

SUPPLEMENTARY TABLES

Supplementary Table 1. Baseline characteristics, morbidities, and physical or lifestyle traits of individuals with or without ICD10-defined F3X affective disorders diagnoses in NHS clinical records since 01.01.1990.

Baseline characteristics	Control (n = 348112)	Diagnosed with F3X (n = 62168)	p-value
Age at recruitment [years]*	56.68 ± 8.05	54.93 ± 8.14	0.00E+00
Sex (male) [%] (counts)	47.03 (163709)	34.34 (21351)	0.00E+00
Deaths [%] (counts)	3.31 (11514)	3.59 (2234)	2.76E-04
Suicides [%] (counts)	0.02 (63)	0.07 (39)	1.79E-10
Age at Death [years]*	70.57 ± 7.19	69.71 ± 7.56	2.50E-07
Morbidities			
Diabetes [%] (counts)	4.79 (16601)	6.30 (3891)	2.32E-56
Cancer [%] (counts)	7.27 (25165)	8.07 (4983)	1.99E-12
Fractured bones in last 5 years [%] (counts)	9.06 (31316)	11.42 (7033)	5.87E-76
Other serious medical condition/disability [%] (counts)	18.61 (63577)	26.94 (16185)	0.00E+00
Cardiovascular disease [%] (counts)	28.79 (99803)	31.27 (19331)	8.54E-36
Blood clots, DVT, bronchitis and emphysema [%] (counts)	3.64 (12634)	5.36 (3313)	2.63E-91
Traits			
Townsend deprivation index*	-1.41 ± 3.01	-0.85 ± 3.25	0.00E+00
Sleep duration [hours]*	7.15 ± 1.06	7.13 ± 1.32	4.26E-08
Smoking [PackYears]*	7.45 ± 14.74	9.98 ± 16.82	3.53E-275
Physical exercise [Summed MET minutes/ week]*	2688.81 ± 2716.01	2586.96 ± 2758.98	2.93E-14
Alcohol intake [weekly units]*	7.48 ± 8.86	6.62 ± 9.48	3.72E-107
BMI [kg/m ²]	27.26 ± 4.64	28.09 ± 5.36	0.00E+00

Suicides are included in the dataset. *Denotes mean ± standard deviation; p-values are obtained with two-tailed t-test for quantitative data and with chi-squared contingency test for categorical data. Abbreviations: DVT: deep vein thrombosis; BMI: body mass index; MET: metabolic equivalent of task.

Supplementary Table 2. Causes of death, conglomerated in ICD10 chapters, in individuals diagnosed with at least one F3X diagnosis since 01.01.1990 or control individuals in the UK Biobank.

Causes of death (IC10 chapters)	Control (n=348049)					Diagnosed with F3X (n= 62129)					Total deaths	p-value (control vs. F3X- diagnosed)
	Deaths	(% of deaths)	% males	Mean age of death	SD age death	Deaths	(% of deaths)	% males	Mean age of death	SD age death		
Certain infectious and parasitic diseases - ICD10 A00-B99	89	0.777%	47.191%	69.174	7.943	25	1.117%	50.990%	69.063	8.456	114	0.14
Neoplasms - ICD10 C00-D48	6023	52.575%	55.371%	69.617	7.047	919	41.063%	49.661%	68.741	7.229	6942	2.79E-23
Diseases of the blood - ICD10 D50-D99	31	0.271%	51.613%	69.316	8.554	4	0.179%	57.735%	71.522	4.091	35	0.58
Endocrine, nutritional and metabolic diseases - ICD10 E00-E99	132	1.152%	65.909%	70.154	7.333	29	1.296%	50.123%	67.154	9.386	161	0.64
Mental, Behavioral and Neurodevelopmental Diseases - ICD10 F00-F99	242	2.112%	60.331%	75.225	5.179	80	3.575%	50.253%	74.281	6.752	322	4.15E-05
Diseases of the nervous system - ICD10 G00-G99	643	5.613%	55.988%	73.129	6.679	188	8.400%	50.131%	73.332	6.157	831	5.63E-07
Diseases of the ear and mastoid process - ICD10 H60-H99	1	0.009%	0.000%	58.000		0	0.000%				1	0.36
Diseases of the circulatory system - ICD10 I00-I99	2324	20.286%	72.504%	70.775	7.105	441	19.705%	47.654%	69.742	7.000	2765	0.55
Diseases of the respiratory system - ICD10 J00-J99	739	6.451%	64.953%	72.063	6.161	199	8.892%	49.051%	70.712	6.769	938	3.54E-05
Diseases of the digestive system - ICD10 K00-K99	428	3.736%	71.963%	69.844	7.874	116	5.183%	50.030%	67.153	8.752	544	1.65E-03
Diseases of the skin and subcutaneous tissue - ICD10 L00-L99	16	0.140%	43.750%	69.313	9.894	3	0.134%	57.735%	72.249	3.547	19	0.81
Diseases of the musculoskeletal system - ICD10 M00-M99	58	0.506%	53.448%	71.498	6.627	17	0.760%	51.450%	71.626	9.175	75	0.18
Diseases of the genitourinary system - ICD10 N00-N99	83	0.725%	68.675%	71.467	7.590	18	0.804%	51.131%	73.764	6.654	101	0.79
Abnormal clinical and laboratory findings - ICD10 R00-R99	23	0.201%	73.913%	65.791	11.439	7	0.313%	53.452%	64.479	7.408	30	0.43
COVID19 - ICD10 U07.1	550	4.801%	68.545%	75.045	5.682	147	6.568%	50.030%	73.134	6.987	697	6.11E-04
Other special purpose codes non-COVID19 - ICD U00-U99	11	0.096%	72.727%	65.073	11.340	4	0.179%	57.735%	62.747	6.858	15	0.46
Self-inflicted - ICD10 X00-X99	63	0.550%	77.778%	60.975	9.000	41	1.832%	48.765%	58.974	7.333	104	3.93E-10
Total	11456	100%	61.129%	70.575	7.186	2238	100%	52.482%	69.713	7.555	13694	

Suicides are included in the dataset. *p*-values were calculated with chi-squared test.

Supplementary Table 3. Suicides in individuals with ICD10-defined F3X affective disorder diagnoses in National Health Service (NHS) clinical records since 01.01.1990 and prescribed lithium or other anti-psychotic drugs, or both.

	Suicides	Other deaths	Total individuals	% Suicides over other deaths	<i>p</i> value vs. lithium	<i>p</i> value vs. other anti-psychotic drugs
Lithium	0	19	348	0	NA	1
Other anti-psychotic drugs	5	164	1,717	2.91	1	NA
Both lithium and other anti-psychotic drug	2	19	203	9.85	0.488	0.173

Significance in proportion of deaths caused by suicides in individuals taking lithium, other anti-psychotic medications, or both, are calculated with chi-squared test.

Supplementary Table 4. Baseline characteristics, morbidities, most frequent ICD10 F3X diagnoses, and physical or lifestyle traits of individuals with ICD10-defined F3X affective disorders diagnoses taking lithium and matched subjects prescribed other anti-psychotic medications.

Baseline characteristics	Lithium users (n = 276)	Other anti- psychotic drug users (n = 552)	p-value
Age at recruitment [years]*	57.58 ± 7.51	56.85 ± 7.74	0.1963
Sex (male) [%] (counts)	40.94 (113)	40.22 (222)	0.8413
Deaths [%] (counts)	4.35 (12)	9.60 (53)	0.0081
Suicides [%] (counts)	0.00 (0)	0.18 (1)	0.4792
Age at Death [years]*	71.49 ± 4.93	70.38 ± 7.52	0.6330
Medication use			
Age at first drug use [years]*	53.08 ± 10.71	53.47 ± 11.48	0.6432
Length of drug use [years]*	16.56 ± 8.37	15.17 ± 8.52	0.0264
ICD10 F3X diagnoses			
F3X episodes per year (counts)	1.71 ± 3.21	3.56 ± 22.02	0.1650
Hypomania [F300]	39.49 (109)	35.14 (194)	0.2208
Bipolar affective disorder, unspecified [F319]	20.65 (57)	20.83 (115)	0.9517
Severe depressive episode with psychotic symptoms [F323]	6.52 (18)	6.16 (34)	0.8395
Depressive episode, unspecified [F329]	14.86 (41)	17.57 (97)	0.3226
Recurrent depressive disorder, current episode mild [F330]	26.45 (73)	25.54 (141)	0.7790
Comorbidities			
Diabetes [%] (counts)	4.71 (13)	4.89 (27)	0.9088
Cancer [%] (counts)	8.70 (24)	8.88 (49)	0.9309
Fractured bones in last 5 years [%] (counts)	7.97 (22)	8.88 (49)	0.6608
Other serious medical condition/disability [%] (counts)	50.00 (138)	51.27 (283)	0.7308
Cardiovascular disease [%] (counts)	23.19 (64)	25.36 (140)	0.4938
Blood clots, DVT, bronchitis and emphysema [%] (counts)	6.16 (17)	6.16 (34)	1.0000
Traits			
Townsend deprivation index*	-1.05 ± 3.21	-0.88 ± 3.39	0.4952
Sleep duration [hours]*	7.47 ± 1.37	7.64 ± 1.59	0.1388
Smoking [PackYears]*	8.50 ± 16.49	8.94 ± 17.39	0.7303
Physical exercise [Summed MET minutes/ week]*	1971.51 ± 2055.12	2379.31 ± 2748.37	0.0472
Alcohol intake [weekly units]*	6.20 ± 8.21	5.08 ± 8.21	0.0669
BMI [kg/m ²]	27.77 ± 4.67	27.94 ± 5.38	0.6588

Suicides are included in the dataset; *denotes mean ± standard deviation. *p*-values are obtained with two-tailed *t* test for quantitative data and with chi-squared contingency test for categorical data. Abbreviations: DVT: deep vein thrombosis; BMI: body mass index; MET: metabolic equivalent of task.

Supplementary Table 5. Causes of death, conglomerated in ICD10 chapters, in individuals diagnosed with at least one F3X diagnosis since 01.01.1990 and taking lithium or 1:2 propensity score matched individuals taking other anti-psychotic medications.

Causes of death (IC10 chapters)	Lithium users					Other anti-psychotic drug users					Total deaths	<i>p</i> -value (lithium vs. other anti- psychotic)
	Deaths	(% of deaths)	% males	Mean age of death	SD age death	Deaths	(% of deaths)	% males	Mean age of death	SD age death		
Certain infectious and parasitic diseases - ICD10 A00-B99	1	8.3%	0.0%	73.232		0	0.0%				1	0.39
Neoplasms - ICD10 C00-D48	5	41.7%	80.0%	71.422	5.201	20	35.1%	65.0%	68.324	6.772	25	9.20E-01
Mental, Behavioral and Neurodevelopmental Diseases - ICD10 F00-F99	0	0.0%				5	8.8%	80.0%	73.486	2.653	5	0.65
Diseases of the nervous system - ICD10 G00-G99	0	0.0%				7	12.3%	71.4%	75.840	3.739	7	4.50E-01
Diseases of the circulatory system - ICD10 I00-I99	4	33.3%	100.0%	71.071	7.587	9	15.8%	44.4%	70.474	5.489	13	0.31
Diseases of the respiratory system - ICD10 J00-J99	2	16.7%	100.0%	71.669	2.428	6	10.5%	50.0%	71.114	5.558	8	9.14E-01
Diseases of the digestive system - ICD10 K00-K99	0	0.0%				2	3.5%	50.0%	69.522	0.995	2	7.73E-01
COVID19 - ICD10 U07.1	0	0.0%				8	14.0%	75.0%	74.702	3.563	8	3.77E-01
Total	12	100.0%	62.1%	71.169	5.854	57	100.0%	83.3%	71.497	5.140	69	

Suicides are excluded from the dataset. *p*-values were calculated with chi-squared test.