

## SUPPLEMENTARY.

**Table S1. Main characteristics of the selected articles for the evaluation of the use of melatonergic antidepressants in comorbid depression and alcohol dependence syndrome conditions**

Author, year	Sample characteristics	Affective disorder	Affective disorder assessment criteria	Details of medication treatment	Concomitant therapy	Duration of follow-up	Primary outcomes	Secondary outcomes	Adverse events	Number of dropouts
Vinnikova et al., 2021	n=175 80% men, mean age 45.3±4.3 years	8% of participants: recurrent affective disorder or F42.x, 92% of participants: depressive disorders due to withdrawal syndrome of ADS	ICD-10	45 participants received Fluvoxamine 50 to 200 mg in the evening, 1–2 times a day	Not specified	30 days	MADRS: ↓p <0.001 (day 7), ↓p <0.01 (day 14) HADS: ↓p <0.001 (day 7)	VAS: ↓p <0.01 (day 7), ↓p <0.01 (day 30)	Not detected	0
Zastrozhin et al., 2020	n=118 100% men, mean age 36.95±8.92 years	F32.x or F34.0	ICD-10	30 participants in the main group and 45 participants in the control group received Fluvoxamine at 100 [50; 150] mg/day; mean dose of 121.7 ± 40.9 mg/day and 136.7 ± 43.2 mg/day, respectively	Some participants received Carbamazepine 200 [100; 200] mg/day	16 days	HAM-D: ↓ in the main and control groups (day 9)  ↓ in the main group, ↑ in the control group (day 16)*	PACS: ↓ on days 9 and 16 in the main and control groups*	UKU ↑ in the main and control groups (day 9), ↓ in the main group, ↑ in the control group (day 16)*	No data
Zastrozhin, Skryabin, Smirnov, Zastrozhina, Grishina, et al., 2021	n=45 100% men, mean age 36.44±9.96 years	Not specified	N/A	Fluvoxamine 100 [50; 150] mg/day	Some participants received Phenazepam	16 days	HAM-D: ↓ on days 9 and 16 of administration* HADS: ↓ on days 9 and 16 of administration* BDI: ↓ on days 9 and 16 of administration*	PACS: ↓ on days 9 and 16 of administration* VAS: ↓ on days 9 and 16 of administration* SoPA: ↓ on days 9 and 16 of administration* Lower efficacy and a higher number of adverse events were found with Fluvoxamine in participants with the GA genotype of the <i>CYP2D6</i> 1846G >A polymorphism	UKU: ↑ on day 9 of administration; ↓ in the group of patients with the GG genotype, ↑ in the group with the GA genotype on day 16*	No data
Zastrozhin, Skryabin, Smirnov, Zastrozhina, Kaverina, et al., 2021	n=105 100% men, mean age 37.5±13.2 years	F32.x	ICD-10	Fluvoxamine Mean dose 117.6 ± 44.3 mg/day	Not specified	8 weeks	No data on changes in the HAM-D score	No data No relationship between the efficacy and safety of Fluvoxamine and the genotype of the participants was found	No data on changes in UKU	No data

Author, year	Sample characteristics	Affective disorder	Affective disorder assessment criteria	Details of medication treatment	Concomitant therapy	Duration of follow-up	Primary outcomes	Secondary outcomes	Adverse events	Number of dropouts
Zastrozhin et al., 2020	n=96 100% men, mean age 39.95±15.4 years	F32.x	ICD-10	Fluvoxamine Mean dose 125.0 ± 50.3 mg/day	Not specified	16 days	HAM-D: ↓ on days 9 and 16 of administration* HADS: ↓ on days 9 and 16 of administration*	PACS: ↓ on days 9 and 16 of administration* VAS: ↓ on days 9 and 16 of administration* Fluvoxamine is more effective and safer in participants with the GG genotype	UKU: ↑ on days 9 and 16 of administration*	No data
Zastrozhin, Smirnov et al., 2018	n=117 100% men, mean age 34.32±8.16 years	F32.x	ICD-10	Fluvoxamine 100 [50; 150] mg/day	Not specified	16 days	HAM-D: ↓ on days 9 and 16 of administration* HADS: ↓ on days 9 and 16 of administration*	PACS: ↓ on days 9 and 16 of administration* VAS: ↓ on days 9 and 16 of administration* Increased activity of the CYP2D6 isoenzyme reduces the effectiveness of fluvoxamine; CYP2D6 polymorphism affects the safety profile	UKU: ↑ on days 9 and 16 of administration*	No data
Zastrozhin, Sorokin et al., 2018	n=118 100% men, mean age 35.95±8.92 years	F32.x or F34.0	ICD-10	30 participants in the main group and 45 participants in the control group received Fluvoxamine at 100 [50; 150] mg/day.	Some participants received Carbamazepine 200 [100; 200] mg/day	16 days	HADS: ↓ on days 9 and 16 of administration* HAM-D: ↓ on day 9 of administration; ↓ on day 16 of administration in the main group, ↑ in the control group* BDI: ↓ on days 9 and 16 of administration*	PACS: ↓ on days 9 and 16 of administration* VAS: ↓ on days 9 and 16 of administration* SoPA: ↓ on day 9 in both groups*, ↓ on day 16 in the main and ↑ in the control group*	UKU: ↓ on day 9 of administration, ↑ on day 16 of administration in the main group, ↑ in the control group*	No data
Zastrozhin, Antonenko et al., 2018	n=45 100% men, mean age 36.44±9.96 years	Not specified	N/A	Fluvoxamine 100 [50; 150] mg/day	Not specified	16 days	HADS: ↓ on day 9 in the GG genotype group and ↑ in the GA genotype group, ↑ on day 16 of administration in both groups* HAM-D: ↑ on day 9 of administration and ↓ on day 16 in both groups*	PACS: ↓ on days 9 and 16 of administration* VAS: ↓ on day 9 of administration and ↑ on day 16 of administration* Gene polymorphism SoPA: ↑ on day 9 in both groups*, ↓ on day 16 in both groups*  CYP2C19*3 does not affect the efficacy and safety of fluvoxamine	UKU: ↑ on day 9 of administration, ↓ on day 16 in both groups*	No data

Note: ADS — Alcohol Dependence Syndrome; ICD-10 — International Classification of Diseases 10<sup>th</sup> Revision; F42.x — Obsessive-Compulsive Disorder; MADRS — Montgomery-Åsberg Depression Rating Scale; HADS — Hospital Anxiety and Depression Scale; VAS — Visual Analogue Scale for Alcohol Craving; F32.x — Depressive Episode; F34.0 — Cyclothymia; HAM-D — Hamilton Depression Rating Scale; PACS — Penn Alcohol Craving Scale; UKU — Udvalg for Kliniske Undersøgelser Side Effect Rating Scale; BDI — Beck Depression Inventory; SoPA — Scale of Pathological Addiction; ↓ — decrease in indicators; ↑ — increase in indicators.\* The authors did not provide data on the statistical significance of changes within the groups, only the statistically significant difference between the main group and the control group.