at Brown, says he has never heard of a formal investigation of Keller or Study 329. “There were claims that some person or personsin the Brown administration had looked into the cases, but not in a formal way, in particular not using an open process, and I don’t believe any formal results of any such investigation were ever made public.” “The big story is that there was no story. There was no formal investigation, no hearing, no faculty forum, no real public discussion,” says Poses. “I don’t understand how Brown has gotten away with what it’s doing. It has essentially decided to ignore the whole thing,” says Paul Thacker, a journalist that investigated Study 329 and Brown as part of his work as a former congressional staffer for Senator Grassley. “The only real investigation we’ve had on the Brown University campus on this drug has been by the Brown Daily Herald,” he said, referring to the student newspaper. The Herald has run at least six stories since 2008 that probe Study 329, Keller’s relationship with the pharmaceutical industry, and Senator Grassley’s investigations into conflicts of interest in clinical research. “I think this is the most thoroughly examined case study of research misconduct in the 2000s, and I don’t know how it has not been retracted yet,” Thacker told The BMJ. “Why would you send your kid to Brown University and pay all that tuition when the only people who seem to know what’s right are the kids on campus?” Retraction Watch’s Oransky says he is notsurprised by Brown’s silence. “Universities have become more corporate than many corporations.” Oransky arguesthat institutionslike Brown should confront the problem. Instead of silence, the message from Brown should be: “There is fraud in science; it’s pretty rare, but here is what we’re doing to get rid of it because we’re upset about it.” “The controversy will not end if they simply stop talking about it. If anything, it will get worse.” Competing interests: I have read and understood BMJ policy on declaration of interests and declare I am the first author of the RIAT declaration, which was coauthored by David Healy, who is part of the group that reanalysed Study 329. I served as a formal peer reviewer for the reanalysis manuscript and provided the Jureidini team with unpaid advice on the RIAT process before the paper was submitted and while it was under review. I am also a graduate of Brown University and member of a Cochrane review of neuraminidase inhibitors that is based in part on clinical study reports provided by GSK for zanamivir. I initiated an inquiry in 2012 that resulted in additional information from clinical study reports of Study 329 and eight other studies being posted on GSK’s website. Provenance: Commissioned, not externally reviewed. 1 Le Noury J, Nardo JM, Healy D, et al. 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