

# 64 - References

## References

394 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 with a heightened risk of stroke recurrence for this reason. Stroke can be embolic or haemorrhagic – SSRIs may protect against the former<sup>46,47</sup> and provoke the latter,<sup>48,49</sup> although the evidence base for this is rather weak<sup>50</sup> (see section on SSRIs and bleeding in this chapter). Other adverse effects may also be problematic; specifically falls, bone fractures and seizures.<sup>19,24</sup> Agomelatine is better tolerated than SSRIs or SNRIs in the post-stroke population and seems not to affect clotting parameters.<sup>33</sup> Antidepressants are clearly effective in post-stroke depression<sup>51</sup> and treatment should not usually be withheld.<sup>52</sup> Inadequate treatment of depression increases the risk of stroke.<sup>11,53</sup> Two network meta-analyses suggested that paroxetine might be the drug of choice when considering both efficacy and tolerability post-stroke, although small sample sizes and a lack of high-quality studies in this area limit the strength of this recommendation.<sup>54,55</sup> Each analysis included only one paroxetine trial, whereas a meta-analysis of four trials of paroxetine found no benefit.<sup>56</sup> A 2020 large network meta-analysis of 51 trials ranked mirtazapine first for response rate, followed by venlafaxine and escitalopram, although the studies were limited to Chinese participants and so may lack generalisability.<sup>57</sup> Box 3.3 shows recommended drugs for use in post-stroke depression. Where SSRIs are given in any patient treated with anticoagulants or aspirin, consideration should be given to the prescription of a proton-pump inhibitor for gastric protection. Nortriptyline, which does not appear to increase risk of bleeding, is an alternative. References

1. Murphy RP, et al. Depressive symptoms and risk of acute stroke: INTERSTROKE case-control study. *Neurology* 2023; 100:e1787–e1798.
2. Ashraf F, et al. Association between depression and stroke risk in adults: a systematic review and meta-analysis. *Front Neurol* 2024; 15:1331300.
3. Gainotti G, et al. Relation between depression after stroke, antidepressant therapy, and functional recovery. *J Neurol Neurosurg Psychiatry* 2001; 71:258–261.
4. Hayee MA, et al. Depression after stroke-analysis of 297 stroke patients. *Bangladesh Med Res Counc Bull* 2001; 27:96–102.
5. Paolucci S, et al. Post-stroke depression, antidepressant treatment and rehabilitation results: a case-control study. *Cerebrovasc Dis* 2001; 12:264–271.
6. Xu XM, et al. Efficacy and feasibility of antidepressant treatment in patients with post-stroke depression. *Medicine (Baltimore)* 2016; 95:e5349.
7. Gainotti G, et al. Determinants and consequences of post-stroke depression. *Curr Opin Neurol* 2002; 15:85–89.
8. Jorge RE, et al. Escitalopram and enhancement of cognitive recovery following stroke. *Arch Gen Psychiatry* 2010; 67:187–196.

9. Gu SC, et al. Early selective serotonin reuptake inhibitors for recovery after stroke: a meta-analysis and trial sequential analysis. *J Stroke Cerebrovasc Dis* 2018; 27:1178–1189. Box 3.3 Post-stroke depression – recommended drugs ■ ■SSRIs\* ■ ■Mirtazapine ■ ■Nortriptyline\* \*Caution is clearly required if the index stroke was known to be haemorrhagic because SSRIs increase the risk of de novo haemorrhagic stroke (although absolute risk is low), especially when combined with warfarin or other anti-platelet drugs.<sup>41,42</sup> If the patient is taking warfarin, suggest citalopram or escitalopram (probably lowest interaction potential<sup>43</sup>) and use the lowest effective dose.<sup>40</sup> Little is known of the pharmacokinetic interaction potential with direct-acting oral anticoagulants (DOACs). Citalopram or escitalopram may again be preferred, as neither drug affects the enzymes associated with DOAC metabolism.<sup>44</sup> The pharmacodynamic interaction always remains – SSRIs increase the risk of major bleeding when combined with anticoagulants.<sup>45</sup>

Depression and anxiety disorders CHAPTER 3 10. Thilarajah S, et al. Factors associated with post-stroke physical activity: a systematic review and meta-analysis. *Arch Phys Med Rehabil* 2018; 27:1178–1189. 11. Krivoy A, et al. Low adherence to antidepressants is associated with increased mortality following stroke: a large nationally representative cohort study. *Eur Neuropsychopharmacol* 2017; 27:970–976. 12. El Husseini N, et al. Depression and antidepressant use after stroke and transient ischemic attack. *Stroke* 2012; 43:1609–1616. 13. Farooq S, et al. Pharmacological interventions for prevention of depression in high risk conditions: systematic review and meta-analysis. *J Affect Disord* 2020; 269:58–69. 14. Woranush W, et al. Preventive approaches for post-stroke depression: where do we stand? A systematic review. *Neuropsychiatr Dis Treat* 2021; 17:3359–3377. 15. Coupland C, et al. Antidepressant use and risk of adverse outcomes in older people: population based cohort study. *BMJ* 2011; 343:d4551. 16. Palomaki H, et al. Prevention of poststroke depression: 1 year randomised placebo controlled double blind trial of mianserin with 6 month follow up after therapy. *J Neurol Neurosurg Psychiatry* 1999; 66:490–494. 17. Lampl C, et al. Amitriptyline in the prophylaxis of central poststroke pain. Preliminary results of 39 patients in a placebo-controlled, long-term study. *Stroke* 2002; 33:3030–3032. 18. Masuccio FG, et al. Post-stroke depression in older adults: an overview. *Drugs Aging* 2024; 41:303–318. 19. Legg LA, et al. Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery. *Cochrane Database Syst Rev* 2021; 11:CD009286. 20. Tay J, et al. Does fluoxetine reduce apathetic and depressive symptoms after stroke? An analysis of the efficacy of fluoxetine – a randomized controlled trial in stroke trial data set. *Int J Stroke* 2023; 18:285–295. 21. AFFINITY Trial Collaboration. Safety and efficacy of fluoxetine on functional outcome after acute stroke (AFFINITY): a randomised, double-blind, placebo-controlled trial. *Lancet Neurol* 2020; 19:651–660. 22. Almeida OP, et al. Depression outcomes among patients treated with fluoxetine for stroke recovery: the AFFINITY randomized clinical trial. *JAMA Neurol* 2021; 78:1072–1079. 23. Cole MG, et al. Feasibility and effectiveness of treatments for post-stroke depression in elderly inpatients: systematic review. *J Geriatr Psychiatry Neurol* 2001; 14:37–41. 24. Mead G, et al. Individual patient data meta-analysis of the effects of fluoxetine on functional outcomes after acute stroke. *Int J Stroke* 2024; 19:798–808. 25. Wu J, et al. The efficacy and safety of fluoxetine versus placebo for stroke recovery: a meta-analysis of randomized controlled trials. *Int J Clin Pharm* 2023; 45:839–846. 26. Cui M, et al. Efficacy and safety of citalopram for the treatment of poststroke depression: a meta-analysis. *J Stroke Cerebrovasc Dis* 2018; 27:2905–2918. 27. Yan N, et al. The safety and efficacy of escitalopram and sertraline in post-stroke depression: a randomized controlled trial. *BMC Psychiatry* 2024; 24:365. 28. Ece Çetin F, et al. Efficacy of citalopram on stroke recurrence: a

randomized clinical trial. *J Clin Neurosci* 2022; 101:168–174. 29. Robinson RG, et al. Nortriptyline versus fluoxetine in the treatment of depression and in short-term recovery after stroke: a placebo-controlled, double-blind study. *Am J Psychiatry* 2000; 157:351–359. 30. Zhang Wh, et al. Nortriptyline protects mitochondria and reduces cerebral ischemia/hypoxia injury. *Stroke* 2008; 39:455–462. 31. Starkstein SE, et al. Antidepressant therapy in post-stroke depression. *Expert Opin Pharmacother* 2008; 9:1291–1298. 32. Niedermaier N, et al. Prevention and treatment of poststroke depression with mirtazapine in patients with acute stroke. *J Clin Psychiatry* 2004; 65:1619–1623. 33. Chen Y, et al. Efficacy and safety of agomelatine versus SSRIs/SNRIs for post-stroke depression: a systematic review and meta-analysis of randomized controlled trials. *Int Clin Psychopharmacol* 2024; 39:163–173. 34. Rampello L, et al. An evaluation of efficacy and safety of reboxetine in elderly patients affected by ‘retarded’ post-stroke depression: a random, placebo-controlled study. *Arch Gerontol Geriatr* 2005; 40:275–285. 35. Eyding D, et al. Reboxetine for acute treatment of major depression: systematic review and meta-analysis of published and unpublished placebo and selective serotonin reuptake inhibitor controlled trials. *BMJ* 2010; 341:c4737. 36. Gamberini G, et al. Safety and efficacy of vortioxetine on depressive symptoms and cognition in post-stroke patients: a pilot study. *J Affect Disord* 2021; 286:108–109. 37. Broman J, et al. Association of post-stroke-initiated antidepressants with long-term outcomes in young adults with ischaemic stroke. *Ann Med* 2022; 54:1757–1766. 38. Douglas I, et al. The use of antidepressants and the risk of haemorrhagic stroke: a nested case control study. *Br J Clin Pharmacol* 2011; 71:116–120. 39. Trajkova S, et al. Use of antidepressants and risk of incident stroke: a systematic review and meta-analysis. *Neuroepidemiology* 2019; 53:142–151. 40. Kim JH, et al. Major adverse cardiovascular events in antidepressant users within patients with ischemic heart diseases: a nationwide cohort study. *J Clin Psychopharmacol* 2020; 40:475–481. 41. Jeong HE, et al. Risk of major adverse cardiovascular events associated with concomitant use of antidepressants and non-steroidal anti-inflammatory drugs: a retrospective cohort study. *CNS Drugs* 2020; 34:1063–1074. 42. Quinn GR, et al. Effect of selective serotonin reuptake inhibitors on bleeding risk in patients with atrial fibrillation taking warfarin. *Am J Cardiol* 2014; 114:583–586. 43. Sayal KS, et al. Psychotropic interactions with warfarin. *Acta Psychiatr Scand* 2000; 102:250–255. 44. Fitzgerald JL, et al. Drug interactions of direct-acting oral anticoagulants. *Drug Saf* 2016; 39:841–845. 45. Bakker S, et al. Selective serotonin reuptake inhibitor use and risk of major bleeding during treatment with vitamin K antagonists: results of a cohort study. *Thromb Haemost* 2023; 123:245–254.

396 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 46. He Y, et al. Effect of fluoxetine on three-year recurrence in acute ischemic stroke: a randomized controlled clinical study. *Clin Neurol Neurosurg* 2018; 168:1–6. 47. Douros A, et al. Degree of serotonin reuptake inhibition of antidepressants and ischemic risk: a cohort study. *Neurology* 2019; 93:e1010–e1020. 48. Trifiro G, et al. Risk of ischemic stroke associated with antidepressant drug use in elderly persons. *J Clin Psychopharmacol* 2010; 30:252–258. 49. Wu CS, et al. Association of cerebrovascular events with antidepressant use: a case-crossover study. *Am J Psychiatry* 2011; 168:511–521. 50. Mortensen JK, et al. Safety of selective serotonin reuptake inhibitor treatment in recovering stroke patients. *Expert Opin Drug Saf* 2015; 14:911–919. 51. Mead GE, et al. Selective serotonin reuptake inhibitors for stroke recovery. *JAMA* 2013; 310:1066–1067. 52. Allida SM, et al. Pharmacological, non-invasive brain stimulation and psychological interventions, and their combination, for treating depression after stroke. *Cochrane Database Syst Rev* 2023; 7:CD003437. 53. Bangalore S, et al. Cardiovascular hazards of insufficient treatment of depression among patients with known cardiovascular disease: a propensity score adjusted analysis. *Eur Heart J Qual Care Clin Outcomes* 2018; 4:258–266. 54. Sun Y, et al. Comparative efficacy and acceptability of

antidepressant treatment in poststroke depression: a multiple-treatments meta-analysis. *BMJ Open* 2017; 7:e016499. 55. Deng L, et al. Interventions for management of post-stroke depression: a Bayesian network meta-analysis of 23 randomized controlled trials. *Sci Rep* 2017; 7:16466. 56. Li L, et al. Effectiveness of paroxetine for poststroke depression: a meta-analysis. *J Stroke Cerebrovasc Dis* 2020; 29:104664. 57. Li X, et al. Comparative efficacy of nine antidepressants in treating Chinese patients with post-stroke depression: a network meta-analysis. *J Affect Disord* 2020; 266:540–548.

---

Revision #1

Created 2026-01-04 20:15:36 UTC by Omar Ayman

Updated 2026-01-04 20:15:36 UTC by Omar Ayman