

Table S1. Demographic overview of drug-specific subsamples. Detailed drug-specific demographics for amitriptyline, mirtazapine, sertraline and venlafaxine for week 1 and week 7.

Week 1 (Baseline)	N	Mean \pm SD (range)	N	Mean \pm SD (range)
	Amitriptyline		Mirtazapine	
Included patients	68		110	
Age [years]	68	47.50 \pm 13.06 (18-73)	110	48.75 \pm 16.61 (18-80)
male/female	34/34		46/64	
Duration of disorder [years]	66	12.41 \pm 10.94 (0.3-40)	106	14.18 \pm 13.62 (0.3-60)
Dose [mg]	68	74.26 \pm 43.33 (25-225)	110	26.18 \pm 12.54 (3-60)
Serum concentration [ng/ml]	45	66.49 \pm 51.65 (0-236)	70	34.97 \pm 20.32 (6-110)
Normal dose range [mg]		50-150		15-45
Normal serum levels [ng/ml]		80-200		30-80
HDRS-21 Baseline	68	24.27 \pm 7.53 (7-39)	110	26.85 \pm 7.52 (9-46)
HDRS-21 Out	67	12.42 \pm 7.25 (2-33)	109	10.14 \pm 6.60 (0-27)
Responder/Nonresponder (Out)	37/29		71/37	
HDRS anxiety-somatization factor Baseline	68	6.60 \pm 2.91 (1-13)	110	7.27 \pm 3.16 (0-15)
HDRS-21 anxiety-somatization factor Out	82	3.23 \pm 2.43 (0-9)	108	2.99 \pm 2.51 (0-10)
aMDD/naMDD Baseline	41/27		68/42	
aMDD/naMDD Out	9/57		12/96	
	Sertraline		Venlafaxine	
Included patients	33		154	
Age [years]	33	52.33 \pm 14.93 (19-75)	154	43.60 \pm 14.32 (18-80)
male/female	12/21		65/89	
Duration of disorder [years]	32	14.63 \pm 13.81 (0.5-49)	150	14.14 \pm 11.95 (0.4-48)
Dose [mg]	33	78.94 \pm 41.52 (5-200)	154	162.25 \pm 87.63 (37.5-375)
Serum concentration [ng/ml]	19	30.21 \pm 18.42 (4-73)	108	93.81 \pm 124.40 (0-616)
Normal dose range [mg]		50-200		75-225
Normal serum levels [ng/ml]		10-150		100-400
HDRS-21 Baseline	33	25 \pm 7.56 (11-39)	154	24.39 \pm 7.66 (7-46)
HDRS-21 Out	33	11.72 \pm 7.29 (1-33)	150	9.97 \pm 6.35 (0-27)
Responder/Nonresponder (Out)	18/15		101/45	
HDRS-21 anxiety-somatization factor Baseline	33	6.85 \pm 2.85 (1-14)	151	6.40 \pm 2.88 (0-14)
HDRS-21 anxiety-somatization factor Out	33	3.18 \pm 2.49 (0-10)	148	2.45 \pm 2.34 (0-10)
aMDD/naMDD Baseline	17/16		74/77	

aMDD/naMDD Out	4/29		9/139	
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Week 7 (Out)	N	Mean \pm SD (range)	N	Mean \pm SD (range)
	Amitriptyline		Mirtazapine	
Included patients	84		98	
Age [years]	84	46.90 \pm 13.49 (18-75)	98	48.81 \pm 16.59 (18-80)
male/female	39/45		43/55	
Duration of disorder [years]	82	12.13 \pm 12.83 (0.5-60)	95	14.20 \pm 13.34 (0-60)
Dose [mg]	84	107.74 \pm 44.09 (25-225)	98	35.10 \pm 12.26 (7.5-60)
Serum concentration [ng/ml]	71	82.44 \pm 32.52 (14-151)	72	42.60 \pm 17.12 (0-94)
Normal dose range [mg]		50-150		15-45
Normal serum levels [ng/ml]		80-200		30-80
HDRS-21 Baseline	84	25.96 \pm 7.47 (7-43)	98	26.29 \pm 7.45 (9-46)
HDRS-21 Out	83	12.77 \pm 7.04 (2-38)	97	9.39 \pm 6.54 (0-27)
Responder/Nonresponder	47/37		72/26	
HDRS-21 anxiety-somatization factor Baseline	84	6.93 \pm 2.61 (1-13)	98	7.19 \pm 3.07 (1-14)
HDRS-21 anxiety-somatization factor Out	82	3.43 \pm 2.43 (0-10)	97	2.96 \pm 2.48 (0-10)
aMDD/naMDD Baseline	52/32		59/39	
aMDD/naMDD Out	11/72		10/87	
		Sertraline	Venlafaxine	
Included patients	35		166	
Age [years]	35	47.37 \pm 16.17 (18-75)	166	43.62 \pm 14.48 (18-76)
male/female	12/23		67/99	
Duration of disorder [years]	35	11.09 \pm 9.93 (0.2-41)	162	13.75 \pm 11.97 (0.4-49)
Dose [mg]	35	145.71 \pm 63.66 (25-250)	166	258.89 \pm 98.89 (37.5-525)
Serum concentration [ng/ml]	33	69.12 \pm 55.49 (0-242)	152	159.39 \pm 144.05 (7-589)
Normal dose range		50-200		75-225
Normal serum levels [ng/ml]		10-150		100-400
HDRS-21 Baseline	35	26.83 \pm 7.40 (9-42)	166	24.54 \pm 7.68 (7-46)
HDRS-21 Out	35	11.31 \pm 6.41 (1-25)	163	10.23 \pm 6.50 (0-27)
Responder/Nonresponder	20/15		106/60	
HDRS-21 anxiety-somatization factor Baseline	35	7.71 \pm 2.99 (1-14)	163	6.31 \pm 2.78 (1-14)
HDRS-21 anxiety-somatization factor Out	34	3.12 \pm 2.40 (0-10)	161	2.58 \pm 2.42 (0-10)
aMDD/naMDD Baseline	22/13		79/84	
aMDD/naMDD Out	4/31		13/148	

N, number of patients; SD, standard deviation; HDRS, Hamilton Depression Rating Scale; aMDD, anxious depressed patients; naMDD, non-anxious depressed patients.

Table S2. Overview of all administered psychiatric drugs.

Psychiatric Drug	N (Dose)	N (Concentration)	Psychiatric Drug	N (Dose)	N (Concentration)
Antidepressants			Antipsychotics		
Venlafaxine	166	152	Quetiapine	162	131
Mirtazapine	98	72	Aripiprazole	26	20
Amitriptyline	84	71	Risperidone	23	12
Sertraline	35	32	Olanzapine	19	17
Bupropion	29	16	Promethazine	3	3
Escitalopram	22	20	Melperone	3	2
Clomipramine	16	14	Pipamperone	3	2
Trazodon	15	12	Perazine	2	0
Doxepin	13	13	Ziprasidone	1	1
Duloxetine	13	9	Clozapine	1	0
Milnacipran	5	4	Antiepileptics		
Nortriptyline	5	4	Pregabalin	33	17
Trimipramine	4	3	Lamotrigine	14	12
Fluoxetine	1	1	Valproic Acid	13	10
Maprotiline	1	1	Gabapentine	6	3
			Levetiracetam	1	1
			Zonisamide	1	1
			Topiramate	1	0

N, number of dose and serum concentration data available for the evaluation.