Prescribing Antidepressants for Adolescents With Major Depression

My comment addresses points raised in the recent Pediatrics article by Coon et al titled "Update on Pediatric Overuse". The section of the article in question is titled "Antidepressants for Adolescents Are Determined to Be Ineffective and Possibly Harmful in Reanalysis of a Pivotal Trial." This section highlights the recent "Restoring Study 329", which raises major methodological concerns about an important original paroxetine and imipramine trial performed in the mid-late 1990s (Study 329). Coon et al conclude that the "current widespread use of antidepressants in adolescents may have been driven in part by misleading results from the initial [Study 329] trial in 2001" and correctly argues for improved data transparency in antidepressant research.

While Coon et al should be applauded for highlighting concerns raised by "Restoring Study 329", their conclusion on antidepressants as a medication class does not seem to consider the broader context of major depression management in adolescents. The notion that paroxetine is not efficacious in adolescents has been well established from other previous studies. A recent network meta-analysis on anti-depressant use in children and adolescents also re-confirmed this finding.

Importantly, this same meta-analysis also confirmed the established evidence that fluoxetine is often efficacious for acute treatment of adolescents with major depressive disorder (MDD). It also finds that among the pediatric population, fluoxetine is better tolerated than many other antidepressants. Importantly, the findings in favor of fluoxetine were observed in both industry-sponsored and non-industry-sponsored trials. This knowledge has largely informed major depression practice parameters that have been in place for the better part of a decade.

USPSTF systematic reviews from 2009 and 2016 describe evidence of good symptom response to combination psychotherapy and fluoxetine in adolescents with MDD. Due to the body of evidence, fluoxetine in addition to psychotherapy is recommended for consideration in moderate to severe depression by both the Royal Australian and New Zealand and the British NICE guidelines for diagnosing and managing depression in pediatrics. Restoring Study 329 raises important concerns about research ethics and the importance of revisiting trial data to reach appropriate conclusions in pediatric research. Likewise, Coon et al crucially identify the need for better trial data transparency to ensure accurate evidence-based antidepressant prescribing practices for adolescents. At the root, however, Coon et al use specific evidence against paroxetine in adolescents to raise concern about the overuse of antidepressants as a class. They do not seem to acknowledge that fluoxetine is used far more often than paroxetine due to strong evidence that suggests it should be considered as first line therapy for many adolescents with major depression. Based on the body of the literature, there is moderate to strong evidence that fluoxetine in combination with psychotherapy is an efficacious and safe option for adolescents with moderate to severe depression. Prescribing this antidepressant to a teenager should be strongly considered when indicated. Primary pediatricians and mental health specialists should not be afraid to use fluoxetine as a tool when an adolescent truly needs help.

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REFERENCES

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Author’s Response

We appreciate Dr. Pitts’ comments on our article. He appears to take issue with the implication that antidepressants as a class are of questionable efficacy in the treatment of adolescents with depression, arguing in particular that there is moderate to strong evidence of fluoxetine’s efficacy and that providers should not be afraid to use it. While Restoring Study 329 and our commentary apply only to imipramine and paroxetine, we do believe the larger body of existing literature similarly calls into question the efficacy of treating adolescent

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