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Letter to the Editor

Updating the position of fluoxetine: Editorial shift or evidence-based evolution?

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To the Editors,

The Maudsley Prescribing Guidelines in Psychiatry have long been regarded as a cornerstone of psychopharmacological practice internationally. In the recently published 15th edition (2025), a notable shift in the positioning of fluoxetine is observed, particularly regarding its use during pregnancy. Fluoxetine is no longer presented as a first-line option without the inclusion of new robust evidence to justify this downgrading.[1,2]

Historically, fluoxetine has been recognized as a first-line SSRI due to its well-established efficacy, favorable tolerability, long half-life protecting against withdrawal symptoms, and safer profile in overdose compared to older antidepressants.[3,4] In the 15th edition, it is stated that "an association between prenatal SSRI use and congenital heart defects has been reported, with some studies suggesting a higher risk with fluoxetine and paroxetine".[1]

The only relevant citation is Reefhuis et al. (2015),[5] which employed Bayesian analysis to reevaluate previous associations. Although a slight increase in risk for specific congenital anomalies (e.g., right ventricular outflow tract obstruction) was identified, the study concludes that the absolute risks are small and that most SSRIs, including fluoxetine, are not significantly associated with specific birth defects.

It is important to highlight that this study was already available at the time of the 14th edition (2021),[2] where fluoxetine continued to be considered an appropriate and safe choice during pregnancy. This raises concerns about whether the change in tone in the 15th edition reflects genuine new scientific developments or simply evolving clinical preferences.

Moreover, current NICE guidelines[6,7] do favor sertraline due to a slightly lower observed risk in pregnancy. However, they also emphasize that women benefiting from an existing SSRI treatment should not be advised to switch medications solely because of pregnancy. Notably, fluoxetine remains the only SSRI officially approved for treating moderate to severe depression in adolescents aged 8–18 years.[8]

While adapting guidelines to evolving prescribing practices is understandable, in authoritative references such as the Maudsley Guidelines, it is crucial to clearly distinguish between evidence-based updates and pragmatic clinical trends. Failure to do so may inadvertently undermine confidence in long-standing, evidence-supported treatments like fluoxetine, ultimately affecting clinical decision-making.

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