

Supplement: Oral glucocorticoids and risk of psychiatric and suicidal behaviour outcomes: a population-based cohort study

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Table S1. Target trial emulation, indication cohorts

Component	Target trial specifications	Target trial emulation
Eligibility criteria	- Age 15-54 years old 1 January 2006 to November 30 2019. - Any autoimmune disorder cohort: first diagnosis of any autoimmune disorder 1 January 2006 to 30 November 2019. - Gastrointestinal autoimmune disorder cohort: first diagnosis of a gastrointestinal autoimmune disorder 1 January 2006 to 30 November 2019. - No glucocorticoid (H02) prescriptions within 180 days before the autoimmune diagnosis.	Same as target trial.
Treatment strategies	- Initiation of a glucocorticoid (H02) within 28 days of the autoimmune diagnosis then continuing to take the treatment for 52 weeks. - No initiation of a glucocorticoid within 28 days of the autoimmune diagnosis and then remaining off treatment for 52 weeks.	Same as target trial. Follow-up starts at the time an individual collects a prescription in individuals assigned as initiators at baseline. The number of days between the autoimmune diagnosis and the dispensation of a glucocorticoid prescription in initiators is randomly assigned to controls – the start of follow-up in controls occurs on this number of days after their autoimmune diagnosis.
Treatment assignment	At baseline, individuals are assigned to a strategy at random and are aware of their assigned strategy.	We classify individuals according to the strategy they are compatible with at baseline. Assignment of treatment strategy is assumed to be random within levels of: sex, age category, year of follow-up start, highest level of attained education of individual and their parents, highest income category between individual and parents, and diagnoses (anxiety, bipolar disorder, depression, schizophrenia spectrum disorders, substance use disorder, and a history of self-harm).
Outcomes	Unplanned specialist inpatient or specialist outpatient contacts for: Anxiety disorder ICD-10: F4 Bipolar disorder ICD-10: F25.0, F30, F31, F340 Depression ICD-10: F32, F33, F34 excl. F34.0, F38, F39	Same as for target trial.

	Schizophrenia spectrum disorders ICD-10: F2, excl. F25.0 Suicidal behaviour ICD-10: X60 - X84; Y10 - Y34	
Follow-up	Follow-up starts at randomization and ends at (whichever occurs first): • 52 weeks after randomization • Outcome • Death • Emigration	Same as for target trial.
Causal contrasts	1. Intention-to-treat effect at 14, 120, and 365 days of follow-up. 2. Per-protocol effect at 14, 120, and 365 days of follow-up.	Observational analog of intention-to-treat and per-protocol effect.
Analysis plan	Separate analyses are run for each outcome type. ITT: Individuals are assumed to remain on the treatment they are assigned at baseline throughout follow-up. Per-protocol: Individuals are censored when they cease adhering to the treatment they are assigned at baseline. To mitigate bias from this censoring, we apply IPW weighting for adherence to treatment using baseline confounders and any specialist outpatient or inpatient healthcare contact for any of the following over follow-up: alcohol use disorder, substance use disorder, depression, anxiety disorders, bipolar disorders, schizophrenia spectrum disorders, or self-harm (see outcome ICD-10 codes). Analyses of a specific psychiatric outcome do not consider healthcare contacts for that outcome type over follow-up as a confounder. We run subgroup analyses by baseline history of any of the events considered as outcomes (past psychiatric diagnosis) for the intention-to-treat analyses.	The same analyses with sequential emulation and additional adjustment for baseline covariates. Same subgroup analyses.

Table S2. ICD-10 codes for autoimmune disorders

	ICD-10	Name
	D68.61	Antiphospholipid syndrome
	D69.0	Allergic purpura
	D69.3	Immune thrombocytopenic purpura
	E05.0	Thyrotoxicosis with diffuse goiter
	E06.3	Autoimmune thyroiditis
	E31.0	Autoimmune polyglandular failure
	G04	Encephalitis, myelitis and encephalomyelitis
		Other systemic atrophy primarily affecting central nervous system in
	G13.1	neoplastic disease
	G35	Multiple sclerosis
	G61.0	Guillain-Barre syndrome
	G70.0	Myasthenia gravis
	I00-I02	Acute rheumatic fever
	A38.9	Scarlet fever
	K50-K51	Crohn's disease; Ulcerative colitis
	K74.3	Primary biliary cirrhosis
	K90.0	Celiac disease
	L10.0	Pemphigus vulgaris
	L12.0	Bullous pemphigoid
	L13	Dermatitis herpetiformis
	L40	Psoriasis
	L63	Alopecia areata
	M06	Rheumatoid arthritis
	M30.0-M30.1	Polyarteritis nodosa; Polyarteritis nodosa with lung involvement
	M30.3	Mucocutaneous lymph node syndrome
	M31.1	Thrombotic microangiopathy
	M31.5	Giant cell arteritis with polymyalgia rheumatica
	M31.7	Microscopic polyangiitis
	M32	Systemic lupus erythematosus
	M33.9	Dermatopolymyositis
	M34	Systemic sclerosis
	M35.0	Sjogren syndrome
	M35.1	Other overlap syndromes
	M35.2-M35.3	Behcet's disease; Polymyalgia rheumatica
	N00-N01	Acute nephritic syndrome; Rapidly progressive nephritic syndrome
	N03	Chronic nephritic syndrome
	N05	Unspecified nephritic syndrome
Gastrointestinal autoimmune disorders	K50	Crohn's disease
	K51	Ulcerative colitis
	K743	Primary biliary cirrhosis
	K900	Coeliac disease
	L13	Dermatitis herpetiformis

Table S3. Characteristics of the individuals followed since an autoimmune disorder diagnosis (indication cohort)

	Before IP weighting			After IP weighting		
	Initiator	Non-initiator	SMD ^a	Initiator	Non-initiator	SMD ^a
N	22621	264745		22122.4	264743.3	
Sex (%)	12132 (53.6)	159862 (60.4)	0.137	13051.7 (59.0)	158462.3 (59.9)	0.017
Age category (years) (%)			0.100			0.016
15-24	5735 (25.4)	58872 (22.2)		5080.1 (23.0)	59515.8 (22.5)	
25-34	5586 (24.7)	61036 (23.1)		5192.4 (23.5)	61377.2 (23.2)	
35-44	5348 (23.6)	70637 (26.7)		5742.4 (26.0)	70006.8 (26.4)	
45-54	5952 (26.3)	74200 (28.0)		6107.4 (27.6)	73843.4 (27.9)	
Year of follow-up start (%)			0.161			0.057
2006	2938 (13.0)	49008 (18.5)		3526.4 (15.9)	47857.3 (18.1)	
2007	1925 (8.5)	23579 (8.9)		1998.3 (9.0)	23497.2 (8.9)	
2008	1687 (7.5)	19847 (7.5)		1692.8 (7.7)	19839.4 (7.5)	
2009	1554 (6.9)	17283 (6.5)		1485.0 (6.7)	17353.8 (6.6)	
2010	1515 (6.7)	16031 (6.1)		1388.7 (6.3)	16164.4 (6.1)	
2011	1525 (6.7)	16171 (6.1)		1405.4 (6.4)	16303.1 (6.2)	
2012	1540 (6.8)	17015 (6.4)		1467.3 (6.6)	17094.8 (6.5)	
2013	1466 (6.5)	16412 (6.2)		1401.4 (6.3)	16469.7 (6.2)	
2014	1460 (6.5)	15840 (6.0)		1365.3 (6.2)	15937.6 (6.0)	
2015	1358 (6.0)	15363 (5.8)		1309.9 (5.9)	15404.3 (5.8)	
2016	1500 (6.6)	15236 (5.8)		1342.3 (6.1)	15419.2 (5.8)	
2017	1423 (6.3)	14997 (5.7)		1294.9 (5.9)	15126.2 (5.7)	
2018	1396 (6.2)	14402 (5.4)		1256.3 (5.7)	14554.1 (5.5)	
2019	1334 (5.9)	13561 (5.1)		1188.3 (5.4)	13722.0 (5.2)	
Family income category (%)			0.027			0.010
<0	210 (0.9)	2396 (0.9)		209.0 (0.9)	2401.5 (0.9)	
0	144 (0.6)	1368 (0.5)		120.9 (0.5)	1392.8 (0.5)	
0-p20	2107 (9.3)	23416 (8.8)		2011.3 (9.1)	23516.6 (8.9)	
p20-p80	13200 (58.4)	153796 (58.1)		12871.0 (58.2)	153849.6 (58.1)	
>p80	6960 (30.8)	83769 (31.6)		6910.1 (31.2)	83582.9 (31.6)	
Education category (%)			0.036			0.011
Primary	1647 (7.3)	18543 (7.0)		1585.5 (7.2)	18603.2 (7.0)	
Secondary	10204 (45.1)	116356 (44.0)		9781.9 (44.2)	116594.6 (44.0)	
Post-secondary	10294 (45.5)	124915 (47.2)		10318.3 (46.6)	124563.2 (47.1)	
NA	476 (2.1)	4931 (1.9)		436.6 (2.0)	4982.3 (1.9)	
Depression (%)	1398 (6.2)	17011 (6.4)	0.010	1418.3 (6.4)	16961.0 (6.4)	<0.001
Bipolar disorder diagnosis (%)	186 (0.8)	2778 (1.0)	0.024	210.6 (1.0)	2730.6 (1.0)	0.008
Anxiety disorder diagnosis (%)	1888 (8.3)	23454 (8.9)	0.018	1945.7 (8.8)	23348.2 (8.8)	0.001
Schizophrenia diagnosis (%)	169 (0.7)	2848 (1.1)	0.035	197.9 (0.9)	2779.3 (1.0)	0.016
Substance abuse disorder (excl. alcohol) diagnosis (%)	595 (2.6)	6743 (2.5)	0.005	570.4 (2.6)	6760.6 (2.6)	0.002
Suicide history (%)	770 (3.4)	8976 (3.4)	0.001	751.0 (3.4)	8978.6 (3.4)	<0.001

^a SMD: Standardized Mean Difference

Table S4. Characteristics of the individuals followed since a gastrointestinal autoimmune disorder diagnosis (indication cohort)

	Before IP weighting			After IP weighting		
	Initiator	Non-initiator	SMD ^a	Initiator	Non-initiator	SMD ^a
N	12360	83669		12155.4	83663.2	
Sex (%)	5400 (43.7)	47526 (56.8)	0.265	6639.9 (54.6)	46122.8 (55.1)	0.010
Age category (years) (%)			0.135			0.012
15-24	4148 (33.6)	28786 (34.4)		4143.3 (34.1)	28690.4 (34.3)	
25-34	3464 (28.0)	18856 (22.5)		2880.5 (23.7)	19439.3 (23.2)	
35-44	2559 (20.7)	18638 (22.3)		2690.0 (22.1)	18472.8 (22.1)	
45-54	2189 (17.7)	17389 (20.8)		2441.6 (20.1)	17060.7 (20.4)	
Year of follow-up start (%)			0.219			0.034
2006	1782 (14.4)	18380 (22.0)		2390.4 (19.7)	17570.9 (21.0)	
2007	1130 (9.1)	8832 (10.6)		1296.5 (10.7)	8682.7 (10.4)	
2008	981 (7.9)	6683 (8.0)		993.0 (8.2)	6678.5 (8.0)	
2009	853 (6.9)	5367 (6.4)		798.7 (6.6)	5417.6 (6.5)	
2010	804 (6.5)	4714 (5.6)		709.3 (5.8)	4807.2 (5.7)	
2011	800 (6.5)	4820 (5.8)		722.7 (5.9)	4895.8 (5.9)	
2012	758 (6.1)	4474 (5.3)		675.8 (5.6)	4558.7 (5.4)	
2013	790 (6.4)	4415 (5.3)		659.8 (5.4)	4531.3 (5.4)	
2014	806 (6.5)	4379 (5.2)		676.5 (5.6)	4518.0 (5.4)	
2015	673 (5.4)	4230 (5.1)		627.5 (5.2)	4271.1 (5.1)	
2016	768 (6.2)	4377 (5.2)		666.6 (5.5)	4483.0 (5.4)	
2017	737 (6.0)	4313 (5.2)		637.6 (5.2)	4396.7 (5.3)	
2018	759 (6.1)	4235 (5.1)		634.1 (5.2)	4347.9 (5.2)	
2019	719 (5.8)	4450 (5.3)		666.8 (5.5)	4503.9 (5.4)	
Family income category (%)			0.061			0.014
<0	88 (0.7)	550 (0.7)		88.0 (0.7)	557.2 (0.7)	
0	64 (0.5)	314 (0.4)		48.2 (0.4)	329.0 (0.4)	
0-p20	1052 (8.5)	5860 (7.0)		910.6 (7.5)	6026.2 (7.2)	
p20-p80	7295 (59.0)	50299 (60.1)		7288.0 (60.0)	50179.4 (60.0)	
>p80	3861 (31.2)	26646 (31.8)		3820.5 (31.4)	26571.4 (31.8)	
Education category (%)			0.067			0.013
Primary	765 (6.2)	4589 (5.5)		699.3 (5.8)	4668.5 (5.6)	
Secondary	5612 (45.4)	36489 (43.6)		5345.2 (44.0)	36676.6 (43.8)	
Post-secondary	5775 (46.7)	41530 (49.6)		5937.1 (48.8)	41210.6 (49.3)	
NA	208 (1.7)	1061 (1.3)		173.8 (1.4)	1107.5 (1.3)	
Depression (%)	711 (5.8)	4688 (5.6)	0.006	700.8 (5.8)	4706.3 (5.6)	0.006
Bipolar disorder diagnosis (%)	79 (0.6)	596 (0.7)	0.009	86.4 (0.7)	588.2 (0.7)	0.001
Anxiety disorder diagnosis (%)	950 (7.7)	6472 (7.7)	0.002	960.2 (7.9)	6469.3 (7.7)	0.006
Schizophrenia diagnosis (%)	81 (0.7)	679 (0.8)	0.018	88.9 (0.7)	661.9 (0.8)	0.007
Substance abuse disorder (excl. alcohol) diagnosis (%)	298 (2.4)	1625 (1.9)	0.032	254.7 (2.1)	1676.4 (2.0)	0.006
Suicide history (%)	406 (3.3)	2495 (3.0)	0.017	372.5 (3.1)	2527.3 (3.0)	0.003

^a SMD: Standardized Mean Difference

Table S5. Psychiatric and suicidal behaviour outcomes in individuals dispensed a glucocorticoid (medication-only cohort) using a within-individual analysis, stratified by sex

Outcome	Males (N=463,397)		Females (N=642,567)	
	N events	HR (95% CI)	N events	HR (95% CI)
Anxiety	48,045	1.26 (1.15, 1.38)	107,863	1.25 (1.19, 1.32)
Bipolar disorder	7,742	1.17 (0.94, 1.45)	21,156	1.25 (1.12, 1.40)
Depression	23,843	1.00 (0.86, 1.15)	53,217	1.12 (1.02, 1.22)
Psychotic disorder	9,996	1.19 (0.99, 1.42)	12,234	1.16 (1.02, 1.33)
Suicidal behaviour	15,773	0.97 (0.80, 1.18)	30,111	1.09 (0.97, 1.23)

Table S6. Psychiatric and suicidal behaviour outcomes in individuals dispensed a glucocorticoid (medication-only cohort) using a within-individual analysis, stratified by age category

Outcome	Age category ^a							
	15-24 years (N=391,888)		25-34 years (N=569,909)		35-44 years (N=658,122)		45-54 years (N=569,912)	
	N events	HR (95% CI)	N events	HR (95% CI)	N events	HR (95% CI)	N events	HR (95% CI)
Anxiety	34231	1.23 (1.09, 1.39)	44293	1.22 (1.09, 1.35)	41706	1.38 (1.25, 1.53)	35678	1.24 (1.13, 1.37)
Bipolar disorder	3897	1.04 (0.77, 1.41)	8086	1.41 (1.13, 1.77)	8518	1.03 (0.81, 1.32)	8397	1.41 (1.19, 1.67)
Depression	16261	1.05 (0.85, 1.30)	20370	1.26 (1.03, 1.53)	21124	1.05 (0.89, 1.24)	19305	1.07 (0.92, 1.24)
Psychotic disorder	2102	1.03 (0.59, 1.79)	5155	1.03 (0.74, 1.42)	6948	1.18 (0.94, 1.47)	8025	1.16 (0.98, 1.38)
Suicidal behaviour	14456	1.19 (0.96, 1.46)	11458	1.20 (0.94, 1.54)	10438	0.91 (0.71, 1.16)	9532	0.93 (0.72, 1.19)

^a Individuals may contribute to more than one age category over follow-up

Table S7. Psychiatric and suicidal behaviour outcomes in individuals dispensed a glucocorticoid (medication-only cohort) using a within-individual analysis, excluding individuals ever dispensing an inhaled glucocorticoid during follow-up

Outcome	Overall cohort	Excluding individuals dispensing an inhaled glucocorticoid^a
	HR (95% CI)	HR (95% CI)
Anxiety	1.25 (1.20, 1.31)	1.29 (1.21, 1.37)
Bipolar disorder	1.23 (1.12, 1.36)	1.20 (1.04, 1.38)
Depression	1.08 (1.00, 1.16)	1.11 (1.01, 1.22)
Psychotic disorder	1.17 (1.05, 1.30)	1.14 (0.99, 1.32)
Suicidal behaviour	1.06 (0.96, 1.17)	1.12 (0.97, 1.29)

^a Inhaled glucocorticoids ATC code: R03BA

Table S8. Psychiatric and suicidal behaviour outcomes in individuals dispensed a glucocorticoid (medication-only cohort) using a within-individual or between-individual analysis, stratified by indication and past psychiatric diagnosis

	Overall cohort (N=1,105,964)		Past psychiatric diagnosis (N=80,952)		Autoimmune disorder cohort (N= 153,848)		Gastrointestinal autoimmune disorder cohort (N= 58,318)	
	Between-individual ^a HR (95% CI)	Within-individual ^b HR (95% CI)	Between-individual ^a HR (95% CI)	Within-individual ^b HR (95% CI)	Between-individual ^a HR (95% CI)	Within-individual ^b HR (95% CI)	Between-individual ^a HR (95% CI)	Within-individual ^b HR (95% CI)
Anxiety	1.70 (1.64, 1.77)	1.25 (1.20, 1.31)	1.36 (1.28, 1.45)	1.15 (1.08, 1.23)	1.03 (0.95, 1.11)	1.09 (0.99, 1.21)	1.12 (0.99, 1.27)	1.05 (0.89, 1.23)
Bipolar disorder	1.49 (1.34, 1.66)	1.23 (1.12, 1.36)	1.20 (1.04, 1.38)	1.27 (1.12, 1.43)	0.80 (0.65, 0.98)	1.30 (1.05, 1.60)	0.86 (0.59, 1.26)	1.23 (0.81, 1.86)
Depression	1.32 (1.25, 1.39)	1.08 (1.00, 1.16)	1.08 (0.99, 1.17)	1.07 (0.95, 1.20)	0.88 (0.79, 0.98)	1.12 (0.96, 1.31)	0.94 (0.79, 1.11)	1.13 (0.87, 1.46)
Schizophrenia spectrum disorder	1.51 (1.32, 1.71)	1.17 (1.05, 1.30)	1.11 (0.97, 1.27)	1.17 (1.03, 1.32)	1.19 (0.92, 1.54)	1.06 (0.84, 1.35)	1.07 (0.72, 1.58)	1.06 (0.69, 1.62)
Suicidal behaviour	1.21 (1.13, 1.30)	1.06 (0.96, 1.17)	0.92 (0.82, 1.03)	0.89 (0.77, 1.04)	0.77 (0.67, 0.89)	1.02 (0.80, 1.32)	0.90 (0.70, 1.15)	1.01 (0.67, 1.53)

^a Adjusted for age and sex

^b Adjusted for age

Table S9. Psychiatric and suicidal behaviour outcomes in individuals dispensed a glucocorticoid (medication-only cohort) using a within-individual analysis, by treatment periods

	Time since treatment start			
	<14 days	14-119 days	120-364 days	>364 days
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Anxiety	1.37 (1.27, 1.47)	1.23 (1.15, 1.31)	1.14 (1.04, 1.25)	1.19 (1.05, 1.35)
Bipolar disorder	1.58 (1.35, 1.85)	1.06 (0.91, 1.24)	1.00 (0.82, 1.23)	1.32 (1.02, 1.70)
Depression	1.17 (1.03, 1.32)	0.98 (0.87, 1.09)	1.20 (1.04, 1.38)	1.03 (0.85, 1.25)
Schizophrenia spectrum disorder	1.18 (0.97, 1.42)	1.11 (0.94, 1.31)	1.25 (1.02, 1.54)	1.19 (0.94, 1.51)
Suicidal behaviour	1.07 (0.90, 1.27)	1.02 (0.88, 1.19)	1.14 (0.93, 1.40)	0.98 (0.72, 1.34)

Table S10. Associations of glucocorticoid treatment with the risk of psychiatric and suicidal behaviour outcomes at low, medium, and high average dosage

	Dosage		
	Low <0.5 DDDs/day	Medium 0.5-1.5 DDDs/day	High >1.5 DDDs/day
Outcome	HR (95% CI)	HR (95% CI)	HR (95% CI)
Anxiety	1.19 (1.12, 1.26)	1.38 (1.26, 1.51)	1.40 (1.22, 1.61)
Bipolar disorder	1.13 (1.01, 1.27)	1.42 (1.17, 1.71)	1.59 (1.18, 2.15)
Depression	1.06 (0.97, 1.15)	1.13 (0.97, 1.32)	1.15 (0.92, 1.44)
Psychotic disorder	1.16 (1.02, 1.31)	1.25 (1.01, 1.54)	1.06 (0.73, 1.56)
Suicidal behaviour	1.03 (0.91, 1.17)	1.12 (0.92, 1.38)	1.09 (0.78, 1.51)

Table S11. Psychiatric and suicidal behaviour outcomes in individuals dispensed a glucocorticoid (medication-only cohort) using a within-individual analysis in the data linkage covering 2006-2020, compared to the data linkage covering 2006-2013 only

	Data linkage 2006-2020 (N= 1,105,964)	Data linkage 2006-2013 (N=680,215)
	HR (95% CI)	HR (95% CI)
Anxiety disorders	1.25 (1.20, 1.31)	1.36 (1.25, 1.49)
Bipolar disorders	1.23 (1.12, 1.36)	1.37 (1.11, 1.71)
Depressive disorders	1.08 (1.00, 1.16)	1.06 (0.92, 1.23)
Schizophrenia-spectrum disorders	1.17 (1.05, 1.30)	0.93 (0.73, 1.20)
Suicidal behaviour	1.06 (0.96, 1.17)	1.11 (0.94, 1.31)

Table S12. Per-protocol analyses in individuals with an autoimmune disorder or gastrointestinal autoimmune disorder diagnosis (indication cohorts)

Outcome	Time	Autoimmune disorder cohort (N = 287,366)			Gastrointestinal disorder cohort (N=96,029)		
		Cumulative Incidence (%)			Cumulative Incidence (%)		
		Initiators	Controls	Hazard Ratio (95% CI)	Initiators	Controls	Hazard Ratio (95% CI)
Anxiety	14 days	0.10 (0.05,0.15)	0.06 (0.05,0.07)	1.64 (0.94,2.86)	0.09 (0.01,0.16)	0.06 (0.04,0.07)	1.46 (0.61,3.51)
	120 days	0.53 (0.36,0.71)	0.40 (0.36,0.43)	1.47 (1.00,2.16)	0.43 (0.21,0.66)	0.38 (0.32,0.45)	1.26 (0.69,2.32)
	365 days	1.05 (0.57,1.54)	0.97 (0.91,1.03)	1.25 (0.90,1.76)	1.07 (0.17,1.96)	0.90 (0.79,1.01)	1.11 (0.64,1.95)
Bipolar disorder	14 days	0.01 (0.00,0.03)	0.01 (0.01,0.02)	1.01 (0.27,3.76)	0.01 (0.00,0.04)	0.01 (0.00,0.02)	1.20 (0.07,19.95)
	120 days	0.12 (0.03,0.22)	0.09 (0.07,0.10)	1.24 (0.49,3.13)	0.11 (0.00,0.25)	0.06 (0.03,0.09)	1.62 (0.38,6.88)
	365 days	0.25 (0.01,0.49)	0.18 (0.15,0.21)	1.44 (0.68,3.05)	0.15 (0.00,0.33)	0.12 (0.07,0.16)	1.66 (0.52,5.34)
Depression	14 days	0.03 (0.00,0.06)	0.04 (0.03,0.04)	0.84 (0.33,2.14)	0.02 (0.00,0.05)	0.03 (0.02,0.05)	0.51 (0.09,3.06)
	120 days	0.23 (0.11,0.34)	0.24 (0.21,0.26)	0.90 (0.47,1.73)	0.22 (0.04,0.39)	0.23 (0.18,0.29)	0.71 (0.27,1.88)
	365 days	0.73 (0.27,1.20)	0.59 (0.54,0.64)	1.04 (0.63,1.72)	0.49 (0.00,1.07)	0.60 (0.51,0.70)	0.88 (0.41,1.92)
Schizophrenia spectrum disorders	14 days	0.02 (0.00,0.04)	0.02 (0.01,0.02)	0.99 (0.21,4.60)	0.01 (0.00,0.04)	0.02 (0.00,0.03)	0.62 (0.00,4934.89)
	120 days	0.12 (0.03,0.20)	0.09 (0.07,0.11)	1.17 (0.46,2.98)	0.06 (0.00,0.14)	0.08 (0.05,0.11)	0.70 (0.00,422.08)
	365 days	0.19 (0.03,0.35)	0.19 (0.16,0.21)	1.20 (0.58,2.50)	0.10 (0.00,0.25)	0.16 (0.11,0.20)	0.72 (0.04,13.27)
Suicidal behaviour	14 days	0.01 (0.00,0.03)	0.02 (0.01,0.02)	0.74 (0.17,3.33)	0.01 (0.00,0.03)	0.02 (0.01,0.03)	0.61 (0.06,6.74)
	120 days	0.07 (0.01,0.14)	0.12 (0.10,0.14)	0.67 (0.21,2.10)	0.09 (0.00,0.19)	0.12 (0.09,0.16)	0.68 (0.17,2.60)
	365 days	0.37 (0.00,0.74)	0.32 (0.28,0.36)	0.71 (0.32,1.57)	0.23 (0.00,0.59)	0.33 (0.26,0.40)	0.72 (0.24,2.15)

Table S13. Intention-to-treat analyses in individuals with a gastrointestinal autoimmune disorder diagnosis (indication cohort)

Outcome	Time	Overall cohort (N = 96,029)			Past psychiatric diagnosis (N= 11,334)		
		Cumulative incidence (%)			Cumulative incidence (%)		
		Initiators	Controls	Hazard Ratio (95% CI)	Initiators	Controls	Hazard Ratio (95% CI)
Anxiety	14 days	0.08 (0.04,0.11)	0.06 (0.05,0.07)	1.31 (0.82,2.09)	0.49 (0.23,0.75)	0.34 (0.26,0.41)	1.47 (0.86,2.51)
	120 days	0.47 (0.34,0.60)	0.39 (0.35,0.43)	1.26 (0.88,1.81)	3.06 (2.16,3.97)	2.16 (1.89,2.44)	1.45 (0.97,2.16)
	365 days	1.06 (0.87,1.25)	0.95 (0.88,1.01)	1.18 (0.92,1.51)	5.81 (4.59,7.03)	4.86 (4.42,5.30)	1.35 (1.03,1.76)
Bipolar disorder	14 days	0.01 (0.00,0.03)	0.01 (0.01,0.02)	1.11 (0.28,4.39)	0.08 (0.00,0.18)	0.09 (0.05,0.13)	0.83 (0.14,5.04)
	120 days	0.07 (0.02,0.12)	0.06 (0.04,0.07)	1.18 (0.41,3.42)	0.46 (0.08,0.83)	0.48 (0.35,0.61)	0.89 (0.23,3.51)
	365 days	0.17 (0.09,0.25)	0.12 (0.10,0.15)	1.29 (0.65,2.53)	1.15 (0.53,1.76)	1.00 (0.81,1.19)	1.00 (0.45,2.23)
Depression	14 days	0.02 (0.01,0.03)	0.03 (0.03,0.04)	0.58 (0.29,1.19)	0.11 (0.02,0.21)	0.19 (0.14,0.24)	0.61 (0.24,1.52)
	120 days	0.21 (0.13,0.28)	0.24 (0.21,0.27)	0.72 (0.42,1.24)	1.09 (0.59,1.59)	1.33 (1.12,1.54)	0.71 (0.36,1.43)
	365 days	0.73 (0.56,0.89)	0.63 (0.58,0.69)	0.96 (0.69,1.33)	3.30 (2.29,4.32)	3.33 (2.96,3.69)	0.88 (0.58,1.33)
Schizophrenia spectrum disorders	14 days	0.01 (0.00,0.02)	0.02 (0.01,0.02)	0.66 (0.18,2.51)	0.06 (0.00,0.15)	0.12 (0.07,0.16)	0.53 (0.09,3.16)
	120 days	0.07 (0.03,0.12)	0.08 (0.06,0.10)	0.79 (0.29,2.16)	0.47 (0.12,0.83)	0.63 (0.47,0.78)	0.64 (0.17,2.39)
	365 days	0.15 (0.09,0.22)	0.16 (0.14,0.19)	0.93 (0.49,1.77)	1.10 (0.55,1.65)	1.21 (0.99,1.42)	0.81 (0.37,1.75)
Suicidal behaviour	14 days	0.01 (0.00,0.03)	0.02 (0.01,0.02)	0.82 (0.33,2.04)	0.13 (0.03,0.23)	0.10 (0.06,0.15)	1.22 (0.49,3.06)
	120 days	0.11 (0.06,0.16)	0.12 (0.10,0.14)	0.87 (0.43,1.75)	0.77 (0.38,1.16)	0.68 (0.52,0.84)	1.17 (0.58,2.37)
	365 days	0.36 (0.25,0.47)	0.34 (0.30,0.38)	0.95 (0.61,1.46)	1.65 (0.96,2.34)	1.67 (1.41,1.93)	1.08 (0.66,1.76)

