Effects of Fluoxetine on Outcomes at 12 Months After Acute Stroke
Results From EFFECTS, a Randomized Controlled Trial

Erik Lundström, MD, PhD; Eva Isaksson, RN, PhD; Nina Greilert Norin, RN; Per Näslund, MD, PhD; Per Wester, MD, PhD; Björn Mårtensson, MD, PhD; Bo Norrving, MD, PhD; Håkan Wallén, MD, PhD; Jörgen Borg, MD, PhD; Graeme J. Hankey, MD; Maree L. Hackett, PhD; Gillian E. Mead, MD; Martin S. Dennis, MD; Katharina S. Sunnerhagen, MD, PhD; on the behalf of the EFFECTS Writing Committee

BACKGROUND AND PURPOSE: The EFFECTS (Efficacy of Fluoxetine—a Randomised Controlled Trial in Stroke) recently reported that 20 mg fluoxetine once daily for 6 months after acute stroke did not improve functional outcome but reduced depression and increased fractures and hyponatremia at 6 months. The purpose of this predefined secondary analysis was to identify if any effects of fluoxetine were maintained or delayed over 12 months.

METHODS: EFFECTS was an investigator-led, randomized, placebo-controlled, double-blind, parallel group trial in Sweden that enrolled adult patients with stroke. Patients were randomized to 20 mg oral fluoxetine or matching placebo for 6 months and followed for another 6 months. The primary outcome was functional outcome (modified Rankin Scale), at 6 months. Predefined secondary outcomes for these analyses included the modified Rankin Scale, health status, quality of life, fatigue, mood, and depression at 12 months.

RESULTS: One thousand five hundred patients were recruited from 35 centers in Sweden between 2014 and 2019; 750 were allocated fluoxetine and 750 placebo. At 12 months, modified Rankin Scale data were available in 715 (95%) patients allocated fluoxetine and 712 (95%) placebo. The distribution of modified Rankin Scale categories was similar in the 2 groups (adjusted common odds ratio, 0.92 [95% CI, 0.76–1.10]). Patients allocated fluoxetine scored worse on memory with a median value of 89 (interquartile range, 75–100) versus 93 (interquartile range, 82–100); P=0.0021 and communication 93 (interquartile range, 82–100) versus 96 (interquartile range, 86–100); P=0.024 domains of the Stroke Impact Scale compared with placebo. There were no other differences in secondary outcomes.

CONCLUSIONS: Fluoxetine after acute stroke had no effect on functional outcome at 12 months. Patients allocated fluoxetine scored worse on memory and communication on the Stroke Impact Scale compared with placebo, but this is likely to be due to chance.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02683213.

GRAPHIC ABSTRACT: An online graphic abstract is available for this article.

Key Words: antidepressive agents • disability studies • fluoxetine • functional status • randomized controlled trial • serotonin uptake inhibitors • stroke

In 2011, the FLAME trial (Fluoxetine for Motor Recovery After Acute Ischemic Stroke) reported that fluoxetine enhanced motor recovery after acute ischemic stroke.1 A Cochrane systematic review of 4059 patients included in 52 randomized controlled trials of SSRIs (selective serotonin reuptake inhibitors) for stroke recovery concluded that SSRIs could reduce disability but in the light of the methodological limitations and...
heterogeneity of the trials, more data were needed. In 2020, the EFFECTS (Efficacy of Fluoxetine—a Randomised Controlled Trial in Stroke) authors reported that 20 mg of fluoxetine once daily for 6 months after acute stroke did not improve functional outcome at 6 months compared with placebo, although the occurrence of depression was reduced and fractures and hyponatremia increased. EFFECTS included 1500 stroke patients from Sweden, and the results were similar to those of 2 other large randomized controlled trials with comparable design. As specified in the protocol and statistical analysis plan, we followed-up participants to 12 months, to examine whether any effects of fluoxetine identified at 6 months were sustained or delayed.

METHODS

The anonymized data that support the findings of this trial are available to other researchers from the corresponding author (Dr Lundström) upon reasonable request following receipt of a written application and proposal for use of the data. Approval by the EFFECTS trial Steering Committee, and establishment of a data sharing agreement by a central medical ethics committee in Stockholm (reference 2013/1265-31/2) and by the Swedish Medical Agency (reference 5.1-2014-43006); all patients provided written informed consent. EFFECTS was registered in the EU Clinical Trials Register and ClinicalTrials.gov. We have followed the CONSORT statement (Consolidated Standards of Reporting Trials). Eligible patients were adults (aged ≥18 years) with a clinical diagnosis of acute stroke within the previous 2 to 15 days, brain imaging consistent with ischemic or hemorrhagic stroke, and a persisting neurological deficit at the time of randomization. Patients were excluded if they were depressed or taking antidepressants; had a contraindication to fluoxetine; were unlikely to be available for follow-up during the subsequent 12 months; had another life-threatening illness that would make 12-month survival unlikely; were enrolled in another clinical trial of an investigational medicinal product or device; and women were excluded if pregnant, breast-feeding, or of child-bearing age and not using contraception. Baseline characteristics and outcome at 6 months are available in Tables I through III in the Data Supplement.

Randomization was via a secure, centralized, web-based system which used a minimization algorithm and assigned patients to fluoxetine or placebo in a 1:1 ratio. Placebo capsules were visually identical to the fluoxetine capsules even when broken open. Fluoxetine 20 mg capsules or matching placebo capsules were administered orally once daily for 6 months.

Patients were followed-up at 6 and 12 months by postal questionnaire or telephone by one research nurse (N. Greilert Norin) in the trial coordinating center at Danderyd Hospital. If the patient was unable to complete the questionnaire, assistance was sought from their next of kin or carer. In this article, we report the following predefined secondary outcomes at 12 months:

1. Functional status, measured with the modified Rankin Scale (mRS). We used the simple mRS questionnaire to derive the mRS score.

2. Health status using the Stroke Impact Scale version 3.0. The Stroke Impact Scale is a 59-item self-reported questionnaire that includes 8 domains: arm, hand, leg, and foot strength; hand function; mobility; communication and understanding; memory and thinking; mood and emotions; daily activities; and participation in work, leisure, and social activities. Four of the subscales (strength, hand function, daily activities, and mobility) can be combined into a composite physical domain. Scores for each domain range from 0 to 100, and higher scores indicate better health. The Stroke Impact Scale also contains a question to assess the patient’s global experience of recovery. The patient is asked to score their recovery on a visual analogue scale ranging from 0 to 100, with 0 meaning no recovery and 100 meaning full recovery.

3. Depression, defined as taking an antidepressant medication (Anatomic Therapeutic Chemical code beginning with NO6A) at 12 months.

4. Mood, using the Mental Health Inventory 5 scale. The Mental Health Inventory 5 is a subscale of the 36-Item Short Form Health Survey containing 5 questions, each with 6 possible answers, with a score of 1 to 6; possible sum of scores ranges from 5 to 30. The total score is transformed into a value between 0 and 100, where 100 represents optimal mental health. A value below 60 has been suggested as moderate-to-poor mental health.

5. Fatigue, using the vitality subscale of the 36-Item Short Form Health Survey. Four questions, each with 5 answers scored from 1 to 5 (sum ranges from 4–20). The sum score is transformed to a value between 0 and 100. Scores below 50 indicate fatigue.

6. Health-related quality of life, measured with the EQ-5D-5L. EQ-5D-5 L includes 5 dimensions: mobility; personal care; usual activities; pain/discomfort; and...
Statistical Analysis

We calculated an EQ-5D index—where 1 indicates the best health imaginable, and 0 indicates the worst health imaginable—using the UK cross-walk value set, since it is the most commonly used.21 The participant, care provider, investigator, and outcomes assessor remained masked to the allocated trial treatment until the 12 month assessment. Except death, we did not collect any adverse event or safety outcome data between 6 and 12 months. Long-term follow-up is planned to at least 3 years using central registries.

RESULTS

EFFECTS recruitment started 20 October, 2014 and ended 28 June, 2019; 750 were assigned to fluoxetine and 750 to placebo. Last 12 months follow-up was 8 July, 2020. Baseline characteristics were well balanced, 87.4% had ischemic stroke, 12.3% had intracerebral hemorrhage, 0.2% had nonstroke. The mean age was 71 years (SD, 11), 38.3% were women, 96.3% were previously independent, and the median National Institutes of Health Stroke Scale score was 3.3 For both groups, the median duration of treatment was 180 days (IQR,
Most patients (1338/1500, 89%) took the trial medication for at least 150 days.\textsuperscript{5}

At 12 months, mRS data were available for 715 (95%) patients in the fluoxetine group and 712 (95%) patients in the placebo group (Figure 1). No patients withdrew consent for follow-up between 6 and 12 months; 4.1% (62/1500) were lost to follow-up at 12 months, and 4.5% (68/1500) died within 12 months (Table IV in the Data Supplement).

Table 1 shows the mRS\textsuperscript{10} scores 12 months after randomization, that is, 6 months after cessation of trial medication. There was no difference in the distribution across mRS categories in the fluoxetine and placebo groups (adjusted common odds ratio, 0.92 [95% CI, 0.76–1.10]). The unadjusted analysis produced similar results (common odds ratio, 0.96 [95% CI, 0.80–1.15]; Table 1).

Table 2 shows the secondary outcomes in the fluoxetine and placebo groups. Patients randomized to fluoxetine had significantly worse values on the memory (median value of 89 [IQR, 75–100] versus 93 [IQR, 82–100]; \(P=0.0021\)) and communication (93 [IQR, 82–100] versus 96 [IQR, 86–100]; \(P=0.024\)) domains of the Stroke Impact Scale v3 compared with placebo. There were no other differences on the secondary outcomes (Table 2).

Six months after randomization, 5.8% (87/1500) of the patients reported that they were taking an open-label antidepressant; 4.8% (36/750) had been randomized to an antidepressant; 4.8% (36/750) had been randomized to placebo.

At 12 months follow-up, 8.8% of the survivors from 6 months (129/1453) were taking an open-label antidepressant; 9.0% (65/725) randomized to fluoxetine, and 8.8% (64/728) to placebo (diff, 0.2% [95% CI, −3.1 to 3.8]; Tables V and VI in the Data Supplement). Of patients on an antidepressant at 6 months, 60% (51/87) patients continued to take antidepressant at 12 months follow-up; 41% (21/51) randomized to fluoxetine, and 59% (30/51) to placebo.

Table 1. Modified Rankin Scale\textsuperscript{10} Score 6 and 12 Months After Randomization

| modified Rankin Scale | 6 months | 12 months |
|-----------------------|----------|----------|
|                       | Fluoxetine, n=737 | Placebo, n=742 | Fluoxetine, n=715 | Placebo, n=712 |
| 0 No symptoms          | 156 (21) | 170 (23) | 160 (22) | 178 (25) |
| 1 No clinically significant disability despite symptoms | 216 (29) | 199 (27) | 224 (31) | 201 (28) |
| 2 Slightly disability: unable to do everything | 94 (13) | 106 (14) | 75 (11) | 88 (12) |
| 3 Moderately disability: unable to live independently but can walk | 168 (23) | 164 (22) | 158 (22) | 141 (20) |
| 4 Moderately disability and unable to walk without help from another person | 46 (6) | 48 (7) | 35 (5) | 42 (6) |
| 5 Severe disability: unable to sit up | 32 (4) | 33 (4) | 29 (4) | 28 (4) |
| 6 Dead                 | 25 (3) | 22 (3) | 34 (5) | 34 (5) |

DISCUSSION

The results of the EFFECTS trial show that fluoxetine 20 mg daily for 6 months after acute stroke had no effect on functional outcome up to 1 year after stroke. Similar results have been found in the FOCUS (Fluoxetine or Control Under Supervision trial)\textsuperscript{6} (n=3124, United Kingdom), and AFFINITY (Assessment of Fluoxetine in Stroke Recovery)\textsuperscript{4} (n=1260, Australia, New Zealand and Vietnam) trials.

Although fluoxetine reduced depression by \(\approx\)4% (from 11% to 7%) at 6 months in EFFECTS, the proportion of patients on an antidepressant was similar for the 2 groups at 12 months (9%). Depression is an episodic disorder for most, and not being on antidepressant right at the 12 months assessment does not exclude they did not take one between 6 and 11 months; we cannot rule out that some patients were successfully treated already and drug not needed. Compared with our 6-month follow-up, no clinical evaluation of depression symptoms was performed at 12 months. In a meta-analysis of observational studies, the pooled frequency of depression 6 to 12 months poststroke was 31% and 33%, respectively,\textsuperscript{22} >3× higher than the observed proportion in EFFECTS. One possible explanation might be that EFFECTS included patients with relatively mild stroke. Another explanation might be that patients showing symptoms of depression before study start were not included.

Our finding of better reported memory and communication for patients in the placebo group compared with those allocated to the fluoxetine group is unexpected and not supported by the results in FOCUS and AFFINITY. We view this result as a chance finding due to random error associated with multiple analyses.

Our study has several limitations. First, we did not routinely collect data on safety after 6 months, except death. Reassuringly, there was no difference between the groups in death, and we plan to follow the patients for at least 3 years via central registries in Sweden, to collect data on...
In conclusion, fluoxetine 20 mg once daily for six months after acute stroke had no effect on functional outcome at 12 months. Patients allocated fluoxetine scored worse on memory and communication on the Stroke Impact Scale compared with placebo, but this is likely to be due to chance. More precise estimates of any effects of fluoxetine will be available from our prospective meta-analysis of individual patient data from the FOCUS, AFFINITY, and EFFECTS trials.

**Table 2. Secondary Outcomes at 6 and 12 Months by Allocated Treatment Group**

|                  | Fluoxetine (n=750) at 6 months | Placebo (n=750) at 6 months | Fluoxetine (n=642) at 12 months follow-up | Placebo (n=638) at 12 months follow-up |
|------------------|--------------------------------|-----------------------------|------------------------------------------|---------------------------------------|
|                  | N*   | Median | IQR | N*   | Median | IQR | P value† | N*   | Median | IQR | P value† | N*   | Median | IQR | P value† |
| Stroke Impact Scale version 3.0‡ domains |
| Strength         | 694  | 75     | (50–94) | 689  | 75     | (50–94) | 0.67 | 662  | 75     | (50–94) | 658  | 75     | (50–94) | 0.88 |
| Hand ability     | 690  | 81     | (50–100) | 692  | 88     | (50–100) | 0.99 | 664  | 81     | (56–100) | 661  | 81     | (50–100) | 0.75 |
| Mobility         | 696  | 89     | (72–100) | 698  | 89     | (72–97) | 1.00 | 665  | 89     | (69–100) | 662  | 89     | (72–100) | 0.84 |
| Motor§           | 697  | 80     | (60–93) | 695  | 81     | (58–94) | 0.95 | 665  | 79     | (60–94) | 661  | 80     | (58–94) | 0.88 |
| Daily Activities | 697  | 88     | (69–98) | 697  | 88     | (68–98) | 0.72 | 667  | 90     | (70–98) | 662  | 90     | (68–98) | 0.97 |
| Physical function§ | 697  | 77     | (56–90) | 697  | 77     | (56–91) | 0.81 | 667  | 76     | (57–91) | 662  | 77     | (55–92) | 0.98 |
| Memory           | 696  | 89     | (79–100) | 698  | 93     | (82–100) | 0.0064 | 666  | 89     | (75–100) | 662  | 93     | (82–100) | 0.0021 |
| Communication    | 695  | 96     | (82–100) | 697  | 92     | (86–100) | 0.83 | 664  | 93     | (82–100) | 661  | 96     | (86–100) | 0.024 |
| Mood and emotional control | 695  | 81     | (67–92) | 696  | 76     | (64–89) | 0.0002 | 665  | 78     | (64–89) | 658  | 78     | (64–89) | 0.63 |
| Participation    | 690  | 66     | (46–89) | 682  | 69     | (44–89) | 0.55 | 663  | 69     | (46–91) | 656  | 71     | (47–93) | 0.79 |
| Recovery (VAS)   | 695  | 70     | (50–90) | 695  | 70     | (50–90) | 0.79 | 666  | 75     | (50–90) | 662  | 80     | (50–90) | 0.58 |
| Fatigue*         | 692  | 56     | (44–69) | 692  | 56     | (44–69) | 0.74 | 662  | 56     | (44–75) | 658  | 56     | (44–75) | 0.22 |
| MHI-5 score†     | 697  | 76     | (64–88) | 695  | 72     | (60–88) | 0.0086 | 667  | 76     | (60–88) | 660  | 76     | (60–88) | 0.57 |
| EQ-5D-SL‡        | 687  | 0.73   | (0.55–0.84) | 684  | 0.71   | (0.54–0.84) | 0.83 | 664  | 0.74   | (0.55–0.84) | 658  | 0.74   | (0.55–0.88) | 0.86 |

Data on Stroke Impact Scale at 6 mo have previously been published. Stroke Impact Scale v 3.0 is a patient-reported design to assess stroke outcome, where higher scores are better. Fatigue was measured with the vitality subscale of the SF-36 questionnaire. Higher scores indicate more energy, less fatigue. The EQ-5D-5L has 5 dimensions: mobility; personal care; usual activities; pain/discomfort; and anxiety/depression. We calculated an EQ-5D index using the UK cross-walk value, where 1 indicates the best health imaginable, and 0 indicates the worst health imaginable. EQ-5D-SL indicates The 5-level EQ-5D version; MHI-5, mental health inventory-5; and VAS, visual analogue scale.

The number of patients with each of the secondary outcome scores. Data were only available for those who survived and who completed sufficient questions to derive a score. Mann-Whitney U test, between fluoxetine and placebo at 6 and 12 mo, respectively. Mean of the strength, hand ability, and mobility domains. Mean of the strength, hand ability, mobility, and daily activities domains.

**Affiliations**

Department of Neuroscience, Neurology, Department of Clinical Sciences (J.B.), Uppsala University, Sweden (E.I.). Department of Clinical Neuroscience, Neurology (E.I.). Department of Clinical Sciences, Danderyd Hospital (N.G.N.). Department of Clinical Sciences (F.W.), Department of Clinical Neurosciences (E.M.), Department of Clinical Sciences (F.W.), Department of Public Health & Clinical Neurology, Umeå University, Sweden (F.W.). Department of Clinical Sciences, Neurology, Lund University, Sweden (F.W.). Medical School, Faculty of Health and Medical Sciences, The University of Western Australia, Perth (G.J.H.). Department of Neuroscience, Sir Charles Gairdner Hospital, Perth, Western Australia (G.J.H.). The George Institute for Global Health, Faculty of Medicine, University of New South Wales Sydney (M.L.H.). The University of Central Lancashire, United Kingdom (M.L.H.). University of Edinburgh, Royal Infirmary, Edinburgh, United Kingdom (G.E.M., M.S.D.). Institute of Neuroscience and Physiology, Clinical Neuroscience, The Sahlgrenska Academy, University of Gothenburg, Sweden (K.S.S.).

**Acknowledgments**

We thank all patients in the EFFECTS trial (Efficacy of Fluoxetine—a Randomised Controlled Trial in Stroke), personnel in the EFFECTS Trial Collaboration, Chief Technical Officer, Kristo Kristianson at EDC Scandinavia, and our monitors Terése Brunelli, Maria Persson, and Ingail Reinholdsson, at Karolinska Trial Alliance. Dr. Lundström was the Chief Investigator was involved in the design of the trial, collected, verified, analyzed data, and wrote the first draft of the article. Dr Isaksson was the trial manager, was involved in the design of the trial, and collected, verified, analyzed data. N. Greilert Norin was the trial manager assistant, collected, verified, and analyzed data. Dr. Nåsmann was involved in the design of the trial, did the statistical analysis, and analyzed data. Dr. Martensson advised on the management of depression within the trial and was involved in the design of the trial. Drs. Wester, Norrving, Wallén, Borg, Hankey, Hackett, Mead, Dennis, and Sunnerhagen were involved in the design of the trial and analyzed data. All contributors have commented on the analyses and drafts and seen and approved the final version of the article.

**Article Information**

Received January 30, 2021; final revision received July 9, 2021; accepted July 16, 2021.

The podcast and transcript are available at https://www.ahajournals.org/str/podcast.

Presented in part at the European Stroke Organisation Conference, virtual, September 1–3, 2021.
**Sources of Funding**

EFFECTS (Efficacy of Fluoxetine—a Randomised Controlled Trial in Stroke) has received funding from the Swedish Research Council (registration number 2014-07072); the Swedish Heart–Lung Foundation (application number 2013-0496 and 2016-0245); the Swedish Brain Foundation (application number FO2017-0115); the Swedish Society of Medicine (ID 692921); King Gustav V and Queen Victoria’s Foundation of Freemasons (year 2014); and the Swedish Stroke Association (STROKE-Riksförbundet; year 2012 and 2013). The funders of the trial had no role in trial design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the trial and had final responsibility for the decision to submit for publication. The sponsor was Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, 182 88 Stockholm, Sweden. The sponsor’s representative was Dr Lundström.

**Disclosures**

Dr Hankey reports grants from the National Health & Medical Research Council of Australia, Vetenskapsrådet (The Swedish Research Council), and United Kingdom National Institute for Health Research Technology (NIHR), during the conduct of the trial; and personal fees from American Heart Association, outside the submitted work. Drs Hackett, Mead, and Dennis report grants from the National Health and Medical Research Council of Australia, Vetenskapsrådet (The Swedish Research Council), and United Kingdom National Institute for Health Research Technology (NIHR), during the conduct of the trial. The other authors report no conflicts.

**Supplemental Materials**

Online Tables I–VI

**REFERENCES**

1. Chollet F, Tardy J, Albucher JF, Thalaimas C, Berard E, Lamy C, Bejot Y, Deltour S, Jaillard A, Niclot P, et al. Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial. Lancet Neurol 2011;10:129–136. doi: 10.1016/S1474-4422(10)70314-8
2. Mårtensson B, Norrving B, Lundström E, Isaksson E, Näsman P, Wester P, Mårtensson B, Norrving B, Wallén H, Borg J, Dennis M, Mead G, et al. Safety and efficacy of fluoxetine on functional recovery after acute stroke (EFFECTS): a randomised, double-blind, placebo-controlled trial. Lancet Neurol 2020;19:661–669. doi: 10.1016/S1474-4422(20)30219-2
3. 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. doi: 10.1016/S1474-4422(20)30207-6
4. Dennis M, Mead G, Forbes J, Graham C, Hackett M, Hankey GJ, House A, Lewis S, Lundström E, Sandercob P, et al. Effects of fluoxetine on functional outcomes after acute stroke (FOCUS): a pragmatic, double-blind, randomised, controlled trial. The Lancet 2019;393:265–274. doi: 10.1016/S0140-6736(18)32693-X
5. Mead G, Hackett ML, Lundström E, Murray V, Hankey GJ, Dennis M. The FOCUS, AFFINITY and EFFECTS trials studying the effect(s) of fluoxetine in patients with a recent stroke: a study protocol for three multicentre randomised controlled trials. Trials 2015;16:396. doi: 10.1186/1745-6215-16-396
6. Lundström E, Isaksson E, Näsman P, Wester P, Mårtensson B, Norrving B, Wallén H, Borg J, Dennis M, Mead G, et al. EFFECTS Trial Collaboration. Update on the EFFECTS study of fluoxetine for stroke recovery: a randomised controlled trial in Sweden. Trials 2020;21:233. doi: 10.1186/s13063-020-4124-7
7. Graham C, Lewis S, Forbes J, Mead G, Hackett ML, Hankey GJ, Gommans J, Nguyen HT, Lundström E, Isaksson E, et al. The FOCUS, AFFINITY and EFFECTS trials studying the effect(s) of fluoxetine in patients with a recent stroke: statistical and health economic analysis plan for the trials and for the individual patient data meta-analysis. Trials 2017;18:627. doi: 10.1186/s13063-017-2395-6
8. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c332. doi: 10.1136/bmj.c332
9. Brott T, Adams HP Jr, Olinger CP, Marler JR, Barsan WG, Biller J, Spilker J, Holleran R, Eberle R, Hertzberg V. Measurements of acute cerebral infarction: a clinical examination scale. Stroke 1989;20:686–680. doi: 10.1161/01.str.20.7.864
10. Bruno A, Akinwuntan AE, Lin C, Close B, Davis K, Baute V, Ayal T, Brooks D, Hess DC, Switzer JA, et al. Simplified modified rankin scale questionnaire: reproducibility over the telephone and validation with quality of life. Stroke 2011;42:2276–2279. doi: 10.1161/STROKEAHA.111.63273
11. Dennis M, Mead G, Doulab F, Graham C. Determining the modified Rankin score after stroke by postal and telephone questionnaires. Stroke 2012;43:851–853. doi: 10.1161/STROKEAHA.111.639708
12. Isaksson E, Wester P, Laska AC, Näsman P, Lundström E. Validation of the simplified modified rankin scale questionnaire. Eur Neurol 2020;83:493–499. doi: 10.1159/0005010721
13. Duncan PW, Reker DM, Horner RD, Samsa GP, Hoening E, LaClair BJ, Dudley TR. Performance of a mail-administered version of a stroke-specific outcome measure, the Stroke Impact Scale. Clin Rehabil 2002;16:493–505. doi: 10.1177/026921550202501001
14. Hoeymans N, Garsse AA, Westert GP, Verhaak PF. Measuring mental health of the Dutch population: a comparison of the GHQ-12 and the MHI-5. Health Qual Life Outcomes. 2004;2:23. doi: 10.1186/1477-7525-2-23
15. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473–483.
16. Kelly MJ, Dunstan FD, Lloyd K, Fone DL. Evaluating cutpoints for the MHI-5 and MCS using the GHQ-12: a comparison of five different methods. BMC Psychiatry. 2008;8:10. doi: 10.1186/1471-244X-8-10
17. Mead G, Lynch J, Greig C, Young A, Lewis S, Sharpe M. Evaluation of fatigue scales in stroke patients. Stroke 2007;38:2090–2095. doi: 10.1161/STROKEAHA.106.478941
18. Hackett ML, Duncan JR, Anderson CS, Broad JB, Monia B, Health-related quality of life among long-term survivors of stroke: results from the Auckland Stroke Study, 1991–1992. Stroke 2000;31:440–447. doi: 10.1161/01.STR.31.2.440
19. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, Bonsel G, Badia X. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res 2011;20:1277–1278. doi: 10.1007/s11136-010-9903-x
20. van Hout B, Janssen MF, Feng YS, Kohlmann T, Busschbach J, Golicki D, Lloyd A, Scalone L, Kind P, Pickard AS. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L value sets. Health Qual Life Outcomes 2012;10:708–715. doi: 10.1186/1477-7525-10-71
21. Hackett ML, Pickles K, Part I: frequency of depression after stroke: an updated systematic review and meta-analysis of observational studies. Int J Stroke 2014;9:1017–1025. doi: 10.1111/ijis.12357
22. Mead G, Graham C, Billot L, Näsman P, Lundström E, Lewis S, Hankey GJ, Hackett ML, Forbes J, Dennis M; FOCUS, AFFINITY and EFFECTS trialists. Update to the FOCUS, AFFINITY and EFFECTS trials studying the effect(s) of fluoxetine in patients with a recent stroke: statistical analysis plan for the trials and for the individual patient data meta-analysis. Trials 2020;21:971. doi: 10.1186/s13063-020-04875-1