Supplementary Table 1. Baseline serum leptin levels by remission status according to initial antidepressant types

Type of antidepressant	Up to 12-week treatment				Up to 12-month treatment			
	Non-remission	Remission	Statistical coefficients	p value	Non-remission	Remission	Statistical coefficients	p value
SSRIs[a]								
Leptin, low:high	168 (47.1):189 (52.9)	190 (60.3):125 (39.7)	$\chi^2 = 11.818$	0.001	80 (51.9):74 (48.1)	221 (54.6):184 (45.4)	$\chi^2 = 0.308$	0.579
NaSSA (mirtazapine)								
Leptin, low:high	58 (39.7):88 (60.3)	59 (52.2):54 (47.8)	$\chi^2 = 4.010$	0.045	28 (47.5):31 (52.5)	67 (44.7):83 (55.3)	$\chi^2 = 0.133$	0.715
SNRIs[b]								
Leptin, low:high	23 (40.4):34 (59.6)	21 (48.8):22 (51.2)	$\chi^2 = 0.716$	0.397	16 (53.3):14 (46.7)	17 (36.2):30 (63.8)	$\chi^2 = 2.203$	0.138
NDRI (bupropion)								
Leptin, low:high	6 (37.5):10 (62.5)	5 (45.5):6 (54.5)	$\chi^2 = 0.171$	0.679	1 (20.0):4 (80.0)	7 (53.8):6 (46.2)	$\chi^2 = 1.675$	0.196
Serotonin modulators and stimulator (vortioxetine)								
Leptin, low:high	1 (20.0):4 (80.0)	2 (33.3):4 (66.7)	$\chi^2 = 0.244$	0.621	2 (50.0):2 (50.0)	1 (20.0):4 (80.0)	$\chi^2 = 0.900$	0.343

Values are presented as number (%).

SSRI, selective serotonin reuptake inhibitor; NaSSA, noradrenergic and specific serotonin antidepressant; SNRI, serotonin-norepinephrine reuptake inhibitor; NDRI, norepinephrine-dopamine reuptake inhibitor.

[a]Escitalopram, sertraline, paroxetine, and fluoxetine were included as SSRIs. [b]Venlafaxine, desvenlafaxine, and duloxetine were included as SNRIs.

Supplementary Table 2. Baseline serum leptin levels by remission status according to treatment steps

Treatment step	Up to 12-week treatment				Up to 12-month treatment			
	Non-remission (n = 596)	Remission (n = 490)	Statistical coefficients	p value	Non-remission (n = 259)	Remission (n = 625)	Statistical coefficients	p value
Step 1								
Leptin, low:high	137 (47.1):154 (52.9)	88 (51.2):84 (48.8)	$\chi^2 = 0.722$	0.396	53 (47.3):59 (52.7)	109 (50.9):105 (49.1)	$\chi^2 = 0.384$	0.536
Step 2								
Leptin, low:high	78 (42.4):106 (57.6)	112 (63.6):64 (36.4)	$\chi^2 = 16.291$	< 0.001	46 (55.4):37 (44.6)	112 (55.2):91 (44.8)	$\chi^2 = 0.001$	0.969
Step 3								
Leptin, low:high	39 (41.5):55 (58.5)	57 (53.8):49 (46.2)	$\chi^2 = 3.012$	0.083	15 (46.9):17 (53.1)	69 (49.3):71 (50.7)	$\chi^2 = 0.061$	0.806
Step 4								
Leptin, low:high	11 (40.7):16 (59.3)	20 (55.6):16 (44.4)	$\chi^2 = 1.355$	0.244	17 (53.1):15 (46.9)	25 (36.8):43 (63.2)	$\chi^2 = 2.391$	0.122

Values are presented as number (%).

Supplementary Table 3. Baseline serum leptin levels by remission status according to treatment strategies

Treatment strategy	Up to 12-week treatment				Up to 12-month treatment			
	Non-remission (n = 596)	Remission (n = 490)	Statistical coefficients	p value	Non-remission (n = 259)	Remission (n = 625)	Statistical coefficients	p value
Monotherapy								
Leptin, low:high	137 (47.1):154 (52.9)	88 (51.2):84 (48.8)	$\chi^2 = 0.722$	0.396	53 (47.3):59 (52.7)	109 (50.9):105 (49.1)	$\chi^2 = 0.384$	0.536
Switch								
Leptin, low:high	19 (39.6):29 (60.4)	24 (57.1):18 (42.9)	$\chi^2 = 2.768$	0.096	15 (53.6):13 (46.4)	24 (53.3):21 (46.7)	$\chi^2 = 0.000$	0.984
Combination								
Leptin, low:high	30 (47.6):33 (52.4)	39 (55.7):31 (44.3)	$\chi^2 = 0.870$	0.351	17 (58.6):12 (41.4)	44 (53.0):39 (47.0)	$\chi^2 = 0.273$	0.602
Augmentation								
Leptin, low:high	39 (39.4):60 (60.6)	65 (69.1):29 (30.9)	$\chi^2 = 17.180$	< 0.001	21 (50.0):21 (50.0)	64 (57.1):48 (42.9)	$\chi^2 = 0.630$	0.427
Switch + Combination								
Leptin, low:high	7 (50.0):7 (50.0)	10 (66.7):5 (33.3)	$\chi^2 = 0.829$	0.362	5 (55.6):4 (44.4)	13 (54.2):11 (45.8)	$\chi^2 = 0.005$	0.943
Switch + Augmentation								
Leptin, low:high	10 (38.5):16 (61.5)	16 (59.3):11 (40.7)	$\chi^2 = 2.292$	0.130	4 (66.7):2 (33.3)	14 (45.2):17 (54.8)	$\chi^2 = 0.931$	0.335
Augmentation + Combination								
Leptin, low:high	18 (39.1):28 (60.9)	32 (55.2):26 (44.8)	$\chi^2 = 2.645$	0.104	7 (38.9):11 (61.1)	33 (45.2):40 (54.8)	$\chi^2 = 0.234$	0.629
Switch + Augmentation + Combination								
Leptin, low:high	5 (55.6):4 (44.4)	3 (25.0):9 (75.0)	$\chi^2 = 2.036$	0.154	9 (60.0):6 (40.0)	14 (32.6):29 (67.4)	$\chi^2 = 3.500$	0.061

Values are presented as number (%).

Supplementary Table 4. Baseline characteristics by BMI in patients with depressive disorders

Variable	Up to 12-week treatment (n = 1,085)			
	BMI < 23 (n = 524)	BMI 23 (n = 561)	Statistical coefficients[a]	p value
Age (yr)	55.6 ± 15.7	58.2 ± 14.0	$t = -2.874$	0.004
Sex, female	375 (71.6)	369 (65.8)	$\chi^2 = 4.214$	0.040
Education (yr)	9.6 ± 4.7	8.6 ± 4.8	$t = 3.579$	< 0.001
Marital status, unmarried	165 (31.5)	161 (28.7)	$\chi^2 = 1.003$	0.317
Living alone	76 (14.5)	91 (16.2)	$\chi^2 = 0.614$	0.433
Religious observance	281 (53.6)	326 (58.1)	$\chi^2 = 2.211$	0.137
Unemployed status	148 (28.2)	168 (29.9)	$\chi^2 = 0.380$	0.537
Monthly income, < 2,000 USD	299 (57.1)	348 (62.0)	$\chi^2 = 2.781$	0.095
Major depressive disorder	444 (84.7)	480 (85.6)	$\chi^2 = 0.147$	0.701
Melancholic feature	82 (15.6)	80 (14.3)	$\chi^2 = 0.411$	0.521
Atypical feature	37 (7.1)	32 (5.7)	$\chi^2 = 0.838$	0.360
Age at onset (yr)	51.0 ± 17.3	52.7 ± 16.1	$t = -1.707$	0.088
Duration of illness (yr)	4.6 ± 8.3	5.5 ± 9.6	$t = -1.589$	0.112
Recurrent depression	273 (52.1)	296 (52.8)	$\chi^2 = 0.048$	0.827
Number of depressive episodes	1.1 ± 1.5	1.1 ± 1.5	$t = -0.622$	0.534
Duration of present episode (mo)	7.2 ± 10.1	7.6 ± 10.7	$t = -0.652$	0.514
Family history of depression	82 (15.6)	76 (13.5)	$\chi^2 = 0.962$	0.327
History of suicide attempt	44 (8.4)	51 (9.1)	$\chi^2 = 0.163$	0.686
Hamilton Depression Rating Scale	21.1 ± 4.3	20.5 ± 4.0	$t = 2.341$	0.019
Hospital Anxiety & Depression Scale-anxiety subscale	12.0 ± 4.0	11.6 ± 4.1	$t = 1.923$	0.055
EuroQol-5D	9.0 ± 1.5	8.9 ± 1.5	$t = 1.448$	0.148
Social and Occupational Functional Assessment Scale	55.9 ± 7.5	56.0 ± 7.5	$t = -0.347$	0.729

Values are presented as mean ± standard deviation or number (%).

BMI, body mass index.

[a]Independent two sample t test or χ^2 test, as appropriate.

Supplementary Table 5. Baseline BMI by 12-week and 12-month remission status

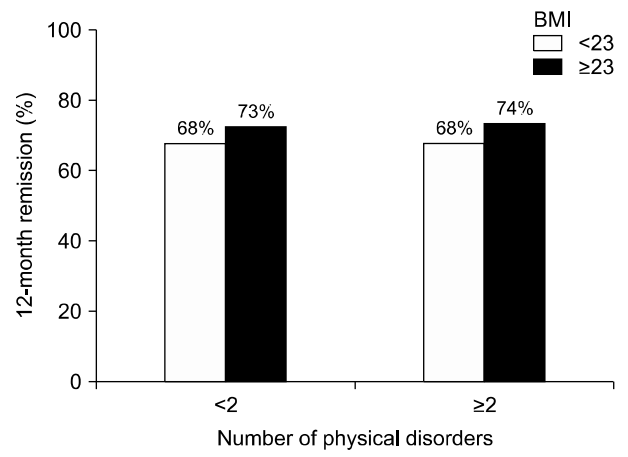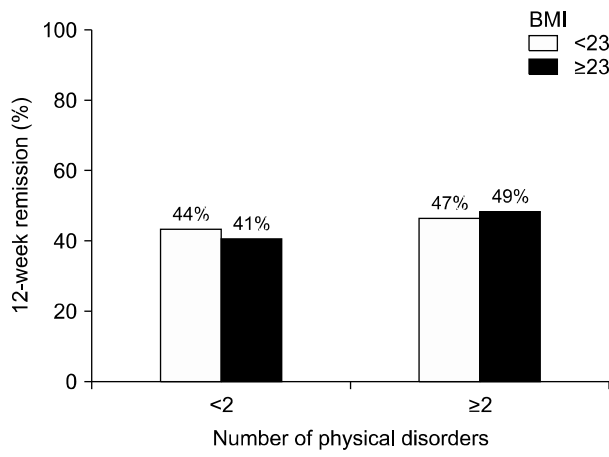| Exposure variable	Up to 12-week treatment (n = 1,085)				Up to 12-month treatment (n = 883)			
	Non-remission (n = 595)	Remission (n = 490)	Statistical coefficients[a]	p value	Non-remission (n = 258)	Remission (n = 625)	Statistical coefficients[a]	p value
BMI (kg/m^2)								
Median (IQR)	23.1 (4.3)	23.1 (4.0)	U = 145,127.5	0.900	22.80 (4.0)	23.4 (4.2)	U = 72,731.0	0.022
< 23; ≥ 23, n (%)	287 (48.2):308 (51.8)	237 (48.4):253 (51.6)	χ^2 = 0.002	0.965	135 (52.3):123 (47.7)	283 (45.3):342 (54.7)	χ^2 = 3.636	0.057

BMI, body mass index; IQR, interquartile range.
[a]Mann–Whitney U test or χ^2 test, as appropriate.

Supplementary Table 6. Multivariate analysis examining the individual and interactive effects of baseline BMI and the number of physical disorders on the 12-week and 12-month remission

Exposure variable	12-week remission		12-month remission	
	Individual effect	Interactive effect	Individual effect	Interactive effect
BMI (≥ 23 vs. < 23)	0.961 (0.753−1.227)	0.695 (0.324−1.488)	1.312 (0.978−1.029)	1.226 (0.487−3.084)
Number of physical disorders (≥ 2 vs. < 2)	1.151 (0.888−1.493)	0.902 (0.417−1.952)	1.011 (0.738−1.385)	0.974 (0.385−2.462)
Leptin × number of physical disorders		0.801 (0.494−1.299)		0.953 (0.530−1.713)

BMI, body mass index; HAMD, Hamilton Depression Rating Scale.
All data were adjusted for age, sex, education, and HAMD.

Supplementary Fig. 1. Rates of remission according to baseline BMI and the number of physical disorders. BMI, body mass index.