**Supplementary Information**

**Interaction effect of serum serotonin level and age on the 12-week pharmacotherapeutic response in patients with depressive disorders**

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| **Supplementary Table 1.**  Baseline characteristics based on age in patients with depressive disorders | | | | | | | |
|  | |  | | **Up to 12-week treatment (N = 1086)** | | | | |
|  |  | | <60 years (N = 567) | | ≥60 years (N = 519) | Statistical coefficientsa | P-value |
| Gender, N (%) female |  | | 385 (67.9) | | 360 (69.4) | χ2 = 0.269 | P = 0.604 |
| Education, mean (SD) years |  | | 11.5 (3.7) | | 6.5 (4.5) | t = 19.548 | P < 0.001 |
| Marital status, N (%) unmarried |  | | 179 (31.6) | | 147 (28.3) | χ2 = 1.359 | P = 0.244 |
| Living alone, N (%) |  | | 61 (10.8) | | 106 (20.4) | χ2 = 19.454 | P < 0.001 |
| Religious observance, N (%) |  | | 287 (50.6) | | 320 (61.7) | χ2 = 13.396 | P < 0.001 |
| Unemployed status, N (%) |  | | 156 (30.2) | | 160 (28.1) | χ2 = 0.614 | P = 0.433 |
| Monthly income, N (%) <2,000 USD |  | | 233 (41.1) | | 415 (80.0) | χ2 = 170.104 | P < 0.001 |
| Body mass index, mean (SD) kg/m2 |  | | 23.1 (3.4) | | 23.4 (3.0) | t = -1.643 | P = 0.101 |
| Major depressive disorder, N (%) |  | | 481 (84.8) | | 444 (85.5) | χ2 = 0.110 | P = 0.740 |
| Melancholic feature, N (%) |  | | 71 (12.5) | | 91 (17.5) | χ2 = 5.362 | P = 0.021 |
| Atypical feature, N (%) |  | | 56 (9.9) | | 13 (2.5) | χ2 = 24.748 | P < 0.001 |
| Age at onset, mean (SD) years |  | | 41.6 (13.0) | | 63.1 (12.5) | t = -27.804 | P < 0.001 |
| Duration of illness, mean (SD) years |  | | 4.3 (7.1) | | 5.9 (10.7) | t = -2.815 | P = 0.005 |
| Recurrent depression, N (%) |  | | 318 (56.1) | | 252 (48.6) | χ2 = 6.161 | P = 0.013 |
| Number of depressive episodes, mean (SD) |  | | 1.2 (1.6) | | 0.9 (1.3) | t = 3.053 | P = 0.002 |
| Duration of present episode, mean (SD) months |  | | 7.4 (10.2) | | 7.4 (10.6) | t = -0.133 | P = 0.894 |
| Family history of depression, N (%) |  | | 100 (17.6) | | 58 (11.2) | χ2 = 9.100 | P = 0.003 |
| History of suicide attempt, N (%) |  | | 76 (13.4) | | 19 (3.7) | χ2 = 32.233 | P < 0.001 |
| Number of physical disorders, mean (SD) |  | | 1.2 (1.2) | | 2.1 (1.3) | t = -11.302 | P < 0.001 |
| Hamilton Depression Rating Scale |  | | 20.8 (4.2) | | 20.7 (4.1) | t = 0.201 | P = 0.841 |
| Hospital Anxiety & Depression Scale-anxiety subscale |  | | 12.4 (4.2) | | 11.2 (3.8) | t = 4.767 | P < 0.001 |
| EuroQol-5D |  | | 8.9 (1.5) | | 9.0 (1.6) | t = -1.431 | P = 0.153 |
| Social and Occupational Functional Assessment Scale |  | | 55.5 (7.3) | | 56.4 (7.6) | t = -1.892 | P = 0.059 |

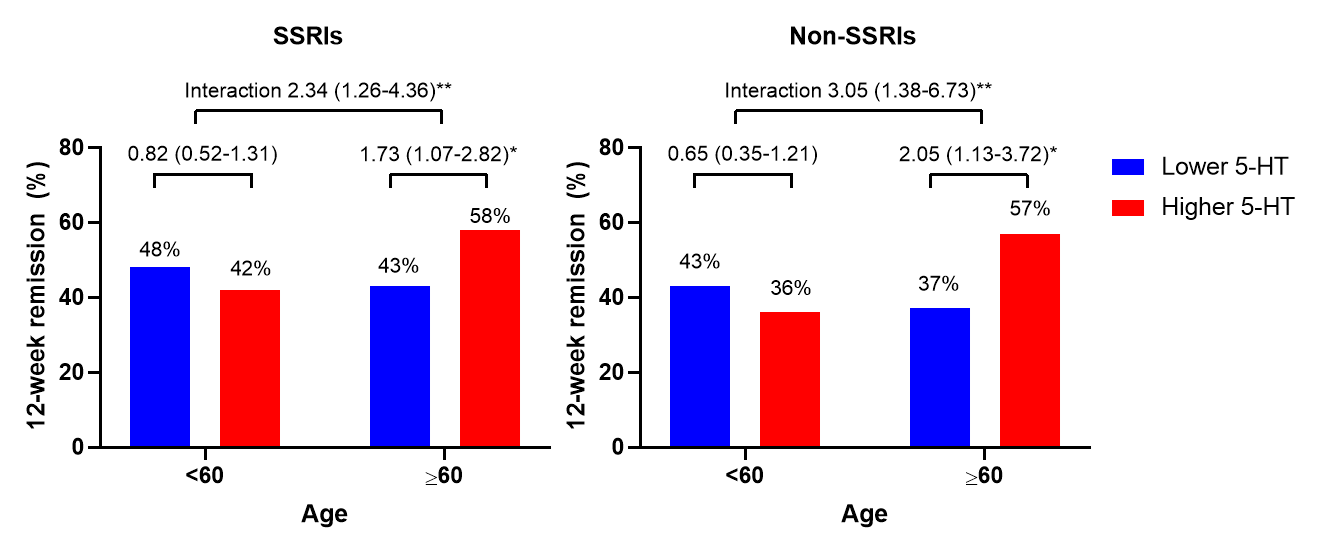
aIndependent two sample *t*-test or χ2 test, as appropriate.

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| **Supplementary Table 2.**  Baseline characteristics based on initial antidepressant type in patients with depressive disorders | | | | | | | |
|  | |  | | **Up to 12-week treatment (N = 1086)** | | | | |
|  |  | | SSRIs (N = 672) | | Non-SSRIs (N = 414) | Statistical coefficientsa | P-value |
| Age, mean (SD) years |  | | 56.1 (15.4) | | 58.3 (14.0) | t = -2.386 | P = 0.017 |
| Gender, N (%) female |  | | 450 (67.0) | | 295 (71.3) | χ2 = 2.191 | P = 0.139 |
| Education, mean (SD) years |  | | 9.2 (4.8) | | 8.9 (4.8) | t = 1.232 | P = 0.218 |
| Marital status, N (%) unmarried |  | | 210 (31.3) | | 116 (28.0) | χ2 = 1.273 | P = 0.259 |
| Living alone, N (%) |  | | 100 (14.9) | | 67 (16.2) | χ2 = 0.334 | P = 0.563 |
| Religious observance, N (%) |  | | 370 (55.1) | | 237 (57.2) | χ2 = 0.497 | P = 0.481 |
| Unemployed status, N (%) |  | | 187 (27.8) | | 129 (31.2) | χ2 = 1.379 | P = 0.240 |
| Monthly income, N (%) <2,000 USD |  | | 392 (58.3) | | 256 (61.8) | χ2 = 1.306 | P = 0.253 |
| Body mass index, mean (SD) kg/m2 |  | | 23.2 (3.1) | | 23.3 (3.4) | t = -0.427 | P = 0.669 |
| Major depressive disorder, N (%) |  | | 564 (83.9) | | 361 (87.2) | χ2 = 2.169 | P = 0.141 |
| Melancholic feature, N (%) |  | | 96 (14.3) | | 66 (15.9) | χ2 = 0.554 | P = 0.457 |
| Atypical feature, N (%) |  | | 44 (6.5) | | 25 (6.0) | χ2 = 0.112 | P = 0.738 |
| Age at onset, mean (SD) years |  | | 1.5 (0.5) | | 1.5 (0.5) | t = 0.036 | P = 0.971 |
| Duration of illness, mean (SD) years |  | | 4.8 (8.9) | | 5.6 (9.2) | t = -1.435 | P = 0.152 |
| Recurrent depression, N (%) |  | | 345 (51.3) | | 225 (54.3) | χ2 = 0.930 | P = 0.335 |
| Number of depressive episodes, mean (SD) |  | | 1.0 (1.4) | | 1.2 (1.6) | t = -1.600 | P = 0.110 |
| Duration of present episode, mean (SD) months |  | | 7.0 (9.8) | | 8.0 (11.4) | t = -1.433 | P = 0.152 |
| Family history of depression, N (%) |  | | 98 (14.6) | | 60 (14.5) | χ2 = 0.002 | P = 0.967 |
| History of suicide attempt, N (%) |  | | 65 (9.7) | | 30 (7.2) | χ2 = 1.889 | P = 0.169 |
| Number of physical disorders, mean (SD) |  | | 1.5 (0.5) | | 1.5 (0.5) | t = -0.083 | P = 0.933 |
| Hamilton Depression Rating Scale |  | | 20.4 (4.0) | | 21.3 (4.4) | t = -3.512 | P < 0.001 |
| Hospital Anxiety & Depression Scale-anxiety subscale |  | | 12.0 (4.2) | | 11.6 (3.8) | t = 1.602 | P = 0.110 |
| EuroQol-5D |  | | 8.9 (1.5) | | 9.0 (1.5) | t = -1.994 | P = 0.046 |
| Social and Occupational Functional Assessment Scale |  | | 56.7 (7.1) | | 54.7 (7.8) | t = 4.465 | P < 0.001 |

aIndependent two sample *t*-test or χ2 test, as appropriate.

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| **Supplementary Table 3**  Individual effects of baseline serum 5-HT level and age on 12-week remission based on type of initial antidepressant | | | | | | | |
| Exposure | Group | 12-week remission | | | | | |
|  |  | SSRIs (N = 672) | | | Non-SSRIs (N = 414) | | |
|  |  | No. (%) presence | OR (95% CI) | | No. (%) presence | OR (95% CI) | |
|  |  |  | Unadjusted | Adjusteda |  | Unadjusted | Adjusteda |
| Serum 5-HT | Lower | 149 (45.4) | 1.00 | 1.00 | 85 (39.5) | 1.00 | 1.00 |
|  | Higher | 166 (48.3) | 1.12 (0.83-1.52) | 1.14 (0.83-1.58) | 90 (45.2) | 1.26 (0.85-1.87) | 1.15 (0.76-1.74) |
| Age | <60 | 162 (44.8) | 1.00 | 1.00 | 80 (39.0) | 1.00 | 1.00 |
|  | ≥60 | 153 (49.4) | 1.20 (0.89-1.63) | 1.00 (0.60-1.66) | 95 (45.5) | 1.30 (0.88-1.93) | 0.86 (0.43-1.70) |

aAdjusted for education, living alone, religious observance, monthly income, melancholic feature, atypical feature, age at onset, duration of illness, recurrent depression, number of depressive episodes, family history of depression, history of suicide attempt, number of physical disorders, HADS-A, and SOFAS.



**Supplementary Figure 1.**

The 12-week remission rates according to baseline serum 5-HT level and age based on initial antidepressant type. Data are presented as odds ratios (95% confidence intervals) adjusted for educational level, living alone, religious observance, monthly income, melancholic features, atypical features, age at onset, duration of illness, recurrent depression, number of depressive episodes, family history of depression, history of suicide attempt, number of physical disorders, HADS-A score, and SOFAS score evaluated at baseline. \*P < 0.05; **\*\***P < 0.01.