PSYCHIATRIKI

Journal Pre-proof

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

Georgios Mikellides, Olympia Evagorou, Marianna Tantele

DOI: https://doi.org/10.22365/jpsych.2025.018

To appear in: Psychiatriki Journal

Received date: 28 April 2025
Accepted date: 7 July 2025

Please cite this article as: Georgios Mikellides, Olympia Evagorou, Marianna Tantele, Updating the Position of Fluoxetine: Editorial Shift or Evidence-Based Evolution?, Psychiatriki (2025), doi: https://doi.org/10.22365/jpsych.2025.018

This is a PDF file of an article that has undergone enhancements after acceptance, such as adding a cover page and metadata, and formatting for readability. Still, it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting, and review before it is published during the production process; errors may be discovered that could affect the content, and all legal disclaimers that apply to the journal pertain.

LETTER TO THE EDITOR

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

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]

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.

Georgios Mikellides
Cyprus rTMS, Nicosia, Cyprus
University of Nicosia Medical School, Nicosia, Cyprus
Email: George.mikellides@gmail.com

Olympia Evagorou
Cyprus rTMS, Nicosia, Cyprus

Journal Pre-proof

Marianna Tantele
Cyprus Mental Health Services, Nicosia, Cyprus

https://doi.org/10.22365/jpsych.2025.018
Received 28 April 2025 / Published Online 5 August 2025

References

1. Taylor D, Barnes TRE, Young AH. *The Maudsley Prescribing Guidelines in Psychiatry*. 15th ed. Wiley-Blackwell; 2025
2. Taylor D, Barnes TRE, Young AH. *The Maudsley Prescribing Guidelines in Psychiatry*. 14th ed. Wiley-Blackwell; 2021
3. Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. *Lancet* 2009, 373(9665):746–758, doi: 10.1016/S0140-6736(09)60046-5
4. Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet* 2018, 391(10128):1357–1366, doi: 10.1176/appi.focus.16407
5. Reefhuis J, Devine O, Friedman JM, et al. Specific SSRIs and birth defects: Bayesian analysis to interpret new data in the context of previous reports. *BMJ* 2015, 351:h3190, doi: 10.1136/bmj.h3190
6. National Institute for Health and Care Excellence. *Antenatal and postnatal mental health: clinical management and service guidance. NICE Clinical Guideline CG192.* NICE, London, 2014
7. National Institute for Health and Care Excellence. *Depression – antenatal and postnatal. Clinical Knowledge Summaries* [Internet]. NICE, London, 2020
8. National Institute for Health and Care Excellence. Fluoxetine for children and young people. In: *BNF for Children* [Internet]. London: NICE; 2024. Available from: https://bnfc.nice.org.uk/drug/fluoxetine.html

Journal Pre-proof