

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

# Antidepressants Administered using Weight- Based Dosing Strategies for Depression: Clinical Effectiveness and Guidelines

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## Research Questions

1. What is the clinical effectiveness of selective serotonin reuptake inhibitors and other antidepressants administered using weight-based dosing strategies for the treatment of individuals with depression?
2. What are the evidence-based guidelines regarding the use of weight-based dosing strategies for selective serotonin reuptake inhibitors and other antidepressants for the treatment of individuals with depression?

## Key Findings

No evidence was identified regarding the clinical effectiveness of selective serotonin reuptake inhibitors and other antidepressants administered using weight-based dosing strategies for the treatment of individuals with depression. One evidence-based guideline was identified regarding the use of weight-based dosing strategies for selective serotonin reuptake inhibitors and other antidepressants for the treatment of individuals with depression.

## Methods

### Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were antidepressants and weight-based drug dosing. No search filters were applied to limit retrieval by study type. An additional search on antidepressant dosing was limited to guidelines only. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2010 and November 30, 2020. Internet links were provided, where available.

### Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available, and relevant recommendations were summarized.

**Table 1: Selection Criteria**

<b>Population</b>	Individuals with depression (any type)
<b>Intervention</b>	Selective serotonin reuptake inhibitors (SSRIs) or other antidepressants administered using weight-based dosing strategies
<b>Comparator</b>	Q1: SSRIs or other antidepressants administered using alternative dosing strategies (e.g., fixed-dose strategies) Q2: Not applicable
<b>Outcomes</b>	Q1: Clinical effectiveness (e.g., severity of depressive symptoms, quality of life, pharmacokinetic outcomes, safety [e.g., adverse events]) Q2: Recommendations regarding best practices (e.g., guidance regarding when weight-based dosing strategies should be used)
<b>Study Designs</b>	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, evidence-based guidelines

## Results

One evidence-based guideline was identified regarding the use of SSRIs and other antidepressants administered using weight-based dosing strategies for the treatment of individuals with depression.<sup>1</sup> No relevant health technology assessments, systematic reviews, randomized controlled trials, or non-randomized studies were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in the appendix.

## Overall Summary of Findings

No relevant literature was found regarding the clinical effectiveness of SSRIs and other antidepressants administered using weight-based dosing strategies for the treatment of individuals with depression; therefore, no summary can be provided. One evidence-based guideline<sup>1</sup> from the National Institute for Health and Care Excellence was identified which considered the weight of pediatric patients when prescribing antidepressants. The guideline recommends that clinicians prescribing fluoxetine or non-fluoxetine antidepressants consider lower starting doses for children with lower body weights, and higher doses for older children with higher body weights.<sup>1</sup>

## References Summarized

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-analyses

No literature identified.

### Randomized Controlled Trials

No literature identified.

## Non-Randomized Studies

No literature identified.

## Guidelines and Recommendations

1. National Institute for Health and Care Excellence. Depression in children and young people: identification and management. (*NICE guideline NG134*); 2019.  
<https://www.nice.org.uk/guidance/ng134/resources/depression-in-children-and-young-people-identification-and-management-pdf-66141719350981>  
*See: How to use antidepressants in children and young people – 1.6.19 (p.23); 1.6.25 (p.24-25)*

## Appendix — Further Information

### Non-Randomized Studies

#### *Alternative Intervention – Association Between Weight and Clinical Effectiveness or Pharmacokinetics*

2. Dale RM, Bryant KA, Thompson NR. Metabolic Syndrome Rather Than Body Mass Index Is Associated With Treatment Response to Ketamine Infusions. *J Clin Psychopharmacol*. 2020 Jan/Feb;40(1):75-79.  
[PubMed: PM31834094](#)
3. Warrings B, Samanski L, Deckert J, Unterecker S, Scherf-Clavel M. Impact of Body Mass Index on Serum Concentrations of Antidepressants and Antipsychotics. *Ther Drug Monit*. 2020 Sep 04.  
[PubMed: PM32910098](#)
4. Greenblatt DJ, Harmatz JS, Chow CR. Vortioxetine Disposition in Obesity: Potential Implications for Patient Safety. *J Clin Psychopharmacol*. 2018 Jun;38(3):172-179.  
[PubMed: PM29596146](#)
5. Jha MK, Wakhlu S, Dronamraju N, Minhajuddin A, Greer TL, Trivedi MH. Validating pre-treatment body mass index as moderator of antidepressant treatment outcomes: Findings from CO-MED trial. *J Affect Disord*. 2018 Jul;234:34-37.  
[PubMed: PM29522941](#)
6. Schoretsanitis G, Haen E, Hiemke C, et al. Sex and body weight are major determinants of venlafaxine pharmacokinetics. *Int Clin Psychopharmacol*. 2018 11;33(6):322-329.  
[PubMed: PM30028351](#)
7. Findling RL, Groark J, Tourian KA, et al. Pharmacokinetics and Tolerability of Single-Ascending Doses of Desvenlafaxine Administered to Children and Adolescents with Major Depressive Disorder. *J Child Adolesc Psychopharmacol*. 2016 12;26(10):909-921.  
[PubMed: PM27428303](#)
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[PubMed: PM27749681](#)
9. Sigurdsson HP, Hefner G, Ben-Omar N, et al. Steady-state serum concentrations of venlafaxine in patients with late-life depression. Impact of age, sex and BMI. *J Neural Transm*. 2015 May;122(5):721-729.  
[PubMed: PM25257248](#)
10. Taurines R, Burger R, Wewetzer C, et al. The relation between dosage, serum concentrations, and clinical outcome in children and adolescents treated with sertraline: a naturalistic study. *Ther Drug Monit*. 2013 Feb;35(1):84-91.  
[PubMed: PM23318280](#)

11. Calarge CA, Miller DD. Predictors of risperidone and 9-hydroxyrisperidone serum concentration in children and adolescents. *J Child Adolesc Psychopharmacol*. 2011 Apr;21(2):163-169.  
[PubMed: PM21486167](#)
12. Unterecker S, Deckert J, Pfuhlmann B. No influence of body weight on serum levels of antidepressants. *Ther Drug Monit*. 2011 Dec;33(6):730-734.  
[PubMed: PM22105590](#)

### *Alternative Intervention – Before and After Bariatric Surgery*

13. Monte SV, Russo KM, Mustafa E, Caruana JA. Impact of Sleeve Gastrectomy on Psychiatric Medication Use and Symptoms. *J Obes*. 2018;2018:8532602.  
[PubMed: PM30410796](#)
14. Krieger CA, Cunningham JL, Reid JM, et al. Comparison of Bioavailability of Single-Dose Extended-Release Venlafaxine Capsules in Obese Patients Before and After Gastric Bypass Surgery. *Pharmacotherapy*. 2017 Nov;37(11):1374-1382.  
[PubMed: PM28845898](#)
15. Marzinke MA, Petrides AK, Steele K, et al. Decreased Escitalopram Concentrations Post-Roux-en-Y Gastric Bypass Surgery. *Ther Drug Monit*. 2015 Jun;37(3):408-412.  
[PubMed: PM25970510](#)

### *Unspecified Intervention – Safety Issues of Weight-Based Dosing*

16. Hirata KM, Kang AH, Ramirez GV, Kimata C, Yamamoto LG. Pediatric Weight Errors and Resultant Medication Dosing Errors in the Emergency Department. *Pediatr Emerg Care*. 2019 Sep;35(9):637-642.  
[PubMed: PM28976456](#)

## Guidelines and Recommendations

### *Unclear Methodology*

17. Canadian Paediatric Society. Medication safety for children with medical complexity. 2020. <https://www.cps.ca/en/documents/position/medication-safety-for-children-with-medical-complexity>  
*See: Factors that contribute to risk of medication errors in CMC*
18. Medicine.com. FLUoxetine. 2020. <https://www.medicines.com/drug/fluoxetine/hcp>  
*See: Dosing: Pediatric – Depression*
19. WellRx. Fluoxetine DR. 2020. <https://www.wellrx.com/fluoxetine%20dr/pediatric-monographs/>  
*See: For the treatment of major depression; Special Populations – Pediatrics – Children and Adolescents*
20. Elsevier. Major Depressive Disorder. 2019. [https://www.elsevier.com/\\_data/assets/pdf\\_file/0018/1010277/Major-depressive-disorder\\_CO\\_300419.pdf](https://www.elsevier.com/_data/assets/pdf_file/0018/1010277/Major-depressive-disorder_CO_300419.pdf)  
*See: Treatment Options – Fluoxetine (p. 6); Amitriptyline (p. 7)*

21. New Hampshire Department of Health and Human Services. FDA approvals for psychotropic medications used in children with mental health disorders. [2017]. <https://www.dhhs.nh.gov/dcyf/adoption/documents/fda-apprv-psych-meds.pdf>  
See: *Prozac/Sarafem, fluoxetine (p.1)*

## Review Articles

### *Alternative Intervention – Ketamine for Depression*

22. Andrade C. Oral Ketamine for Depression, 2: Practical Considerations. *J Clin Psychiatry*. 2019 04 09;80(2):09.  
[PubMed: PM30997961](#)

### *Alternative Intervention – Antidepressants Not Specified*

23. Pan SD, Zhu LL, Chen M, Xia P, Zhou Q. Weight-based dosing in medication use: what should we know? *Patient Prefer Adherence*. 2016 Apr 12;10:549-60.  
[PubMed: PM27110105](#)
24. Kendrick JG, Carr RR, Ensom MH. Pediatric Obesity: Pharmacokinetics and Implications for Drug Dosing. *Clin Ther*. 2015 Sep 1;37(9):1897-923.  
[PubMed: PM26361823](#)
25. Pai MP. Drug dosing based on weight and body surface area: mathematical assumptions and limitations in obese adults. *Pharmacotherapy*. 2012 Sep;32(9):856-68.  
[PubMed: PM22711238](#)
26. Cella M, Knibbe C, Danhof M, Della Pasqua O. What is the right dose for children? *Br J Clin Pharmacol*. 2010 Oct;70(4):597-603.  
[PubMed: PM21087295](#)  
See: *Scaling for function, not for size*
27. Mulla H, Johnson TN. Dosing dilemmas in obese children. *Arch Dis Child Educ Pract Ed*. 2010 Aug;95(4):112-7.  
[PubMed: PM20585055](#)

### *Bariatric Surgery and Pharmacokinetics of Antidepressants*

28. Bland CM, Quidley AM, Love BL, Yeager C, McMichael B, Bookstaver PB. Long-term pharmacotherapy considerations in the bariatric surgery patient. *Am J Health Syst Pharm*. 2016 Aug 15;73(16):1230-1242.  
[PubMed: PM27354038](#)
29. Stein J, Stier C, Raab H, Weiner R. Review article: The nutritional and pharmacological consequences of obesity surgery. *Aliment Pharmacol Ther*. 2014 Sep;40(6):582-609.  
[PubMed: PM25078533](#)
30. Yska JP, van der Linde S, Tapper VV, et al. Influence of bariatric surgery on the use and pharmacokinetics of some major drug classes. *Obes Surg*. 2013 Jun;23(6):819-825.  
[PubMed: PM23430479](#)

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