**Supplementary Table 1:** Baseline information divided by gender on 482 patients with bipolar disorder from the CHOICE study (199 male and 283 female) and 283 patients with bipolar disorder from the LiTMUS study (123 male and 160 female), depending on white blood cell counts (WBC) at study entry.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Bipolar CHOICE | Total | WBC<4.5 | 4.5≤WBC<6 | 6≤WBC<7 | 7≤WBC<8 | 8≤WBC<10 | WBC≥10 |
| Men | 199 (100) | 13 (6.5) | 54 (27.1) | 43 (21.6) | 28 (14.1) | 36 (18.1) | 25 (12.6) |
| Agegroup ≤30 31-45 ≥45 | 52 (26.1)77 (38.7)70 (35.2) | 4 (30.8)3 (23.1)6 (46.1) | 10 (18.5)21 (38.9)23 (42.6) | 11 (25.6)13 (30.2)19 (44.2) | 9 (32.1)12 (42.9)7 (25.0) | 13 (36.1)16 (44.4)7 (19.4) | 5 (20.0)12 (48.0)8 (32.0) |
| Current smoking  | 108 (54.3) | 6 (46.2) | 26 (48.1) | 18 (41.9) | 14 (50.0) | 25 (69.4) | 19 (76.0) |
| BMI <20 20-24.99 25-29.99 ≥30 | 8 (4.1)44 (22.3)70 (35.5)75 (38.1) | 3 (23.1)4 (30.8)1 (7.8)5 (38.5) | 2 (3.7)7 (13.0)23 (42.6)22 (40.7) | 1 (2.4)17 (40.4)15 (35.7)9 (21.4) | 0 (0.0)4 (14.3)10 (35.7)14 (50.0) | 1 (2.9)8 (22.9)14 (40.0)12 (34.3) | 1 (4.0)4 (16.0)7 (28.0)13 (52.0) |
| Medical conditions Diabetes Hypertension Hyperlipidemia | 9 (4.5)41 (20.6)49 (24.6) | 0 (0.0)3 (23.1)2 (15.4) | 2 (3.7)11 (20.4)16 (29.6) | 5 (11.6)5 (11.6)13 (30.2) | 1 (3.6)2 (7.1)4 (14.3) | 1 (2.8)8 (22.2)5 (13.9) | 0 (0.0)12 (48.0)9 (36.0) |
| Women | 283 (100) | 19 (6.7) | 77 (27.3) | 57 (20.2) | 42 (14.9) | 63 (22.3) | 24 (8.5) |
| Agegroup ≤30 31-45 ≥45 | 101 (35.7)90 (31.8)92 (32.5) | 5 (26.3)6 (31.6)8 (42.1) | 23 (29.8)27 (35.1)27 (35.1) | 24 (42.1)11 (19.3)22 (38.6) | 19 (45.2)14 (33.3)9 (21.4) | 17 (27.0)25 (39.7)21 (33.3) | 13 (54.2)6 (25.0)5 (20.8) |
| Current smoking  | 141 (49.8) | 5 (26.3) | 35 (45.5) | 27 (47.4) | 21 (50.0) | 33 (52.4) | 19 (79.2) |
| BMI <20 20-24.99 25-29.99 ≥30 | 17 (6.1)63 (22.4)64 (22.8)137 (48.8) | 1 (5.3)5 (26.3)4 (21.1)9 (47.4) | 4 (5.2)21 (27.3)17 (22.1)35 (45.5) | 3 (5.3)15 (26.3)11 (19.3)28 (49.1) | 5 (11.9)6 (14.3)13 (31.0)18 (42.9) | 3 (4.8)14 (22.6)15 (24.2)30 (48.4) | 1 (4.4)2 (8.7)4 (17.4)16 (69.6) |
| Medical conditions Diabetes Hypertension Hyperlipidemia | 21 (7.4)49 (17.3)54 (19.1) | 2 (10.5)3 (15.8)3 (15.8) | 5 (6.5)16 (20.8)17 (22.1) | 1 (1.2)8 (14.0)13 (22.8) | 3 (7.1)7 (16.7)4 (9.5) | 6 (9.5)9 (14.3)12 (19.1) | 4 (16.7)6 (25.0)5 (20.8) |
| LiTMUS | **Total** | **WBC<4.5** | **WBC<6** | **6≤WBC<7** | **7≤WBC<8** | **8≤WBC<10** | **WBC≥10** |
| Men | 123 (100) | 6 (4.9) | 34 (27.6) | 19 (15.5) | 17 (13.8) | 35 (28.5) | 12 (9.8) |
| Agegroup ≤30 31-45 ≥45 | 33 (26.8)51 (41.5)39 (31.7) | 1 (16.7)30 (50.0)2 (33.3) | 6 (17.7)15 (44.1)13 (38.2) | 7 (36.8)9 (47.4)3 (15.8) | 9 (52.9)5 (29.4)3 (17.7) | 4 (11.4)14 (40.0)17 (48.6) | 6 (50.0)5 (41.7)1 (8.3) |
| Current smoking  | 69 (56.1) | 1 (16.7) | 20 (58.8) | 9 (47.4) | 6 (35.3) | 23 (65.7) | 10 (83.3) |
| BMI <20 20-24.99 25-29.99 ≥30 | 0 (0.0)31 (26.1)50 (42.0)38 (31.9) | 0 (0.0)3 (50.0)1 (16.7)2 (33.3) | 0 (0.0)9 (26.5)20 (58.8)4 (11.8) | 0 (0.0)5 (26.3)6 (31.6)8 (42.1) | 0 (0.0)2 (11.8)6 (35.3)9 (52.9) | 0 (0.0)8 (25.0)13 (40.6)11 (34.4) | 0 (0.0)4 (33.3)4 (33.3)4 (33.3) |
| Medical conditions Diabetes Hypertension  Hyperlipidemia | 7 (5.7)23 (18.7)18 (14.8) | 1 (16.7)2 (33.3)1 (16.7) | 1 (2.9)8 (23.5)5 (14.7) | 0 (0.0)1 (5.3)1 (5.3) | 2 (11.8)4 (23.5)3 (17.7) | 3 (8.6)7 (20.0)6 (17.7) | 0 (0.0)1 (8.3)2 (16.7) |
| Women | 160 (100) | 15 (9.4) | 30 (18.8) | 27 (16.9) | 26 (16.3) | 39 (24.4) | 23 (14.4) |
| Agegroup ≤30 31-45 ≥45 | 54 (33.8)53 (33.1)53 (33.1) | 7 (46.7)4 (26.7)4 (26.7) | 7 (23.3)11 (36.7)12 (40.0) | 9 (33.3)10 (37.1)8 (29.6) | 7 (26.9)8 (30.8)11 (42.3) | 17 (43.6)11 (28.2)11 (28.2) | 7 (30.4)9 (39.1)7 (30.4) |
| Current smoking  | 81 (50.6) | 4 (26.7) | 14 (46.7) | 10 (38.5) | 11 (42.3) | 26 (66.7) | 16 (69.6) |
| BMI <20 20-24.99 25-29.99 ≥30 | 8 (5.1)44 (27.9)41 (26.0)65 (41.1) | 2 (13.3)10 (66.7)2 (13.3)1 (6.7) | 4 (13.3)7 (23.3)13 (43.3)5 (16.7) | 0 (0.0)5 (18.5)11 (40.7)11 (40.7) | 1 (3.9)7 (26.9)5 (19.2)13 (50.0) | 0 (0.0)10 (25.6)7 (18.0)22 (56.4) | 1 (4.6)5 (22.7)3 (13.6)13 (59.1) |
| Medical conditions Diabetes Hypertension  Hyperlipidemia | 8 (5.1)25 (15.6)24 (15.1) | 0 (0.0)0 (0.0)1 (6.7) | 1 (3.3)1 (3.3)5 (16.7) | 1 (3.9)7 (25.9)3 (11.1) | 0 (0.0)4 (15.4)3 (11.5) | 3 (7.7)8 (20.5)10 (26.3) | 3 (13.0)5 (21.7)2 (8.7) |

**Supplementary Table 2:** Multinomial logistic regression analyses\* showing the relative risk ratio (RRR) for the ten specific MADRS items depending on baseline white blood cell (WBC) levels among 322 male patients with bipolar disorder from the CHOICE and LiTMUS studies. Individuals with WBC 7-7.99x109/L were set as the reference group.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| MEN (N=322) | RRR# (95%-CI) | RRR# (95%-CI) | RRR# (95%-CI) | RRR# (95%-CI) |
| MADRS overall | MADRS<7 | 7≤MADRS<20 | 20≤MADRS<35 | MADRS≥35 |
|  WBC<4.5 | 1.00 (ref.) | 4.93 (0.62; 39.30) | 3.94 (0.54; 28.70) | 2.22 (0.13; 39.41) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.71 (0.11; 4.63) | 1.11 (0.20; 6.32) | 2.87 (0.26; 31.77) |
|  6≤WBC<7 | 1.00 (ref.) | 1.59 (0.12; 21.98) | 0.82 (0.08; 8.76) | 1.21 (0.03; 52.87) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.13 (0.10; 13.40) | 0.57 (0.06; 5.05) | 0.89 (0.04; 22.02) |
|  WBC≥10 | 1.00 (ref.) | 2.18 (0.19; 25.21) | 2.52 (0.23; 27.42) | 16.23 (0.97; 272.59) |
| Reported Sadness | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 1.49 (0.34; 6.55) | 2.01 (0.52; 7.71) | 3.56 (0.25; 49.90) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.00 (0.26; 3.78) | 0.87 (0.21; 3.69) | 2.54 (0.10; 68.97) |
|  6≤WBC<7 | 1.00 (ref.) | 1.24 (0.35; 4.40) | 1.87 (0.53; 6.55) | 5.59 (0.42; 74.10) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.38 (0.12; 1.23) | 0.73 (0.24; 2.22) | 2.35 (0.20; 27.02) |
|  WBC≥10 | 1.00 (ref.) | 2.85 (0.44; 18.60) | 6.02 (0.99; 36.62) | ***18.70 (2.21; 78.23)*** |
| Apparent Sadness | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 0.56 (0.14; 2.17) | 0.75 (0.22; 2.62) | 0.20 (0.01; 2.92) |
|  4.5≤WBC<6 | 1.00 (ref.) | 2.06 (0.30; 14.12) | 1.63 (0.26; 10.29) | 2.66 (0.27; 26.47) |
|  6≤WBC<7 | 1.00 (ref.) | 0.90 (0.26; 3.19) | 0.59 (0.18; 1.97) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.51 (0.15; 1.71) | 0.35 (0.11; 1.11) | 0.53 (0.09; 3.27) |
|  WBC≥10 | 1.00 (ref.) | 3.41 (0.51; 22.92) | 2.46 (0.38; 15.78) | **10.84 (1.10; 107.01)** |
| Inner Tension | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | **5.04 (1.11; 22.90)** | 2.25 (0.59; 8.51) | 0.78 (0.05; 13.17) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.56 (0.39; 6.23) | 2.67 (0.75; 9.49) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | **4.87 (1.39; 17.07)** | 1.05 (0.31; 3.59) | 1.64 (0.20; 13.27) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | **5.64 (1.55; 20.56)** | 3.00 (0.92; 9.81) | 4.37 (0.61; 31.46) |
|  WBC≥10 | 1.00 (ref.) | 2.36 (0.51; 10.95) | 3.07 (0.77; 12.31) | 6.51 (0.75; 56.63) |
| Reduced Sleep | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 4.12 (0.73; 23.26) | 2.76 (0.50; 15.13) | 3.02 (0.52; 17.46) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.57 (0.23; 10.66) | 2.44 (0.37; 16.09) | 4.64 (0.68; 31.51) |
|  6≤WBC<7 | 1.00 (ref.) | 0.41 (0.11; 1.46) | 0.38 (0.11; 1.35) | 0.31 (0.07; 1.31) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | **0.24 (0.06; 0.90)** | 0.37 (0.10; 1.32) | 0.92 (0.26; 3.25) |
|  WBC≥10 | 1.00 (ref.) | 0.29 (0.06; 1.34) | 0.24 (0.05; 1.18) | 0.95 (0.22; 4.05) |
| Reduced Appetite | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 1.78 (0.45; 7.15) | 2.38 (0.70; 8.12) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.00 (0.28; 3.52) | 1.29 (0.31; 5.33) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 2.37 (0.76; 7.44) | 1.19 (0.34; 4.15) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | **3.40 (1.12; 10.37)** | 2.27 (0.72; 7.12) | n.a. |
|  WBC≥10 | 1.00 (ref.) | 1.43 (0.37; 5.52) | 1.63 (0.43; 6.18) | n.a. |
| Concentration difficulties | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 0.42 (0.09; 1.95) | 1.04 (0.28; 3.79) | 3.84 (0.31; 47.12) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.36 (0.09; 1.46) | 0.87 (0.23; 3.30) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 0.48 (0.14; 1.70) | 0.61 (0.18; 2.02) | 2.67 (0.24; 30.35) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.53 (0.15; 1.80) | 0.75 (0.24; 2.39) | 4.06 (0.40; 41.18) |
|  WBC≥10 | 1.00 (ref.) | 0.24 (0.05; 1.15) | 0.92 (0.25; 3.40) | 2.20 (0.15; 32.31) |
| Lassitude | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 0.87 (0.30; 2.54) | 1.42 (0.50; 4.03) | 0.97 (0.16; 5.83) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.42 (0.10; 1.75) | 1.07 (0.29; 3.91) | 0.95 (0.09; 9.58) |
|  6≤WBC<7 | 1.00 (ref.) | 1.06 (0.32; 3.54) | 0.83 (0.25; 2.74) | 2.00 (0.27; 14.59) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.61 (0.19; 1.98) | 0.96 (0.32; 2.90) | 1.38 (0.21; 9.18) |
|  WBC≥10 | 1.00 (ref.) | 0.50 (0.11; 2.24) | 0.89 (0.23; 3.41) | 4.13 (0.60; 28.57) |
| Inability to feel | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 1.20 (0.33; 4.35) | 1.73 (0.50; 6.00) | 0.83 (0.04; 17.28) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.64 (0.18; 2.31) | 0.89 (0.25; 3.20) | 3.51 (0.22; 55.09) |
|  6≤WBC<7 | 1.00 (ref.) | 0.75 (0.23; 2.46) | 2.05 (0.66; 6.36) | 1.69 (0.12; 22.94) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.55 (0.18; 1.68) | 1.18 (0.41; 3.42) | 3.34 (0.32; 34.37) |
|  WBC≥10 | 1.00 (ref.) | 1.45 (0.31; 6.72) | **4.58 (1.10; 18.95)** | ***20.75 (1.61; 268.23)*** |
| Pessimistic thoughts | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 0.93 (0.31; 2.77) | 1.19 (0.37; 3.80) | 1.05 (0.21; 5.19) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.78 (0.20; 3.07) | 0.68 (0.14; 3.21) | 2.52 (0.33; 19.03) |
|  6≤WBC<7 | 1.00 (ref.) | 0.54 (0.15; 1.94) | 1.51 (0.41; 5.57) | 0.86 (0.21; 6.07) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.42 (0.13; 1.36) | 0.82 (0.24; 2.80) | 0.83 (0.14; 4.75) |
|  WBC≥10 | 1.00 (ref.) | 0.91 (0.21; 4.01) | 1.79 (0.39; 8.15) | 3.15 (0.42; 23.87) |
| Suicidal thoughts | 0 | 1-2 | 3-6^ |  |
|  WBC<4.5 | 1.00 (ref.) | 0.73 (0.24; 2.23) | 0.55 (0.10; 2.92) |  |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.55 (0.50; 4.95) | 3.71 (0.70; 19.71) |  |
|  6≤WBC<7 | 1.00 (ref.) | 1.26 (0.50; 3.36) | 0.48 (0.08; 3.10) |  |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |  |
|  8≤WBC<10 | 1.00 (ref.) | 0.70 (0.26; 1.89) | 0.91 (0.21; 3.88) |  |
|  WBC≥10 | 1.00 (ref.) | 1.77 (0.55; 5.69) | 2.94 (0.58; 14.90) |  |

Bold values indicate results with p<0.05, and values in italic indicate results that passed the corrected p-value of 0.0033.

\* The results are adjusted for age, BMI, current smoking, race, and a diagnosis of diabetes, hypertension or hyperlipidemia.

^ Because of too few observations, severity on the item “suicidal thoughts” was divided into 3-6 instead of 3-4 and 5-6.

# For each symptom, we corrected for multiple testing by dividing the p-value of 0.05 with the amount of tests performed (15 for each specific symptom), hence the corrected p-value was 0.0033 (except for suicidal thoughts, were the corrected p-value was 0.05/10 = 0.005).

**Supplementary Table 3:** Multinomial logistic regression analyses\* showing the relative risk ratio (RRR) for the ten specific MADRS items depending on baseline white blood cell (WBC) levels among 443 female patients with bipolar disorder from the CHOICE and LiTMUS studies. Individuals with WBC 7-7.99x109/L were set as the reference group.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| WOMEN (N=443) | RRR# (95%-CI) | RRR# (95%-CI) | RRR# (95%-CI) | RRR# (95%-CI) |
| MADRS overall | MADRS<7 | 7≤MADRS<20 | 20≤MADRS<35 | MADRS≥35 |
|  WBC<4.5 | 1.00 (ref.) | 0.26 (0.02; 3.33) | 0.73 (0.06; 8.97) | 0.39 (0.03; 5.82) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.33 (0.02; 4.57) | 1.34 (0.10; 18.44) | 0.33 (0.02; 6.07) |
|  6≤WBC<7 | 1.00 (ref.) | 0.18 (0.01; 3.03) | 0.53 (0.03; 8.54) | 0.43 (0.02; 8.47) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.23 (0.02; 3.19) | 0.57 (0.04; 7.64) | 0.16 (0.01; 3.15) |
|  WBC≥10 | 1.00 (ref.) | 0.43 (0.02; 10.04) | 1.15 (0.05; 8.34) | 0.34 (0.01; 13.34) |
| Reported Sadness | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 0.97 (0.25; 3.80) | 2.57 (0.73; 9.09) | 1.35 (0.25; 7.21) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.38 (0.36; 5.34) | 2.28 (0.57; 9.02) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 0.45 (0.15; 1.38) | 1.37 (0.47; 3.97) | 0.69 (0.15; 3.18) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.91 (0.31; 2.69) | 1.56 (0.53; 4.61) | 0.64 (0.14; 2.83) |
|  WBC≥10 | 1.00 (ref.) | 1.00 (0.27; 3.65) | 1.74 (0.50; 6.10) | 0.56 (0.09; 3.54) |
| Apparent Sadness | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 1.91 (0.58; 6.31) | 3.21 (0.99; 10.47) | 1.67 (0.18; 15.10) |
|  4.5≤WBC<6 | 1.00 (ref.) | 2.86 (0.27; 30.61) | 3.18 (0.30; 33.37) | 1.29 (0.09; 18.31) |
|  6≤WBC<7 | 1.00 (ref.) | 1.48 (0.47; 4.71) | 1.63 (0.50; 5.31) | 0.37 (0.05; 2.78) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.41 (0.47; 4.30) | 1.96 (0.64; 6.02) | 3.03 (0.67; 13.70) |
|  WBC≥10 | 1.00 (ref.) | 0.91 (0.25; 3.28) | 1.72 (0.48; 6.11) | 0.31 (0.03; 3.75) |
| Inner Tension | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 0.52 (0.15; 1.74) | 0.57 (0.18; 1.73) | 1.07 (0.13; 8.63) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.75 (0.24; 2.29) | 0.83 (0.27; 2.56) | 0.41 (0.05; 3.33) |
|  6≤WBC<7 | 1.00 (ref.) | 1.41 (0.49; 4.06) | 1.09 (0.38; 3.15) | 1.39 (0.23; 8.28) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.97 (0.35; 2.65) | 0.62 (0.23; 1.69) | 1.15 (0.22; 6.03) |
|  WBC≥10 | 1.00 (ref.) | 0.77 (0.23; 2.62) | 0.77 (0.24; 2.45) | 1.18 (0.17; 8.09) |
| Reduced Sleep | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 3.95 (1.07; 14.59) | 1.95 (0.57; 6.62) | 2.89 (0.80; 10.49) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.64 (0.49; 5.45) | 0.78 (0.24; 2.56) | 0.82 (0.24; 2.74) |
|  6≤WBC<7 | 1.00 (ref.) | 1.45 (0.47; 4.47) | 1.69 (0.61; 4.65) | 1.48 (0.51; 4.29) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.16 (0.39; 3.44) | 1.40 (0.54; 3.64) | 0.99 (0.35; 2.80) |
|  WBC≥10 | 1.00 (ref.) | 0.47 (0.12; 1.79) | 0.53 (0.16; 1.71) | 1.19 (0.38; 3.80) |
| Reduced Appetite | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 2.40 (0.66; 8.65) | 1.43 (0.49; 4.19) | 1.38 (0.10; 19.56) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.54 (0.50; 4.76) | 2.20 (0.71; 6.86) | 2.46 (0.18; 33.98) |
|  6≤WBC<7 | 1.00 (ref.) | **4.29 (1.55; 11.88)** | 1.77 (0.64; 4.89) | 5.28 (0.48; 57.76) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.18 (0.40; 3.52) | 1.88 (0.74; 4.82) | 2.55 (0.23; 27.87) |
|  WBC≥10 | 1.00 (ref.) | **4.02 (1.23; 13.11)** | **3.61 (1.15; 11.36)** | 9.03 (0.77; 106.10) |
| Concentration difficulties | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 1.14 (0.32; 4.10) | 1.47 (0.47; 4.60) | 1.03 (0.18; 6.04) |
|  4.5≤WBC<6 | 1.00 (ref.) | 4.39 (0.81; 23.77) | **6.13 (1.10; 34.15)** | 3.77 (0.34; 42.00) |
|  6≤WBC<7 | 1.00 (ref.) | 0.83 (0.27; 2.61) | 2.53 (0.90; 7.12) | 0.33 (0.03; 3.63) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.34 (0.48; 3.78) | 1.19 (0.44; 3.21) | 1.60 (0.35; 7.28) |
|  WBC≥10 | 1.00 (ref.) | 1.76 (0.44; 7.11) | 2.52 (0.68; 9.31) | **8.05 (1.43; 45.30)** |
| Lassitude | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 2.36 (0.69; 8.10) | 2.19 (0.73; 6.55) | 0.91 (0.19; 4.31) |
|  4.5≤WBC<6 | 1.00 (ref.) | 2.05 (0.53; 7.85) | 2.29 (0.70; 7.51) | 1.38 (0.30; 6.34) |
|  6≤WBC<7 | 1.00 (ref.) | 1.91 (0.63; 5.80) | 2.09 (0.79; 5.54) | 1.61 (0.44; 5.88) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.88 (0.29; 2.60) | 1.66 (0.67; 4.10) | 1.33 (0.39; 4.56) |
|  WBC≥10 | 1.00 (ref.) | 2.27 (0.58; 8.95) | 2.83 (0.86; 9.37) | 3.59 (0.78; 16.63) |
| Inability to feel | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 2.93 (0.90; 9.53) | **3.01 (1.02; 8.83)** | 2.36 (0.30; 18.68) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.96 (0.58; 6.59) | 2.27 (0.74; 6.98) | 2.30 (0.36; 14.56) |
|  6≤WBC<7 | 1.00 (ref.) | 1.71 (0.61; 4.78) | 2.47 (0.98; 6.25) | 2.30 (0.45; 11.84) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.45 (0.89; 6.77) | **3.06 (1.20; 7.76)** | 3.77 (0.78; 18.31) |
|  WBC≥10 | 1.00 (ref.) | 3.00 (0.77; 11.63) | ***5.54 (1.64; 18.68)*** | 1.34 (0.10; 17.41) |
| Pessimistic thoughts | 0 | 1-2 | 3-4 | 5-6 |
|  WBC<4.5 | 1.00 (ref.) | 2.48 (0.68; 8.95) | 3.15 (0.90; 10.95) | 4.26 (0.54; 33.65) |
|  4.5≤WBC<6 | 1.00 (ref.) | 3.49 (0.86; 14.20) | 3.94 (0.95; 16.37) | 0.79 (0.11; 5.90) |
|  6≤WBC<7 | 1.00 (ref.) | 1.99 (0.69; 5.76) | 1.85 (0.63; 5.38) | 1.01 (0.19; 5.44) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.89 (0.97; 8.62) | **3.53 (1.18; 10.59)** | 1.51 (0.29; 8.00) |
|  WBC≥10 | 1.00 (ref.) | 1.24 (0.36; 4.26) | 2.29 (0.70; 7.52) | 0.80 (0.10; 6.31) |
| Suicidal thoughts | 0 | 1-2 | 3-6 |  |
|  WBC<4.5 | 1.00 (ref.) | 0.77 (0.32; 1.85) | 1.15 (0.25; 5.16) |  |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.87 (0.37; 2.07) | 1.41 (0.24; 8.20) |  |
|  6≤WBC<7 | 1.00 (ref.) | 0.81 (0.37; 1.76) | 2.09 (0.54; 8.10) |  |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |  |
|  8≤WBC<10 | 1.00 (ref.) | 0.59 (0.28; 1.27) | 1.16 (0.28; 4.73) |  |
|  WBC≥10 | 1.00 (ref.) | 0.81 (0.33; 2.03) | 1.68 (0.34; 8.32) |  |

Bold values indicate results with p<0.05, and values in italic indicate results that passed the corrected p-value of 0.0033.

\* The results are adjusted for age, BMI, current smoking, race, and a diagnosis of diabetes, hypertension or hyperlipidemia.

^ Because of too few observations, severity on the item “suicidal thoughts” was divided into 3-6 instead of 3-4 and 5-6.

# For each symptom, we corrected for multiple testing by dividing the p-value of 0.05 with the amount of tests performed (15 for each specific symptom), hence the corrected p-value was 0.0033 (except for suicidal thoughts, were the corrected p-value was 0.05/10 = 0.005).

**Supplementary Table 4:** Multinomial logistic regression analyses\* showing the relative risk ratio (RRR) for the 34 BISS symptoms which are not covered by the MADRS, depending on baseline white blood cell (WBC) levels among 199 male patients with bipolar disorder from the Bipolar CHOICE study. Individuals with WBC 7-7.99x109/L were set as the reference group.

|  |  |  |  |
| --- | --- | --- | --- |
| WBC |  |  |  |
| Depressive symptoms |
| 07: Feeling of Inadequacy | 0 | 1-2# | 3-4# |
|  WBC<4.5 | 1.00 (ref.) | 2.83 (0.26; 30.83) | 4.47 (0.41; 48.71) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.98 (0.30; 3.19) | 1.03 (0.32; 3.39) |
|  6≤WBC<7 | 1.00 (ref.) | 1.13 (0.28; 4.53) | 3.14 (0.83; 11.91) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.97 (0.25; 3.71) | 1.75 (0.48; 6.40) |
|  WBC≥10 | 1.00 (ref.) | 0.61 (0.13; 2.96) | 1.77 (0.42; 7.41) |
| 09: Psychomotor slowing | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.51 (0.10; 2.51) | 3.15 (0.30; 32.97) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.35 (0.12; 1.00) | 1.55 (0.27; 7.73) |
|  6≤WBC<7 | 1.00 (ref.) | 0.37 (0.12; 1.15) | 2.23 (0.37; 13.36) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | **0.26 (0.08; 0.85)** | 2.05 (0.34; 12.33) |
|  WBC≥10 | 1.00 (ref.) | 0.43 (0.13; 1.50) | 0.77 (0.08; 7.10) |
| 11: Social withdrawal | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 3.58 (0.55; 23.54) | 3.60 (0.45; 28.97) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.60 (0.51; 5.01) | 3.16 (0.93; 10.80) |
|  6≤WBC<7 | 1.00 (ref.) | 1.04 (0.32; 3.41) | 1.48 (0.41; 5.35) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.59 (0.45; 5.66) | **3.83 (1.02; 13.34)** |
|  WBC≥10 | 1.00 (ref.) | 1.55 (0.34; 7.13) | **6.16 (1.36; 27.85)** |
| 12: Reduced sex drive | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.26 (0.02; 4.23) | 2.59 (0.56; 11.97) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.60 (0.15; 2.40) | 1.21 (0.43; 3.36) |
|  6≤WBC<7 | 1.00 (ref.) | 0.39 (0.08; 1.85) | 1.09 (0.37; 3.23) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.66 (0.15; 2.96) | 0.83 (0.27; 2.55) |
|  WBC≥10 | 1.00 (ref.) | 0.80 (0.14; 4.64) | 1.19 (0.35; 4.07) |
| 18: Excessive sleep | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.51 (0.10; 2.52) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.79 (0.28; 2.29) | 2.21 (0.40; 12.31) |
|  6≤WBC<7 | 1.00 (ref.) | 1.12 (0.37; 3.37) | 2.18 (0.33; 14.47) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.71 (0.23; 2.22) | 0.76 (0.09; 6.09) |
|  WBC≥10 | 1.00 (ref.) | 0.64 (0.19; 2.24) | 0.49 (0.04; 6.07) |
| 20: Increased appetite | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 3.27 (0.53; 20.12) | 0.68 (0.06; 8.09) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.31 (0.30; 5.71) | 1.66 (0.45; 6.15) |
|  6≤WBC<7 | 1.00 (ref.) | 2.29 (0.52; 10.10) | 2.11 (0.50; 8.81) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.19 (0.25; 5.79) | 0.99 (0.22; 4.42) |
|  WBC≥10 | 1.00 (ref.) | 1.88 (0.37; 9.49) | 0.43 (0.06; 2.98) |
| Mania symptoms |
| 26: Hyperactive | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.35 (0.25; 7.37) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.49 (0.41; 5.38) | 0.84 (0.23; 3.02) |
|  6≤WBC<7 | 1.00 (ref.) | 0.68 (0.16; 2.86) | 0.39 (0.09; 1.69) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.38 (0.64; 8.93) | 1.16 (0.30; 4.55) |
|  WBC≥10 | 1.00 (ref.) | 0.48 (0.08; 2.96) | 0.59 (0.12; 2.89) |
| 27: Energetic | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 4.79 (0.81; 28.25) | 0.73 (0.09; 5.87) |
|  4.5≤WBC<6 | 1.00 (ref.) | 2.15 (0.53; 8.80) | 0.79 (0.21; 3.00) |
|  6≤WBC<7 | 1.00 (ref.) | 1.79 (0.41; 7.82) | 0.37 (0.07; 1.88) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 4.00 (0.97; 16.55) | 0.79 (0.18; 3.52) |
|  WBC≥10 | 1.00 (ref.) | 1.53 (0.29; 7.95) | 0.70 (0.14; 3.59) |
| 28: Increased social interest | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 7.45 (0.63; 88.09) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 6.39 (0.74; 55.05) | 0.34 (0.05; 2.37) |
|  6≤WBC<7 | 1.00 (ref.) | 6.04 (0.67; 54.38) | 0.17 (0.01; 1.97) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | ***12.24 (1.40; 106.81)*** | 1.07 (0.18; 6.27) |
|  WBC≥10 | 1.00 (ref.) | 4.58 (0.46; 46.12) | 0.43 (0.04; 4.83) |
| 29: Racing thoughts reported | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 3.15 (0.61; 16.35) | 0.16 (0.01; 1.93) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.00 (0.28; 3.60) | 1.65 (0.55; 4.93) |
|  6≤WBC<7 | 1.00 (ref.) | 1.70 (0.48; 6.09) | 0.60 (0.17; 2.08) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.31 (0.59; 9.11) | 2.45 (0.70; 8.54) |
|  WBC≥10 | 1.00 (ref.) | 2.29 (0.37; 14.11) | **6.10 (1.32; 28.00)** |
| 30: Pressured speech observed | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.70 (0.14; 3.48) | 0.35 (0.03; 4.15) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.13 (0.38; 3.39) | 0.89 (0.22; 3.56) |
|  6≤WBC<7 | 1.00 (ref.) | 0.43 (0.12; 1.55) | 0.47 (0.10; 2.10) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.67 80.53; 5.20) | 0.80 (0.16; 4.05) |
|  WBC≥10 | 1.00 (ref.) | 0.91 (0.24; 3.47) | 1.73 (0.37; 8.01) |
| 31: Increased sexuality | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.79 (0.05; 12.10) | 1.74 (0.09; 33.83) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.50 (0.26; 8.64) | 3.48 (0.38; 31.74) |
|  6≤WBC<7 | 1.00 (ref.) | 1.94 (0.33; 11.57) | 1.69 (0.15; 18.65) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 4.36 (0.83; 22.81) | 0.94 (0.05; 16.13) |
|  WBC≥10 | 1.00 (ref.) | 1.35 (0.17; 10.97) | 5.43 (0.54; 54.84) |
| 32: Less need for sleep | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 4.47 (0.77; 25.90) | 0.75 (0.06; 9.73) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.43 (0.33; 6.12) | 1.53 (0.36; 6.51) |
|  6≤WBC<7 | 1.00 (ref.) | 1.79 (0.41; 7.82) | 0.59 (0.10; 3.45) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.07 (0.21; 5.38) | 1.29 (0.27; 6.18) |
|  WBC≥10 | 1.00 (ref.) | 1.01 (0.18; 5.82) | 1.08 (0.19; 6.30) |
| 33: Grandiose | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.33 (0.03; 3.65) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 2.70 (0.78; 9.33) | 1.01 (0.21; 4.97) |
|  6≤WBC<7 | 1.00 (ref.) | 1.39 (0.36; 5.33) | 0.54 80.09; 3.23) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.97 (0.52; 7.45) | 0.93 (0.16; 5.32) |
|  WBC≥10 | 1.00 (ref.) | 0.95 (0.21; 4.39) | n.a. |
| 34: Elated | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.35 (0.06; 2.18) | 0.22 (0.02; 3.15) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.99 (0.35; 2.79) | 0.67 (0.13; 3.48) |
|  6≤WBC<7 | 1.00 (ref.) | 0.48 (0.15; 1.54) | 0.29 (0.05; 1.83) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.21 (0.41; 3.59) | 0.45 (0.06; 3.29) |
|  WBC≥10 | 1.00 (ref.) | 0.99 (0.30; 3.35) | 0.30 (0.03; 3.36) |
| 35: Sharpened thinking | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.00 (0.23; 4.26) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.65 (0.24; 1.77) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 0.62 (0.21; 1.83) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.80 80.27; 2.33) | n.a. |
|  WBC≥10 | 1.00 (ref.) | 0.59 (0.18; 1.96) | n.a. |
| 36: Elevated evening energy | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.08 (0.22; 5.35) | 1.03 (0.07; 15.01) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.83 (0.27; 2.51) | 0.99 (0.17; 2.52) |
|  6≤WBC<7 | 1.00 (ref.) | 0.73 (0.22; 2.40) | 0.72 (0.10; 5.25) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.56 (0.16; 1.96) | 1.11 (0.16; 7.50) |
|  WBC≥10 | 1.00 (ref.) | 0.77 (0.20; 2.98) | 1.95 (0.30; 12.74) |
| 37: Impulsive | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.70 (0.35; 8.19) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.63 (0.22; 1.81) | 0.53 (0.11; 2.45) |
|  6≤WBC<7 | 1.00 (ref.) | **0.25 (0.08; 0.80)** | **0.09 (0.01; 0.97)**  |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.72 (0.23; 2.26) | 1.05 (0.23; 4.82) |
|  WBC≥10 | 1.00 (ref.) | 0.73 (0.21; 2.54) | 1.17 (0.22; 6.24) |
| 38: Distractible | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.55 (0.28; 8.52) | 0.61 (0.08; 4.60) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.72 (0.23; 2.20) | 0.82 (0.24; 2.76) |
|  6≤WBC<7 | 1.00 (ref.) | 0.96 (0.30; 3.11) | 0.51 (0.13; 2.04) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.63 (0.41; 6.48) | 3.30 (0.80; 13.52) |
|  WBC≥10 | 1.00 (ref.) | 1.08 (0.27; 4.27) | 1.53 (0.29; 5.77) |
| 39: Risky behavior | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.55 (0.33; 7.32) | 0.83 (0.13; 5.45) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.93 (0.29; 2.97) | 0.85 (0.24; 3.04) |
|  6≤WBC<7 | 1.00 (ref.) | 1.48 (0.48; 4.61) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.11 (0.67; 6.68) | 0.17 (0.02; 1.63) |
|  WBC≥10 | 1.00 (ref.) | 1.96 (0.54; 7.18) | 1.47 (0.34; 6.38) |
| 40: Affective lability | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.59 (0.12; 2.89) | 0.80 (0.10; 6.25) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.52 (0.18; 1.52) | 1.80 (0.46; 7.08) |
|  6≤WBC<7 | 1.00 (ref.) | 0.32 (0.10; 1.00) | 0.63 (0.14; 2.83) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.89 (0.28; 2.78) | 1.94 (0.45; 8.46) |
|  WBC≥10 | 1.00 (ref.) | 1.07 (0.30; 3.82) | 2.59 (0.52; 13.00) |
| Irritability symptoms |
| 06: Guilt | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.61 (0.09; 4.32) | 2.37 (0.40; 14.09) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.09 (0.34; 3.47) | 0.75 (0.22; 2.58) |
|  6≤WBC<7 | 1.00 (ref.) | 1.36 (0.38; 4.85) | 1.30  |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.85 (0.22; 3.26) | 2.09 (0.57; 7.66) |
|  WBC≥10 | 1.00 (ref.) | 2.95 (0.59; 14.89) | 3.62 (0.70; 18.82) |
| 23: Irritability reported | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.39 (0.07; 2.27) | 0.61 (0.09; 4.13) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.75 (0.21; 2.70) | 1.62 (0.42; 6.23) |
|  6≤WBC<7 | 1.00 (ref.) | 0.61 (0.16; 2.27) | 0.75 (0.18; 3.16 |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.03 (0.41; 9.96) | 4.12 (0.79; 21.42) |
|  WBC≥10 | 1.00 (ref.) | 1.39 (0.27; 7.15) | 2.53 (0.46; 13.81) |
| 24: Irritability observed | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.64 (0.11; 3.51) | 0.40 (0.03; 5.90) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.60 (0.56; 4.61) | 1.61 (0.35; 7.36) |
|  6≤WBC<7 | 1.00 (ref.) | 1.00 (0.33; 3.08) | 0.34 (0.05; 2.48) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.78 (0.57; 5.57) | 1.80 (0.36; 9.13) |
|  WBC≥10 | 1.00 (ref.) | 1.00 (0.28; 3.51) | 1.18 (0.19; 7.24) |
| 25: Aggressive behavior | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.96 (0.21; 4.26) | 0.47 (0.04; 5.64) |
|  4.5≤WBC<6 | 1.00 (ref.) | 2.38 (0.82; 6.91) | 2.98 (0.75; 11.89) |
|  6≤WBC<7 | 1.00 (ref.) | 0.47 (0.15; 1.46) | 0.52 (0.12; 2.35) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.75 (0.23; 2.41) | 2.67 (0.67; 10.67) |
|  WBC≥10 | 1.00 (ref.) | 1.07 (0.31; 3.73) | 2.33 (0.50; 10.80) |
| Anxiety symptoms |
| 05: Worrying | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | n.a. | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.50 (0.11; 2.15) | 1.17 (0.31; 4.49) |
|  6≤WBC<7 | 1.00 (ref.) | 0.29 (0.06; 1.34) | 0.44 (0.11; 1.83) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.94 (0.18; 4.97) | 1.83 (0.39; 8.62) |
|  WBC≥10 | 1.00 (ref.) | 0.48 (0.07; 3.50) | 1.21 (0.20; 7.20) |
| 13: Anxiety reported | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.32 (0.05; 2.16) | 0.96 (0.16; 5.66) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.84 (0.25; 2.83) | 1.54 (0.43; 5.56) |
|  6≤WBC<7 | 1.00 (ref.) | 0.32 (0.08; 1.22) | 1.08 (0.28; 4.10) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.30 (0.47; 11.32) | **5.55 (1.09; 28.20)** |
|  WBC≥10 | 1.00 (ref.) | 1.68 (0.31; 9.22) | 2.28 (0.39; 13.28) |
| 14: Anxiety observed | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.55 (0.12; 2.56) | 0.89 (0.07; 11.50) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.87 (0.32; 2.40) | 1.36 (0.29; 6.50) |
|  6≤WBC<7 | 1.00 (ref.) | 0.39 (0.12; 1.24) | 1.10 (0.20; 6.03) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.79 (0.26; 2.40) | 1.30 (0.24; 6.96) |
|  WBC≥10 | 1.00 (ref.) | 1.27 (0.36; 4.52) | 1.25 (0.16; 9.50) |
| 15: Somatic anxiety | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | n.a.  | 1.83 (0.35; 9.65) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.61 (0.46; 5.69) | 2.03 (0.60; 6.82) |
|  6≤WBC<7 | 1.00 (ref.) | 2.19 (0.55; 8.76) | 2.88 (0.77; 10.68) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.65 80.40; 6.87) | **4.30 (1.20; 15.39)** |
|  WBC≥10 | 1.00 (ref.) | 3.67 (0.75; 18.02) | **5.52 (1.27; 24.03)** |
| 16: Fearfulness | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | **8.51 (1.18; 61.50)** | 2.69 (0.10; 69.74) |
|  4.5≤WBC<6 | 1.00 (ref.) | 2.39 (0.45; 12.72) | 3.01 (0.30; 30.39) |
|  6≤WBC<7 | 1.00 (ref.) | 0.38 (0.04; 3.20) | 1.68 (0.13; 21.97) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 3.25 (0.57; 18.52) | 2.15 (0.18; 26.09) |
|  WBC≥10 | 1.00 (ref.) | 1.60 (0.22; 11.67) | 3.53 (0.25; 48.94) |
| Psychotic symptoms |
| 41: Persecutory ideas | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | n.a. | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.32 (0.40; 4.35) | 1.37 (0.11; 16.50) |
|  6≤WBC<7 | 1.00 (ref.) | 1.70 (0.50; 5.80) | 2.62 (0.25; 27.84) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.68 (0.81; 8.90) | 2.00 (0.17; 24.13) |
|  WBC≥10 | 1.00 (ref.) | 1.26 (0.31; 5.13) | 2.98 (0.24; 36.80) |
| 42: Delusions | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 3.40 (0.48; 23.84) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.52 (0.28; 8.21) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 0.87 (0.13; 5.66) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.64 (0.28; 9.72) | 0.90 (0.5; 15.75) |
|  WBC≥10 | 1.00 (ref.) | 4.07 (0.73; 22.77) | n.a. |
| 43: Hallucinations | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | n.a. | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | n.a. | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | n.a. | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | n.a. | 1.73 (0.15; 20.23) |
|  WBC≥10 | 1.00 (ref.) | n.a. | 2.49 (0.21; 29.57) |
| 44: Impaired insights | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.27 (0.03; 2.54) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.69 (0.21; 2.23) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 0.26 (0.06; 1.15) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.60 (0.16; 2.23) | n.a. |
|  WBC≥10 | 1.00 (ref.) | 0.92 (0.24; 3.53) | n.a. |

Bold values indicate significant results (p<0.05), and values in italic indicate results that passed the corrected p-value of 0.005.

\* The results are adjusted for age, BMI, current smoking, race, and a diagnosis of diabetes, hypertension or hyperlipidemia.

# For each symptom, we corrected for multiple testing by dividing the p-value of 0.05 with the amount of tests performed (10 for each specific symptom), hence the corrected p-value was 0.005.

**Supplemental Table 5:** Multinomial logistic regression analyses\* showing the relative risk ratio (RRR) for the 34 BISS symptoms, which are not covered by the MADRS, depending on baseline white blood cell (WBC) levels among 283 female patients with bipolar disorder from the CHOICE study. Individuals with WBC 7-7.99x109/L were set as the reference group.

|  |  |  |  |
| --- | --- | --- | --- |
| WBC |  |  |  |
| Depressive symptoms |
| 07: Feeling of Inadequacy | 0# | 1-2# | 3-4# |
|  WBC<4.5 | 1.00 (ref.) | 1.00 (0.09; 11.34) | 2.65 (0.26; 27.35) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.57 (0.15; 2.18) | 0.72 (0.19; 2.72) |
|  6≤WBC<7 | 1.00 (ref.) | 0.93 (0.19; 4.44) | 2.05 (0.44; 9.42) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.87 (0.21; 3.63) | 0.96 (0.23; 4.01) |
|  WBC≥10 | 1.00 (ref.) | 1.63 (0.15; 18.01) | 3.64 (0.35; 37.63) |
| 09: Psychomotor slowing | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.22 (0.38; 3.93) | 0.65 (0.11; 3.93) |
|  4.5≤WBC<6 | 1.00 (ref.) | 2.14 (0.89; 5.14) | **3.80 (1.17; 12.30)** |
|  6≤WBC<7 | 1.00 (ref.) | 1.55 (0.62; 3.89) | 2.58 (0.75; 8.80) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.86 (0.76; 4.54) | 2.21 (0.64; 7.65) |
|  WBC≥10 | 1.00 (ref.) | 1.03 (0.31; 3.45) | 2.43 (0.55; 10.73) |
| 11: Social withdrawal | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.02 (0.20; 5.20) | 1.36 (0.28; 6.66) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.33 (0.42; 4.17) | 1.36 (0.44; 4.24) |
|  6≤WBC<7 | 1.00 (ref.) | 0.89 (0.27; 2.94) | 1.27 (0.40; 4.10) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.85 (0.26; 2.75) | 1.28 (0.41; 4.02) |
|  WBC≥10 | 1.00 (ref.) | 1.09 (0.24; 4.84) | 0.89 (0.20; 4.04) |
| 12: Reduced sex drive | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.38 (0.20; 9.62) | **4.45 (1.16; 17.10)** |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.86 (0.62; 5.58) | **2.55 (1.04; 6.23)** |
|  6≤WBC<7 | 1.00 (ref.) | 2.13 (0.60; 7.56) | ***4.65 (1.74; 12.41)*** |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.43 (0.11; 1.72) | 2.11 (0.86; 5.17) |
|  WBC≥10 | 1.00 (ref.) | 0.69 (0.11; 4.20) | 2.43 (0.75; 7.84) |
| 18: Excessive sleep | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.63 (0.47; 5.73) | 0.81 (0.07; 8.89) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.76 (0.29; 1.98 ) | 1.84 (0.45; 7.44) |
|  6≤WBC<7 | 1.00 (ref.) | 1.43 (0.55; 3.73) | 1.21 (0.26; 5.68) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.04 (0.80; 5.20) | 2.06 (0.47; 9.01) |
|  WBC≥10 | 1.00 (ref.) | 0.51 (0.12; 2.21) | 3.28 (0.65; 16.51) |
| 20: Increased appetite | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | n.a. | 0.58 (0.16; 2.10) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.52 (0.17; 1.56) | 0.56 (0.22; 1.41) |
|  6≤WBC<7 | 1.00 (ref.) | 0.69 (0.22; 2.16) | 0.47 (0.17; 1.26) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.58 (0.56; 4.51) | 0.80 (0.30; 2.12) |
|  WBC≥10 | 1.00 (ref.) | 1.30 (0.36; 4.76) | 0.39 (0.10; 1.53) |
| Mania symptoms |
| 26: Hyperactive | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | **4.08 (1.09; 15.29)** | 1.32 (0.22; 8.02) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.86 (0.65; 5.32) | 1.74 (0.56; 5.40) |
|  6≤WBC<7 | 1.00 (ref.) | 1.18 (0.37; 3.81) | 1.96 (0.61; 6.32) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.22 (0.40; 3.76) | 1.11 (0.33; 3.76) |
|  WBC≥10 | 1.00 (ref.) | 0.57 (0.10; 3.14) | 1.41 (0.33; 5.98) |
| 27: Energetic | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.19 (0.33; 4.32) | 0.45 (0.05; 4.32) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.48 (0.17; 1.35) | 1.53 (0.48; 4.82) |
|  6≤WBC<7 | 1.00 (ref.) | 0.49 (0.16; 1.48) | 1.47 (0.44; 4.93) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.56 (0.29; 3.50) | 1.01 (0.29; 3.50) |
|  WBC≥10 | 1.00 (ref.) | 0.27 (0.05; 1.42) | 0.84 (0.17; 4.13) |
| 28: Increased social interest | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | **11.21 (1.11; 113.08)** | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 3.97 (0.46; 34.55) | 0.28 (0.06; 1.27) |
|  6≤WBC<7 | 1.00 (ref.) | 5.46 (0.62; 47.86) | 0.39 (0.09; 1.77) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | **10.43 (1.26; 86.07)** | n.a. |
|  WBC≥10 | 1.00 (ref.) | 3.05 (0.25; 37.02) | n.a. |
| 29: Racing thoughts reported | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.07 (0.23; 5.06) | 1.15 (0.32; 4.17) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.61 (0.56; 4.62) | 0.92 (0.37; 2.29) |
|  6≤WBC<7 | 1.00 (ref.) | 1.33 (0.43; 4.11) | 1.05 (0.40; 2.78) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.72 (0.23; 2.21) | 0.73 (0.29; 1.82) |
|  WBC≥10 | 1.00 (ref.) | 0.75 (0.16; 3.42) | 0.82 (0.24; 2.73) |
| 30: Pressured speech observed | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.53 (0.42; 5.61) | 1.38 (0.33; 5.75) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.37 (0.57; 3.32) | 0.49 (0.16; 1.50) |
|  6≤WBC<7 | 1.00 (ref.) | 1.62 (0.63; 4.15) | 0.79 (0.25; 2.47) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.15 (0.45; 2.92) | 0.82 (0.28; 2.39) |
|  WBC≥10 | 1.00 (ref.) | 0.78 (0.23; 2.70) | 0.54 (0.13; 2.37) |
| 31: Increased sexuality | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.51 (0.22; 10.36) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.03 (0.23; 4.72) | 1.38 (0.32; 5.97) |
|  6≤WBC<7 | 1.00 (ref.) | 2.18 (0.53; 9.02) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 2.12 (0.49; 9.09) | 2.20 (0.52; 9.31) |
|  WBC≥10 | 1.00 (ref.) | 0.42 (0.04; 4.64) | 0.52 (0.05; 5.56) |
| 32: Less need for sleep | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.44 (0.05; 4.09) | 1.34 (0.32; 5.61) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.82 (0.25; 2.67) | 0.80 (0.27; 2.39) |
|  6≤WBC<7 | 1.00 (ref.) | 0.50 (0.13; 1.98) | 0.67 (0.21; 2.20) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.89 (0.26; 3.02) | 0.90 (0.29; 2.77) |
|  WBC≥10 | 1.00 (ref.) | 0.74 (0.15; 3.54) | 0.38 (0.07; 2.16) |
| 33: Grandiose | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 2.08 (0.53; 8.23) | 1.09 (0.09; 13.81) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.22 (0.42; 3.54) | 0.47 (0.06; 3.62) |
|  6≤WBC<7 | 1.00 (ref.) | 0.90 (0.28; 2.89) | 0.34 (0.03; 3.99) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.93 (0.30; 2.90) | 0.56 (0.07; 4.32) |
|  WBC≥10 | 1.00 (ref.) | 0.51 (0.09; 2.86) | 1.19 (0.10; 14.77) |
| 34: Elated | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.46 (0.11; 1.95) | 0.48 (0.05; 4.95) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.52 (0.21; 1.32) | 0.78 (0.19; 3.12) |
|  6≤WBC<7 | 1.00 (ref.) | 0.50 (0.18; 1.35) | 0.48 (0.10; 2.45) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.67 (0.26; 1.71) | 0.64 (0.14; 2.90) |
|  WBC≥10 | 1.00 (ref.) | 0.41 (0.11; 1.53) | n.a. |
| 35: Sharpened thinking | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.87 (0.25; 3.07) | 6.26 (0.48; 81.80) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.65 (0.27; 1.56) | 2.48 (0.25; 24.21) |
|  6≤WBC<7 | 1.00 (ref.) | 0.34 (0.12; 0.91) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.46 (0.18; 1.18) | 1.22 (0.10; 14.59) |
|  WBC≥10 | 1.00 (ref.) | n.a. | 2.45 (0.13; 45.97) |
| 36: Elevated evening energy | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.64 (0.15; 2.85) | 2.01 (0.45; 9.03) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.64 (0.24; 1.69) | 1.55 (0.51; 4.69) |
|  6≤WBC<7 | 1.00 (ref.) | 0.94 (0.36; 2.46) | 0.78 (0.21; 2.97) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.72 (0.27; 1.95) | 0.96 (0.29; 3.21) |
|  WBC≥10 | 1.00 (ref.) | 0.48 (0.13; 1.72) | 0.25 (0.03; 2.38) |
| 37: Impulsive | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.51 (0.15; 1.70) | 1.22 (0.17; 8.79) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.85 (0.38; 1.91) | 1.88 (0.45; 7.95) |
|  6≤WBC<7 | 1.00 (ref.) | 1.42 (0.60; 3.36) | 1.35 (0.26; 7.11) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.90 (0.39; 2.09) | 1.86 (0.42; 8.18) |
|  WBC≥10 | 1.00 (ref.) | 0.67 (0.22; 2.01) | 1.29 (0.17; 9.49) |
| 38: Distractible | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 2.41 (0.52; 11.11) | 1.41 (0.28; 7.14) |
|  4.5≤WBC<6 | 1.00 (ref.) | 3.52 (1.22; 10.12) | 1.40 (0.45; 4.29) |
|  6≤WBC<7 | 1.00 (ref.) | 2.71 (0.88; 8.37) | 1.96 (0.60; 6.38) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.15 (0.43; 3.09) | 0.46 (0.15; 1.35) |
|  WBC≥10 | 1.00 (ref.) | 1.78 (0.41; 7.58) | 2.26 (0.52; 9.92) |
| 39: Risky behavior | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.56 (0.15; 2.11) | 0.84 (0.14; 5.05) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.52 (0.22; 1.27) | 0.56 (0.15; 2.05) |
|  6≤WBC<7 | 1.00 (ref.) | 1.14 (0.47; 2.77) | 0.83 (0.21; 3.24) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.69 (0.28; 1.70) | 0.74 (0.20; 2.74) |
|  WBC≥10 | 1.00 (ref.) | 0.90 (0.29; 2.79) | 0.65 (0.11; 3.79) |
| 40: Affective lability | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 2.99 (0.74; 12.12) | 1.25 (0.25; 6.39) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.39 (0.54; 3.56) | 1.01 (0.37; 2.75) |
|  6≤WBC<7 | 1.00 (ref.) | 1.53 (0.56; 4.15) | 1.12 (0.39; 3.24) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.97 (0.37; 2.58) | 0.90 (0.32; 2.49) |
|  WBC≥10 | 1.00 (ref.) | 0.54 (0.15; 1.87) | 0.44 (0.11; 1.70) |
| Irritability symptoms |
| 06: Guilt | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.59 (0.12; 2.83) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.51 (0.17; 2.58) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 0.74 (0.22; 2.53) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.43 (0.14; 1.36) | n.a. |
|  WBC≥10 | 1.00 (ref.) | 0.50 (0.12; 2.05) | n.a. |
| 23: Irritability reported | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | n.a. | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.66 (0.19; 2.27) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 0.81 (0.22; 3.00) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.61 (0.17; 2.13) | n.a. |
|  WBC≥10 | 1.00 (ref.) | 0.69 (0.13; 3.60) | n.a. |
| 24: Irritability observed | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 2.03 (0.65; 6.30) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.18 (0.54; 2.55) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 1.24 (0.55; 2.83) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.77 (0.34; 1.74) | n.a. |
|  WBC≥10 | 1.00 (ref.) | 1.74 (0.60; 5.06) | n.a. |
| 25: Aggressive behavior | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 3.10 (0.75; 12.86) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.42 (0.61; 3.29) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 1.50 (0.61; 3.64) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.85 (0.75; 4.56) | n.a. |
|  WBC≥10 | 1.00 (ref.) | 1.55 (0.48; 4.99) | n.a. |
| Anxiety symptoms |
| 05: Worrying | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.99 (0.12; 7.93) | 2.82 (0.49; 16.32) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.36 (0.50; 3.67) | 2.23 (0.68; 7.31) |
|  6≤WBC<7 | 1.00 (ref.) | 1.31 (0.29; 5.89) | 3.70 (0.99; 13.90) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.88 (0.20; 3.79) | 3.08 (0.88; 10.80) |
|  WBC≥10 | 1.00 (ref.) | 0.24 (0.02; 3.42) | 3.27 (0.56; 19.14) |
| 13: Anxiety reported | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.61 (0.13; 2.78) | 1.10 (0.27; 4.54) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.87 (0.62; 5.61) | 1.75 (0.57; 5.37) |
|  6≤WBC<7 | 1.00 (ref.) | 1.91 (0.57; 6.47) | 2.81 (0.83; 9.55) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.29 (0.40; 4.15) | 2.39 (0.76; 7.53) |
|  WBC≥10 | 1.00 (ref.) | 4.39 (0.46; 42.32) | 6.67 (0.70; 63.21) |
| 14: Anxiety observed | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.50 (0.44; 5.14) | 2.71 (0.41; 17.90) |
|  4.5≤WBC<6 | 1.00 (ref.) | 1.01 (0.43; 2.33) | 2.38 (0.58; 9.84) |
|  6≤WBC<7 | 1.00 (ref.) | 0.61 (0.25; 1.52) | 2.37 (0.56; 10.05) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.81 (0.33; 1.98) | 3.11 (0.75; 12.85) |
|  WBC≥10 | 1.00 (ref.) | 0.62 (0.18; 2.12) | 3.83 (0.74; 19.87) |
| 15: Somatic anxiety | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.42 (0.09; 2.10) | 1.09 (0.27; 4.42) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.79 (0.27; 2.31) | 0.75 (0.26; 2.14) |
|  6≤WBC<7 | 1.00 (ref.) | 1.29 (0.39; 4.28) | 1.49 (0.46; 4.80) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | **0.28 (0.08; 0.91)** | 1.00 (0.35; 2.83) |
|  WBC≥10 | 1.00 (ref.) | 0.33 (0.07; 1.52) | 0.85 (0.22; 3.28) |
| 16: Fearfulness | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 2.42 (0.70; 8.39) | 2.04 (0.11; 37.87) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.96 (0.37; 2.49) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 1.14 (0.41; 3.15) | 4.60 (0.50; 42.36) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.12 (0.42; 3.03) | 4.61 (0.53; 40.30) |
|  WBC≥10 | 1.00 (ref.) | 1.89 (0.56; 6.46) | 7.95 (0.70; 89.96) |
| Psychotic symptoms |
| 41: Persecutory ideas | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 3.17 (0.86; 11.72) | 0.78 (0.08; 7.84) |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.97 (0.33; 2.85) | 0.54 (0.33; 2.85) |
|  6≤WBC<7 | 1.00 (ref.) | 2.30 (0.79; 6.67) | 0.45 (0.08; 2.64) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.43 (0.49; 4.17) | 0.34 (0.06; 2.02) |
|  WBC≥10 | 1.00 (ref.) | 1.95 (0.54; 7.06) | n.a. |
| 42: Delusions | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | n.a. | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.62 (0.14; 2.69) | n.a. |
|  6≤WBC<7 | 1.00 (ref.) | 0.52 (0.11; 2.53) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.58 (0.12; 2.82) | n.a. |
|  WBC≥10 | 1.00 (ref.) | 1.22 (0.24; 6.14) | n.a. |
| 43: Hallucinations | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 0.72 (0.07; 7.68) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.95 (0.21; 4.29) | 1.13 (0.10; 13.09) |
|  6≤WBC<7 | 1.00 (ref.) | 0.66 (0.12; 3.51) | 3.04 (0.29; 31.40) |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 0.72 (0.13; 3.84) | 1.29 (0.11; 15.01) |
|  WBC≥10 | 1.00 (ref.) | 2.57 (0.51; 12.96) | 4.71 (0.39; 57.22) |
| 44: Impaired insights | 0 | 1-2 | 3-4 |
|  WBC<4.5 | 1.00 (ref.) | 1.09 (0.24; 4.94) | n.a. |
|  4.5≤WBC<6 | 1.00 (ref.) | 0.98 (0.33; 2.90) | 0.52 (0.03; 9.28) |
|  6≤WBC<7 | 1.00 (ref.) | 1.72 (0.59; 5.04) | n.a. |
|  7≤WBC<8 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
|  8≤WBC<10 | 1.00 (ref.) | 1.23 (0.41; 3.64) | n.a. |
|  WBC≥10 | 1.00 (ref.) | 1.17 (0.29; 4.66) | n.a. |

Bold values indicate significant results (p<0.05), and values in italic indicate results that passed the corrected p-value of 0.005.

\* The results are adjusted for age, BMI, current smoking, race, and a diagnosis of diabetes, hypertension or hyperlipidemia.

# For each symptom, we corrected for multiple testing by dividing the p-value of 0.05 with the amount of tests performed (10 for each specific symptom), hence the corrected p-value was 0.005.