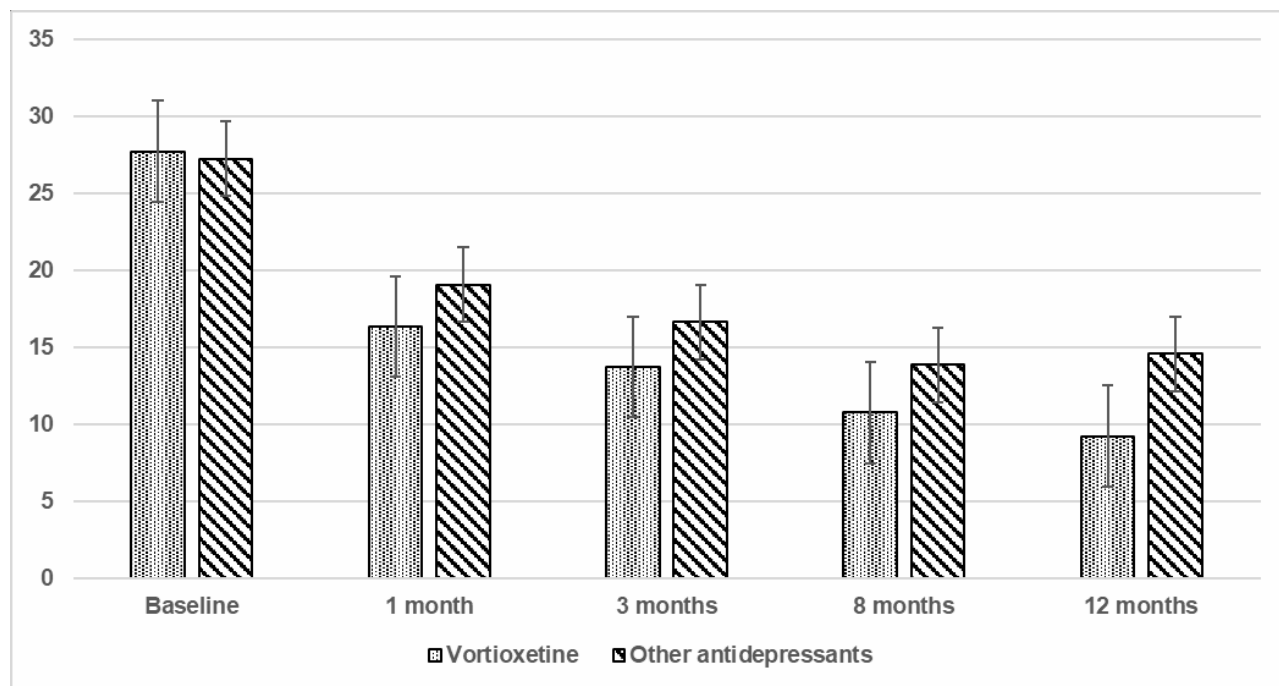


Supplementary Material

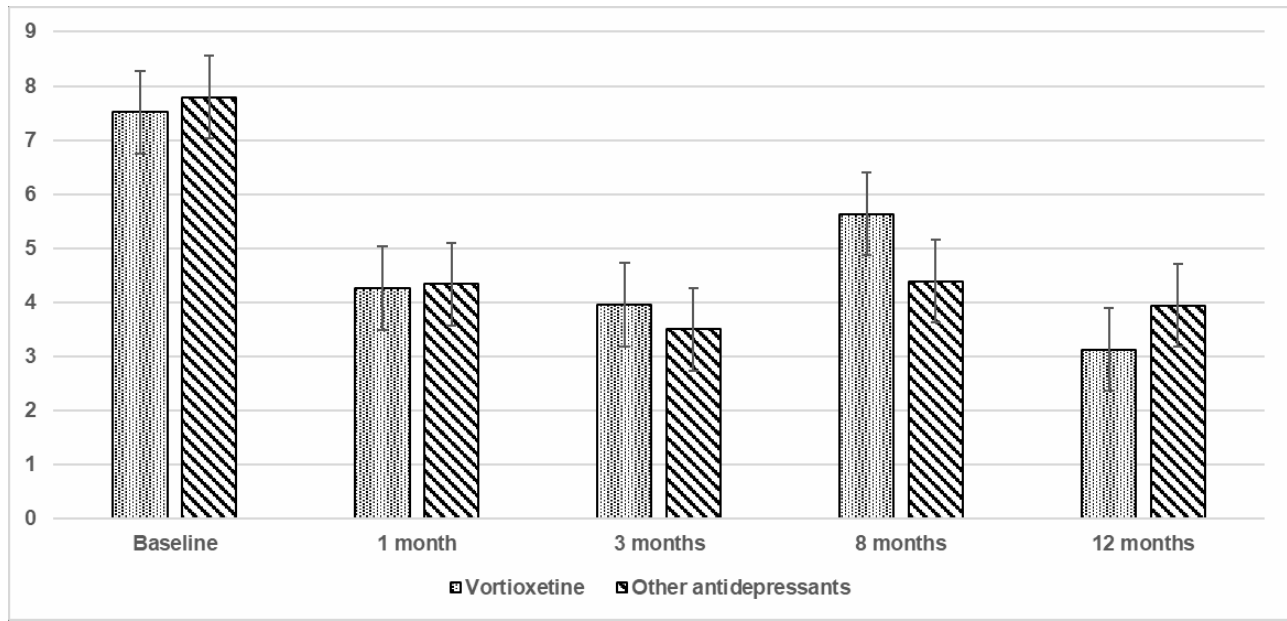
Vortioxetine vs. Other Antidepressants in Patients with Major Depressive Episode with or Without Substance Use Disorder

Georgios D. Kotzalidis^{1,2,*}, Ginevra Lombardozi^{1,3}, Marta Matrone^{1,4}, Emanuela Amici¹, Filippo Perrini^{1,5}, Ilaria Cuomo⁶ and Sergio De Filippis¹

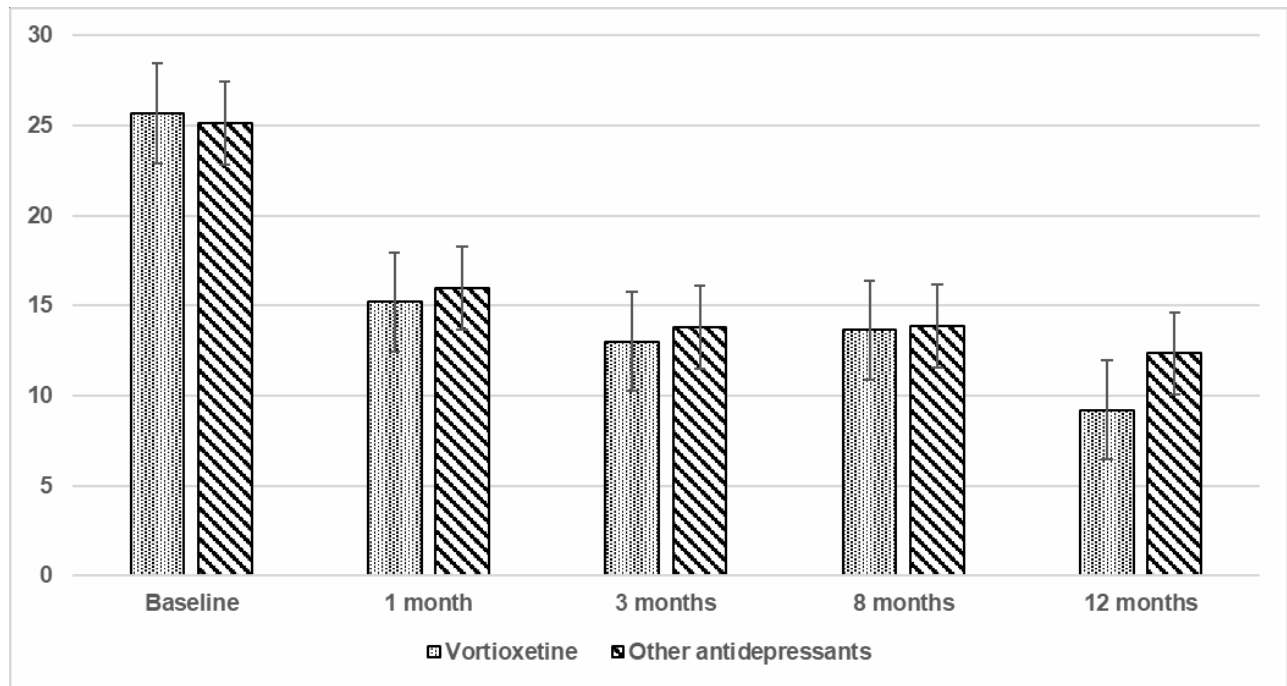
¹Clinica Villa von Siebenthal Neuropsychiatric Hospital, Genzano di Rona, Via della Madonnina 1, 00045 Genzano di Roma RM, Italy; ²NESMOS Department, Faculty of Medicine and Psychology, Sapienza University of Rome, Via di Grottarossa 1035-1039, 00189 Roma RM, Italy; ³U.O.C. Psichiatria e Psicologia Clinica, Dipartimento Benessere della Salute Mentale e Neurologica, Dentale e degli Organi Sensoriali, Tor Vergata University, Rome, Italy; ⁴Department of Neuroscience and Reproductive and Odontostomatologic Sciences, Federico II University, Naples, Italy; ⁵Istituto A.T. Beck-Diagnostic Centre, Research and Training in Cognitive-Behavioral Psychotherapy, Rome, Italy; ⁶UOC I Distretto ASL Roma 1, C.C. Regina Coeli, Rome, Italy



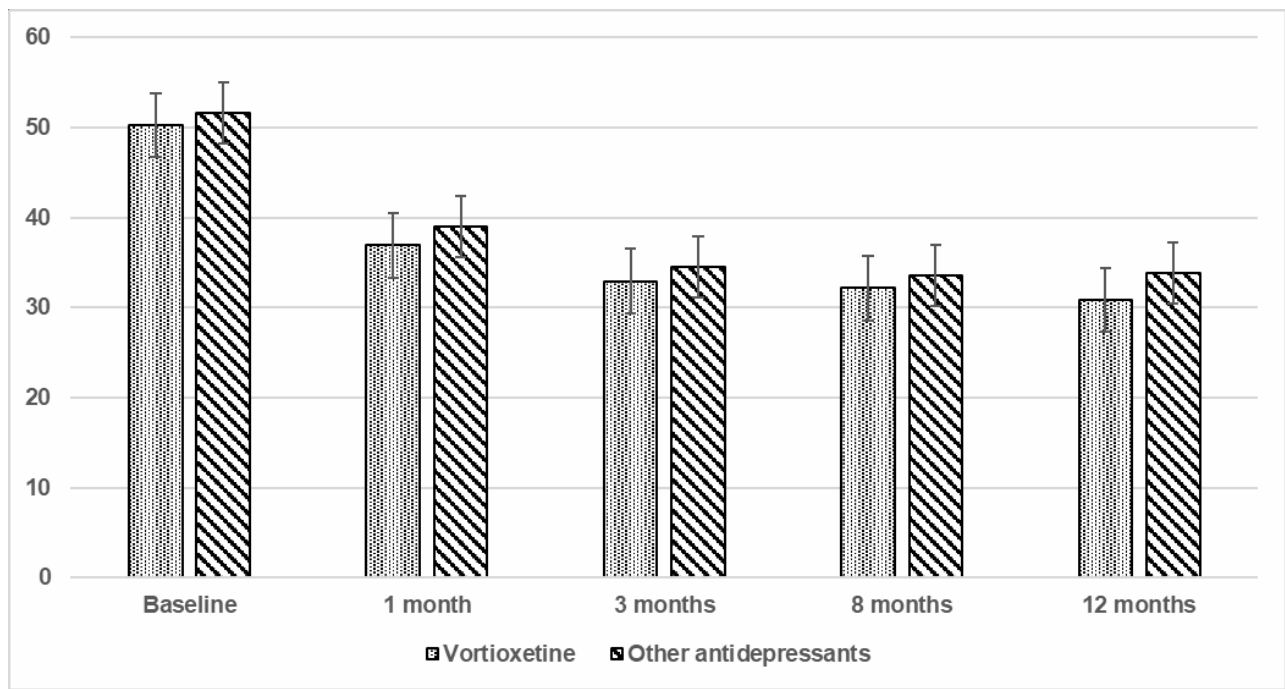
Suppl. Fig. 1. Time course of MADRS scores in the two treatment groups. In no timepoint did the two treatments differ from one another significantly.



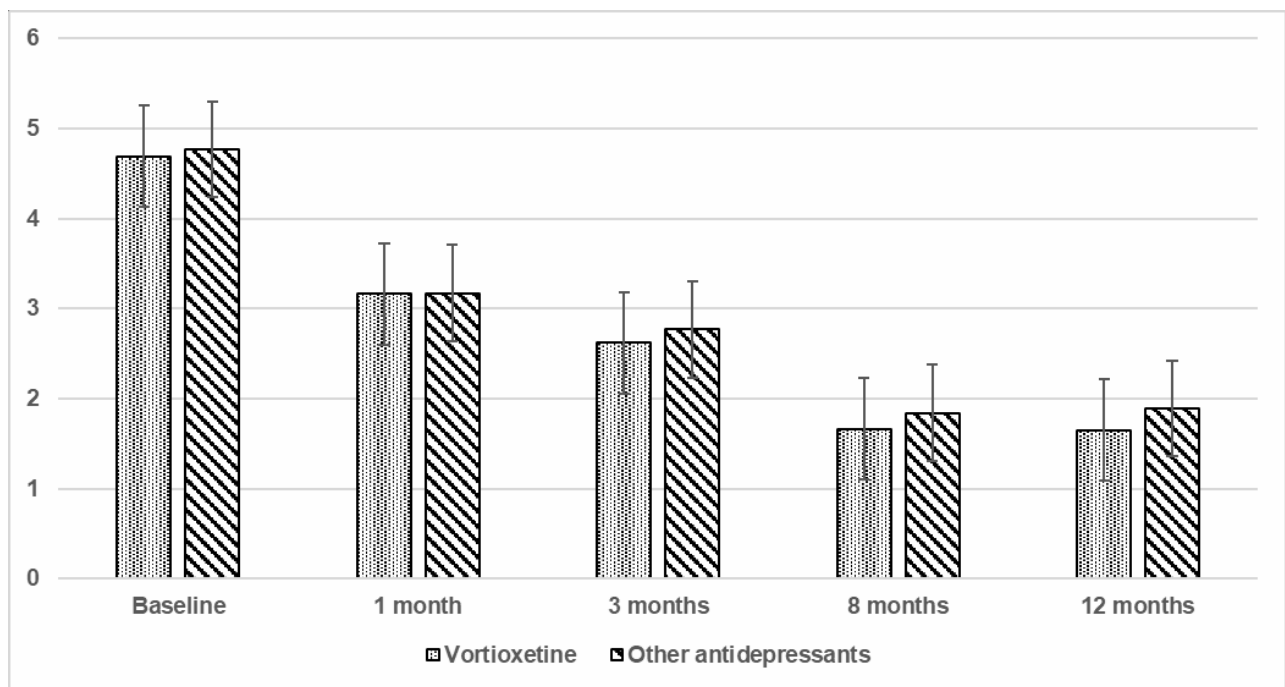
Suppl. Fig. 2. Time course of YMRS scores in the two treatment groups; between-groups differences were not significant at all timepoints.



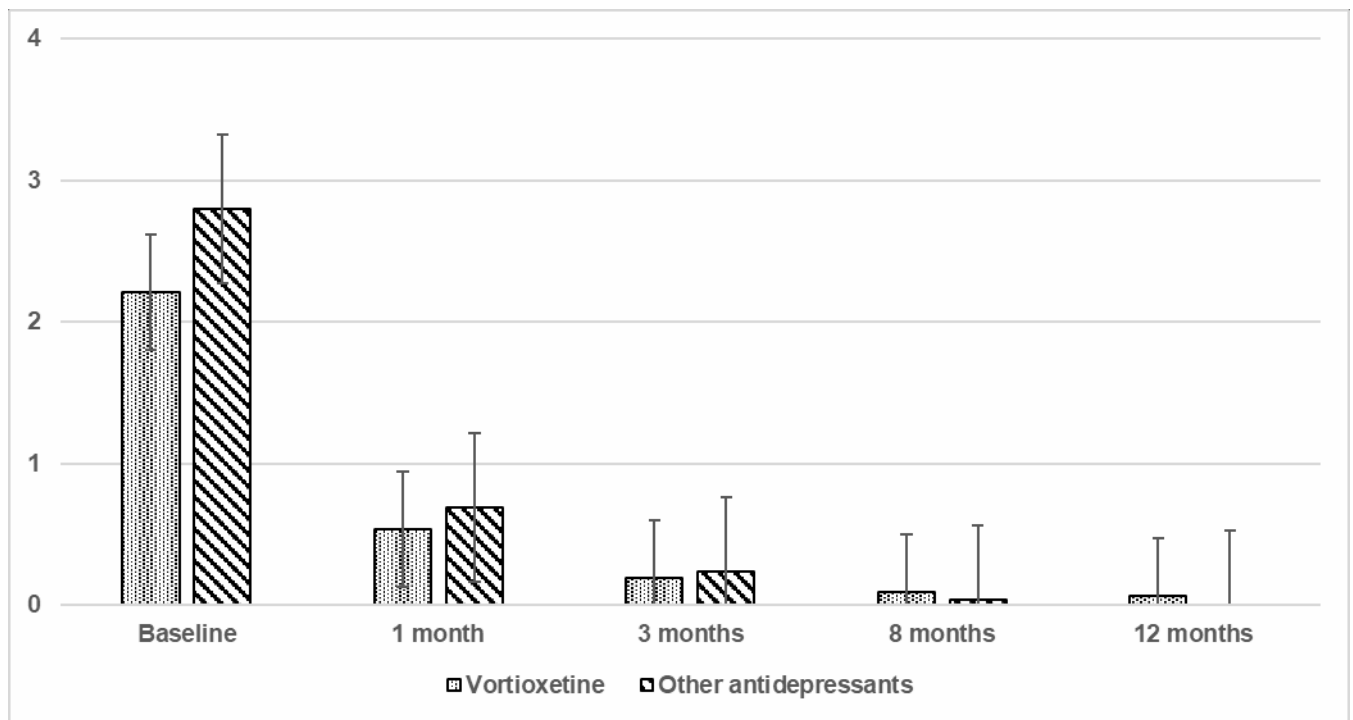
Suppl. Fig. 3. Time course of HAM-A scores in the two treatment groups; between-groups differences were not significant at all timepoints.



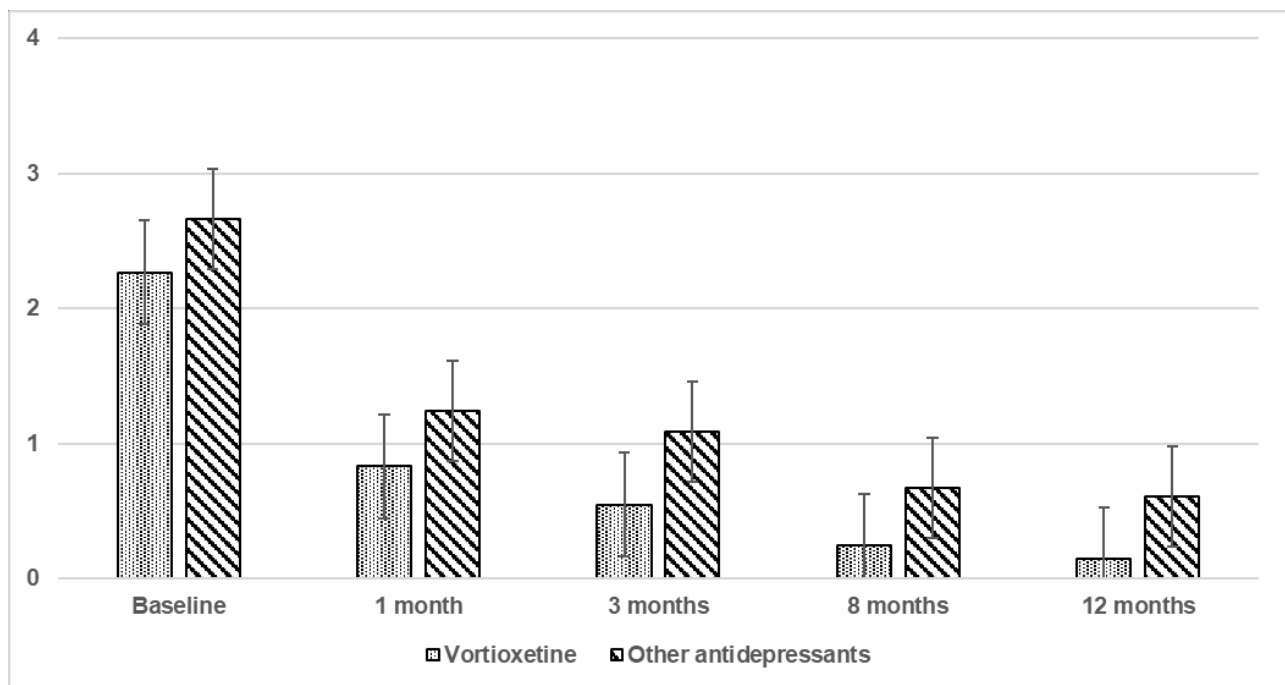
Suppl. Fig. 4. Time course of BPRS scores in the two treatment groups; between-groups differences were not significant.



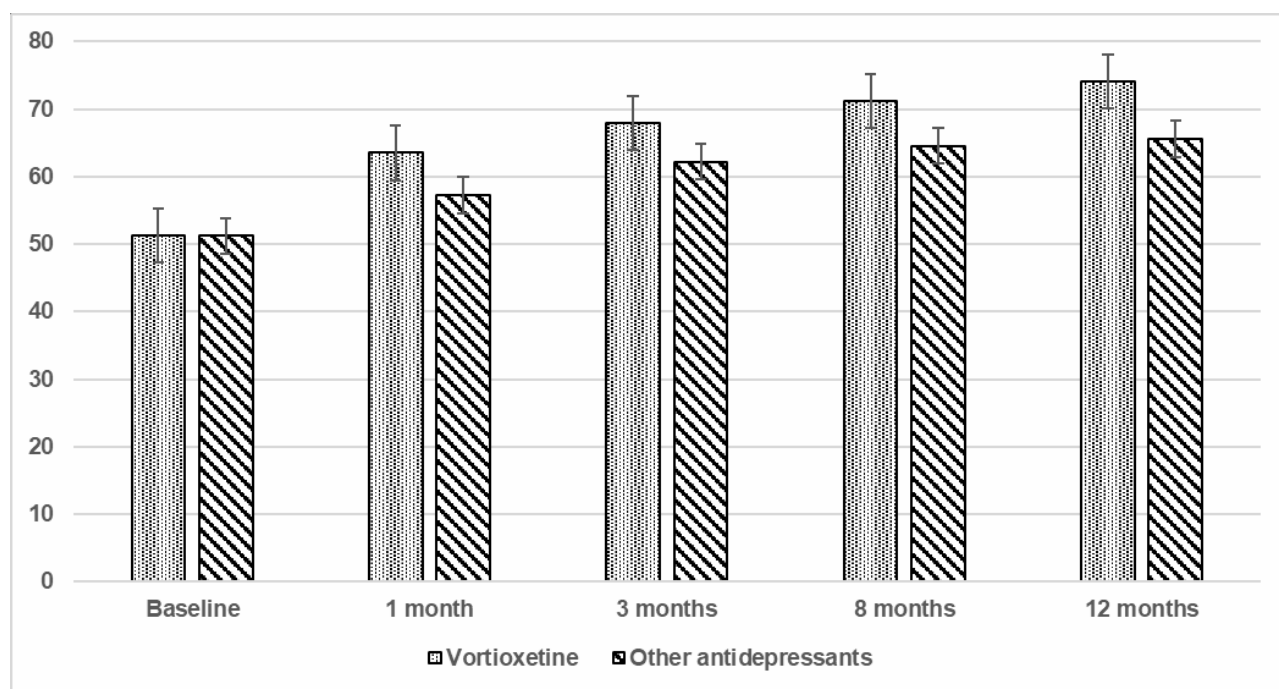
Suppl. Fig. 5. Time course of CGI-S scores in the two treatment groups; the two groups showed a significant reduction in severity, without differing significantly from one another.



Suppl. Fig. 6. Time course of C-SSRS scores in the two treatment groups; the two groups showed a significant reduction in suicidal scores, but did not differ significantly from one another.



Suppl. Fig. 7. Time course of VAScrav scores in the two treatment groups. With vortioxetine, scores dropped more steeply than with other antidepressants from 1 to 12 months, although the two treatments did not differ significantly.



Suppl. Fig. 8. Time course of WHOQOL scores in the two treatment groups. The two treatments did not differ on their scores on quality-of-life.

Supplementary Table 1. Response/remission rates according to the CGI-S 1 or 2/1 and MADRS $\geq 60\%$ drop from BL and final MADRS score ≤ 10 /MADRS < 7 criteria per treatment group and SUD comorbidity.

Treatment group (N)	Criterion	Responders, N (%)	Remitters, N (%)
Vortioxetine (N=126)	CGI-S	99 (78.57%)	77 (61.11%)
	MADRS	87 (69.05%)	67 (53.17%)
	Both	70 (55.56%)	59 (46.82%)
NonSUD (N=84)	CGI-S	64 (76.19%)	48 (57.14%)
	MADRS	56 (66.67%)	42 (50%)
	Both	53 (63.10%)	37 (44.04%)
SUD (N=42)	CGI-S	35 (83.33%)	29 (69.04%)
	MADRS	31 (73.81%)	25 (59.52%)
	Both	30 (71.43%)	22 (52.38%)
Other antidepressants (ADs) (N=100)	CGI-S	75 (75%)	51 (51%)
	MADRS	36 (36%)	15 (15%)
	Both	36 (36%)	12 (12%)
NonSUD (N=62)	CGI-S	44 (70.97%)	31 (50%)
	MADRS	23 (37.10%)	12 (19.35%)
	Both	33 (53.23%)	16 (25.81%)
SUD (N=38)	CGI-S	31 (81.58%)	20 (52.63%)
	MADRS	13 (34.21%)	3 (7.89%)
	Both	13 (34.21%)	2 (5.26%)

Abbreviations: BL, baseline; CGI-S, Clinical Global Impressions-Severity; MADRS, Montgomery-Åsberg Depression Rating Scale; SUD, substance use disorder.

Supplementary Table 2. Effect size (expressed as Cohen's *d*) based on CGI-S score variations between baseline and end-point according to treatment group and SUD comorbidity.

Treatment group	Co-	Cohen's clas-		Sawilowsky's
Vortioxetine (<i>N</i> =126)	4.64	L		H
NonSUD (<i>N</i> =84)	3.51	L		H
SUD (<i>N</i> =42)	4.23	L		H
Other ADs (<i>N</i> =100)	3.09	L		H
NonSUD (<i>N</i> =62)	3.00	L		H
SUD (<i>N</i> =38)	3.25	L		H
NonSUD, both groups	3.00	L		H
SUD, both groups	3.70	L		H

Abbreviations: ADs, antidepressants; CGI-S, Clinical Global Impressions-Severity; SUD, substance use disorder.