Supplementary material

Contents

Table S1. SSRIs prescribed in Sweden during the study period

ATC	Name
N06AB03	Fluoxetine
N06AB04	Citalopram
N06AB05	Paroxetine
N06AB06	Sertraline
N06AB08	Fluvoxamine
N06AB10	Escitalopram

Table S2. Included CNS drugs

ATC	Name
N02AA01	morphine
N02AA05	oxycodone
N02AA59	codeine, combinations excl. psycholeptics
N02AB01	ketobemidone
N02AC04	dextropropoxyphene
N02AE01	buprenorphine
N02AX02	tramadol
N03AE01	clonazepam
N03AF01	carbamazepine
N03AG01	valproic acid
N03AX09	lamotrigine
N03AX11	topiramate
N03AX12	gabapentin
N03AX16	pregabalin
N05AA02	levomepromazine
N05AD01	haloperidol
N05AF01	flupentixol
N05AF05	zuclopenthixol
N05AH03	olanzapine
N05AH04	quetiapine
N05AN01	lithium
N05AX08	risperidone
N05AX12	aripiprazole
N05BA01	diazepam
N05BA04	oxazepam
N05BA06	lorazepam
N05BA12	alprazolam
N05BB01	hydroxyzine
N05BE01	buspirone
N05CD02	nitrazepam
N05CD03	flunitrazepam
N05CF01	zopiclone
N05CF02	zolpidem
N05CF03	zaleplon
N05CH01	melatonin
N05CM02	clomethiazole
N05CM06	propiomazine
N06AA04	clomipramine
N06AA09	amitriptyline
N06AX03	mianserin
N06AX11	mirtazapine
N06AX12	bupropion
N06AX16	venlafaxine
N06AX18	reboxetine
N06AX21	duloxetine
N06AX22	agomelatine
N06BA04	methylphenidate
N06BA09	atomoxetine
N07BA01	nicotine
N07BA03	varenicline
N07BB01	disulfiram
N07BB03	acamprosate
N07BB04	naltrexone

Table S3. Frequency of add-on drug instances and suicide events by baseline treatment with no or any SSRI

CNS drug		No SSRI	Any SSRI
N02AA01	No. individuals	88877	5530
	Events baseline	336	41
	Events comparator	305	48
N02AA05	No. individuals	251847	13380
	Events baseline	971	126
	Events comparator	772	118
N02AA59	No. individuals	1000740	44314
	Events baseline	2482	306
	Events comparator	2034	301
N02AB01	No. individuals	29187	2118
	Events baseline	105	20
	Events comparator	109	25
N02AC04	No. individuals	198480	9591
	Events baseline	411	59
	Events comparator	448	79
N02AE01	No. individuals	28878	3145
	Events baseline	103	30
	Events comparator	88	22
N02AX02	No. individuals	797738	37859
	Events baseline	3004	294
	Events comparator	2653	300
N03AE01	No. individuals	11868	1914
	Events baseline	236	86
	Events comparator	264	87
N03AF01	No. individuals	29409	2911
	Events baseline	374	101
	Events comparator	299	66
N03AG01	No. individuals	23234	3382
	Events baseline	473	143
	Events comparator	363	101
N03AX09	No. individuals	39863	9414
	Events baseline	903	370
	Events comparator	654	257
N03AX11	No. individuals	9150	1555
	Events baseline	148	66
	Events comparator	109	51
N03AX12	No. individuals	57330	4844
	Events baseline	254	57
	Events comparator	200	51
N03AX16	No. individuals	91708	14986
	Events baseline	1121	362
	Events comparator	998	333
N05AA02	No. individuals	23414	5274
	Events baseline	905	317
	Events comparator	739	248
N05AD01	No. individuals	10474	1756
	Events baseline	228	75
	Events comparator	207	64
N05AF01	No. individuals	7568	2134
	Events baseline	107	39
	Events comparator	106	40
N05AF05	No. individuals	7152	1221
	Events baseline	209	69
	Events comparator	182	58
N05AH03	No. individuals	39272	8200
	Events baseline	1152	334
	Events comparator	895	274
N05AH04	No. individuals	37246	10772
	Events baseline	1367	483

	Events comparator	905	317
N05AN01	No. individuals	12877	2739
	Events baseline	468	164
	Events comparator	270	85
N05AX08	No. individuals	24257	5899
	Events baseline	522	200
	Events comparator	382	158
N05AX12	No. individuals	18401	5319
	Events baseline	495	195
	Events comparator	354	160
N05BA01	No. individuals	184198	23464
	Events baseline	1206	366
	Events comparator	1369	391
N05BA04	No. individuals	248028	44439
	Events baseline	1650	562
	Events comparator	1651	520
N05BA06	No. individuals	6998	1036
	Events baseline	108	32
	Events comparator	112	23
N05BA12	No. individuals	43274	9710
	Events baseline	483	152
	Events comparator	593	208
N05BB01	No. individuals	473920	63047
	Events baseline	2660	978
	Events comparator	2277	730
N05BE01	No. individuals	9500	4221
	Events baseline	231	92
	Events comparator	165	59
N05CD02	No. individuals	23259	3781
	Events baseline	425	126
	Events comparator	431	100
N05CD03	No. individuals	18673	2056
	Events baseline	102	18
	Events comparator	144	36
N05CF01	No. individuals	435969	51101
	Events baseline	2627	837
	Events comparator	2616	694
N05CF02	No. individuals	356070	36919
	Events baseline	1228	445
	Events comparator	1480	430
N05CF03	No. individuals	15116	2327
	Events baseline	113	42
	Events comparator	108	36
N05CH01	No. individuals	68959	9126
	Events baseline	523	223
	Events comparator	437	159
N05CM02	No. individuals	5159	1126
	Events baseline	123	20
	Events comparator	135	28
N05CM06	No. individuals	336184	48694
	Events baseline	2838	974
	Events comparator	2421	729
N06AA04	No. individuals	16939	1528
	Events baseline	294	34
	Events comparator	285	36
N06AA09	No. individuals	156233	9847
	Events baseline	374	62
	Events comparator	364	51
N06AX03	No. individuals	17516	8117
	Events baseline	221	138
	Events comparator	162	112
N06AX11	No. individuals	165601	38891
	Events baseline	2513	757
	Events comparator	1698	518
N06AX12	No. individuals	66788	9446

	Events baseline	460	122
	Events comparator	388	104
N06AX16	No. individuals	85354	7854
	Events baseline	1262	152
	Events comparator	1086	122
N06AX18	No. individuals	5366	3096
	Events baseline	77	46
	Events comparator	51	42
N06AX21	No. individuals	72152	5500
	Events baseline	915	121
	Events comparator	697	96
N06AX22	No. individuals	9373	2011
	Events baseline	152	43
	Events comparator	123	35
N06BA04	No. individuals	91864	8087
	Events baseline	636	183
	Events comparator	552	133
N06BA09	No. individuals	28261	2286
	Events baseline	261	55
	Events comparator	217	40
N07BA01	No. individuals	19515	2191
	Events baseline	81	21
	Events comparator	60	18
N07BA03	No. individuals	110353	6890
	Events baseline	134	23
	Events comparator	152	31
N07BB01	No. individuals	48008	9070
	Events baseline	1117	468
	Events comparator	661	221
N07BB03	No. individuals	23291	4898
	Events baseline	515	201
	Events comparator	296	102
N07BB04	No. individuals	18999	3882
	Events baseline	475	176
	Events comparator	240	85

Table S4. Statistically significant IRRs for the risk of suicidal behavior associated with CNS drug initiation during treatment with any SSRI or outside of SSRI treatment

CNS initiation ATC	Name	Type of treatment: Any SSRI (IRR, 95% CrI)	Type of treatment: No SSRI (IRR, 95%CrI)	Ratio (any SSRI vs. no SSRI)
N02AA05	oxycodone	0.97 (0.75, 1.25)	0.80 (0.73, 0.88)*	1.21 (0.93, 1.58)
N02AA59	codeine, combinations excl. psycholeptics	1.02 (0.87, 1.19)	0.82 (0.77, 0.87)*	1.24 (1.05, 1.46)*
N02AX02	tramadol	1.05 (0.90, 1.23)	0.88 (0.84, 0.93)*	1.19 (1.01, 1.41)*
N03AF01	carbamazepine	0.67 (0.50, 0.92)*	0.80 (0.69, 0.93)*	0.84 (0.60, 1.18)
N03AG01	valproic acid	0.73 (0.57, 0.94)*	0.76 (0.67, 0.88)*	0.96 (0.72, 1.26)
N03AX09	lamotrigine	0.72 (0.62, 0.85)*	0.72 (0.65, 0.79)*	1.01 (0.83, 1.22)
N03AX11	topiramate	0.80 (0.56, 1.14)	0.73 (0.57, 0.94)*	1.09 (0.71, 1.67)
N03AX12	gabapentin	0.92 (0.64, 1.32)	0.79 (0.66, 0.95)*	1.16 (0.78, 1.73)
N03AX16	pregabalin	0.94 (0.81, 1.09)	0.89 (0.82, 0.97)*	1.06 (0.89, 1.25)
N05AA02	levomepromazine	0.81 (0.69, 0.96)*	0.82 (0.74, 0.90)*	0.99 (0.82, 1.20)
N05AH03	olanzapine	0.83 (0.71, 0.97)*	0.78 (0.72, 0.85)*	1.06 (0.89, 1.27)
N05AH04	quetiapine	0.67 (0.58, 0.77)*	0.66 (0.60, 0.72)*	1.02 (0.86, 1.21)
N05AN01	lithium	0.55 (0.42, 0.71)*	0.57 (0.49, 0.66)*	0.96 (0.71, 1.29)
N05AX08	risperidone	0.79 (0.64, 0.97)*	0.74 (0.65, 0.84)*	1.07 (0.84, 1.38)
N05AX12	aripiprazole	0.84 (0.69, 1.03)	0.72 (0.62, 0.82)*	1.17 (0.92, 1.50)
N05BA01	diazepam	1.10 (0.96, 1.26)	1.15 (1.06, 1.24)*	0.95 (0.82, 1.12)
N05BA12	alprazolam	1.39 (1.13, 1.71)*	1.25 (1.10, 1.40)*	1.12 (0.88, 1.43)
N05BB01	hydroxyzine	0.77 (0.70, 0.84)*	0.87 (0.82, 0.92)*	0.88 (0.79, 0.99)*
N05BE01	buspirone	0.66 (0.48, 0.91)*	0.72 (0.59, 0.87)*	0.93 (0.64, 1.35)
N05CD03	flunitrazepam	1.83 (1.11, 3.07)*	1.41 (1.10, 1.82)*	1.30 (0.74, 2.30)
N05CF01	zopiclone	0.84 (0.76, 0.93)*	1.00 (0.95, 1.06)	0.84 (0.75, 0.94)*
N05CF02	zolpidem	0.99 (0.87, 1.13)	1.21 (1.13, 1.31)*	0.82 (0.71, 0.95)*
N05CH01	melatonin	0.73 (0.60, 0.90)*	0.84 (0.74, 0.96)*	0.87 (0.69, 1.11)
N05CM06	propiomazine	0.75 (0.69, 0.83)*	0.86 (0.82, 0.91)*	0.88 (0.78, 0.98)*
N06AX03	mianserin	0.81 (0.64, 1.04)	0.73 (0.60, 0.89)*	1.11 (0.81, 1.52)
N06AX11	mirtazapine	0.69 (0.62, 0.77)*	0.68 (0.64, 0.73)*	1.01 (0.89, 1.15)
N06AX12	bupropion	0.92 (0.71, 1.19)	0.84 (0.73, 0.95)*	1.10 (0.83, 1.47)
N06AX16	venlafaxine	0.92 (0.73, 1.16)	0.82 (0.75, 0.88)*	1.12 (0.88, 1.44)
N06AX18	reboxetine	0.95 (0.64, 1.40)	0.66 (0.47, 0.93)*	1.43 (0.85, 2.43)
N06AX21	duloxetine	0.88 (0.68, 1.14)	0.74 (0.67, 0.81)*	1.19 (0.90, 1.57)
N06BA04	methylphenidate	0.76 (0.60, 0.94)*	0.87 (0.78, 0.97)*	0.87 (0.68, 1.11)
N06BA09	atomoxetine	0.76 (0.51, 1.14)	0.84 (0.70, 0.99)*	0.91 (0.59, 1.41)
N07BB01	disulfiram	0.49 (0.42, 0.58)*	0.59 (0.54, 0.65)*	0.83 (0.69, 1.00)
N07BB03	acamprosate	0.52 (0.41, 0.66)*	0.57 (0.50, 0.66)*	0.91 (0.68, 1.20)
N07BB04	naltrexone	0.50 (0.39, 0.65)*	0.50 (0.43, 0.59)*	1.00 (0.74, 1.34)

Inclusion in table: significance of either IRR, or of ratio.

Table S5. Statistically significant IRRs for the risk of suicidal behavior associated with CNS drug initiation during treatment with specific SSRIs

		Type of SSRI treatment				
CNS initiation ATC	**Name**	**Fluoxetine (IRR, 95% CrI)**	**Citalopram (IRR, 95% CrI)**	**Paroxetine (IRR, 95% CrI)**	**Sertraline (IRR, 95% CrI)**	**Escitalopram (IRR, 95% CrI)**
N03AG01	valproic acid	0.72 (0.45, 1.13)	1.16 (0.66, 2.02)	0.71 (0.35, 1.34)	0.86 (0.54, 1.38)	0.57 (0.34, 0.93)*
N03AX11	topiramate	0.95 (0.58, 1.60)	0.92 (0.44, 1.98)	0.71 (0.31, 1.66)	0.51 (0.26, 0.96)*	1.00 (0.54, 1.87)
N05AA02	levomepromazine	0.99 (0.73, 1.33)	0.68 (0.45, 1.02)	0.44 (0.24, 0.84)*	0.78 (0.56, 1.08)	0.95 (0.65, 1.34)
N05AF05	zuclopenthixol	0.86 (0.48, 1.50)	0.47 (0.23, 0.98)*	0.69 (0.30, 1.59)	0.91 (0.51, 1.64)	0.93 (0.48, 1.77)
N05AH03	olanzapine	0.88 (0.64, 1.20)	0.83 (0.56, 1.23)	0.82 (0.47, 1.44)	0.71 (0.53, 0.95)*	0.92 (0.67, 1.25)
N05AH04	quetiapine	0.77 (0.57, 1.02)	0.73 (0.48, 1.10)	0.45 (0.26, 0.77)*	0.71 (0.55, 0.90)*	0.72 (0.53, 0.97)*
N05AN01	lithium	0.67 (0.42, 1.03)	0.53 (0.28, 0.98)*	0.53 (0.26, 1.09)	0.51 (0.33, 0.80)*	0.61 (0.38, 0.96)*
N05BB01	hydroxyzine	0.86 (0.71, 1.05)	0.68 (0.55, 0.83)*	0.99 (0.69, 1.41)	0.83 (0.69, 1.00)*	0.73 (0.57, 0.94)*
N05CF01	zopiclone	1.06 (0.84, 1.32)	0.78 (0.62, 0.97)*	0.92 (0.62, 1.33)	0.93 (0.77, 1.11)	0.86 (0.67, 1.10)
N05CM06	propiomazine	0.83 (0.68, 1.02)	0.63 (0.51, 0.79)*	0.80 (0.53, 1.19)	0.81 (0.67, 0.96)*	0.79 (0.62, 1.00)
N06AX11	mirtazapine	0.76 (0.57, 1.02)	0.60 (0.48, 0.75)*	0.88 (0.57, 1.34)	0.72 (0.58, 0.87)*	0.66 (0.51, 0.87)*
N06AX21	duloxetine	0.98 (0.56, 1.64)	0.56 (0.32, 0.99)*	0.77 (0.36, 1.59)	0.79 (0.46, 1.33)	0.80 (0.47, 1.37)
N07BB01	disulfiram	0.57 (0.40, 0.82)*	0.49 (0.36, 0.67)*	0.49 (0.30, 0.78)*	0.45 (0.34, 0.60)*	0.55 (0.38, 0.77)*
N07BB03	acamprosate	0.77 (0.48, 1.22)	0.51 (0.33, 0.79)*	0.53 (0.28, 1.03)	0.46 (0.29, 0.73)*	0.48 (0.28, 0.82)*
N07BB04	naltrexone	0.71 (0.44, 1.15)	0.43 (0.26, 0.71)*	0.50 (0.24, 1.03)	0.55 (0.34, 0.85)*	0.43 (0.26, 0.72)*

Inclusion in table: significance of either IRR, or of ratio.

Table S6. Statistically significant IRRs for the risk of suicidal behavior associated with CNS drug initiation during any SSRI treatment, by sex

		Sex		
CNS initiation ATC	**Name**	**Males (IRR, 95% CrI)**	**Females (IRR, 95% CrI)**	**Ratio (females vs males)**
N03AF01	carbamazepine	0.60 (0.39, 0.94)*	0.75 (0.50, 1.14)	1.25 (0.68, 2.27)
N03AG01	valproic acid	0.77 (0.47, 1.24)	0.72 (0.54, 0.96)*	0.94 (0.54, 1.64)
N03AX09	lamotrigine	0.73 (0.50, 1.05)	0.73 (0.60, 0.86)*	1.00 (0.67, 1.50)
N05AA02	levomepromazine	0.77 (0.56, 1.08)	0.81 (0.67, 0.98)*	1.05 (0.71, 1.54)
N05AH04	quetiapine	0.69 (0.51, 0.93)*	0.67 (0.57, 0.78)*	0.97 (0.69, 1.37)
N05AN01	lithium	0.38 (0.22, 0.64)*	0.61 (0.46, 0.81)*	1.60 (0.89, 2.94)
N05AX08	risperidone	0.91 (0.63, 1.30)	0.74 (0.58, 0.94)*	0.81 (0.53, 1.26)
N05AX12	aripiprazole	0.62 (0.39, 0.97)*	0.91 (0.72, 1.14)	1.47 (0.89, 2.46)
N05BA04	oxazepam	0.77 (0.61, 0.98)*	1.03 (0.89, 1.17)	1.32 (1.01, 1.74)*
N05BA12	alprazolam	1.41 (0.97, 2.05)	1.36 (1.07, 1.73)*	0.96 (0.62, 1.50)
N05BB01	hydroxyzine	0.77 (0.64, 0.93)*	0.77 (0.69, 0.86)*	1.00 (0.79, 1.24)
N05BE01	buspirone	1.01 (0.57, 1.76)	0.57 (0.39, 0.83)*	0.57 (0.29, 1.12)
N05CD02	nitrazepam	1.07 (0.66, 1.71)	0.72 (0.52, 0.98)*	0.67 (0.38, 1.17)
N05CF01	zopiclone	0.89 (0.73, 1.07)	0.84 (0.74, 0.94)*	0.94 (0.75, 1.18)
N05CH01	melatonin	0.59 (0.37, 0.90)*	0.80 (0.64, 0.98)*	1.36 (0.83, 2.23)
N05CM06	propiomazine	0.67 (0.55, 0.80)*	0.79 (0.71, 0.88)*	1.19 (0.96, 1.49)
N06AX11	mirtazapine	0.65 (0.54, 0.80)*	0.70 (0.62, 0.81)*	1.08 (0.85, 1.38)
N06BA04	methylphenidate	0.72 (0.47, 1.08)	0.76 (0.59, 0.99)*	1.06 (0.66, 1.76)
N06BA09	atomoxetine	0.47 (0.24, 0.93)*	0.93 (0.59, 1.50)	1.97 (0.89, 4.35)
N07BB01	disulfiram	0.55 (0.43, 0.71)*	0.45 (0.37, 0.55)*	0.81 (0.59, 1.11)
N07BB03	acamprosate	0.57 (0.38, 0.82)*	0.49 (0.36, 0.66)*	0.87 (0.54, 1.38)
N07BB04	naltrexone	0.39 (0.25, 0.58)*	0.59 (0.43, 0.80)*	1.51 (0.88, 2.58)

Inclusion in table: significance of either IRR, or of ratio.

eMethods

I. Logic behind the choice of model to account for multiple testing

The issue of multiple testing is that, as the numbers of tests increases, so do the number of chance findings that are statistically significant even in a situation where the null hypothesis is true. That is, the number of "false findings" increases as the number of tests increase. In a frequentist framework, it is not clear what tests to consider in relation to one another when adjusting for multiplicity – in theory, all tests in the world may have to be taken into account. In a Bayesian framework, by contrast, any tests that are not independent (=where either the hypotheses tested or the data used are dependent) are relevant to adjust for one another, which puts at least a theoretical limit on the extent of adjustment necessary (Sjölander and Vansteelandt 2019).[1] A further strength of the Bayesian approach is that it allows for adjustment of effect sizes, as opposed to only significance thresholds (p-values), as in the case of the Bonferroni correction in a frequentist framework. In practice, however, the extent of adjustment necessary in even the Bayesian framework may become impractical, as the number of dependent tests may be very large. Still, this is the case for any type of practically feasible multiplicity adjustment.

In the Bayesian framework, adjustment can be done by taking into account external information about the data. In our case, the ATC subgroup of the CNS drug that is initiated reflects the type of chemical compound and the disease it is used to treat. Based on prior knowledge, we can therefore expect effect estimates within these groups to carry some information about one another. Information on the effect estimates from CNS drug initiations within these ATC subgroups can be "borrowed" from one another through the use of hierarchical modelling (Witte et al. 2000), thereby reducing the likelihood of implausible "false findings".

II. Mathematical description of model

For our main analysis, we employed a two-stage Bayesian Poisson regression model, as per Witte et al. (2000),[2] to investigate the impact of initiating a CNS drug during treatment with any SSRI or outside of any SSRI treatment. The analysis was adjusted for age, sex, and type of SSRI treatment (SSRI or no SSRI). We have used the stan_glmer function from the R package rstanarm for the hierarchical analyses.

If we were to use a conventional Poisson model for our main analyses, it could be denoted as follows:

$$\ln(\mu) = \alpha + X\underline{\beta} + W\underline{\gamma}$$

Where μ is the rate of suicidal behavior over a specified time period, α is the intercept term, X is the matrix of unique combinations of CNS drugs and SSRI "treatments" (treatment with any SSRI or no treatment with SSRIs), $\underline{\beta}$ is the vector of regression coefficients for these combinations, W is the matrix of sex, age, and SSRI treatment data, and $\underline{\gamma}$ is the vector of regression coefficients for these features.

In order to account for multiple testing, we have introduced a second-stage linear model to improve estimates of $\underline{\beta}$ by taking into account information across the CNS drug categories that are initiated. That is, we "borrow" information from the effect estimates across a CNS drug category (e.g. "N02A") to inform the effect estimates for specific CNS drug-SSRI treatment combinations. We do this by introducing a second-stage linear regression model for $\underline{\beta}$:

$$\underline{\beta} = Z\underline{\pi} + \underline{\delta}$$

Here, Z is the matrix of the specific type of CNS drug that is initiated, $\underline{\pi}$ is the vector of coefficients associated with the specific CNS drug, and $\underline{\delta}$ is a vector of normal random variables with variances τ_i^2 and

mean 0 (this reflects the residual variance in $\underline{\beta}$ after taking into account the effect estimates of the individual CNS drug types).

The full two-stage model that we use in our paper can therefore be expressed as:

$$\ln(\mu) = \alpha + XZ\underline{\pi} + X\underline{\delta} + W\underline{\gamma}$$

where $\underline{\pi}$, $\underline{\gamma}$, and $\underline{\delta}$ are all treated as random coefficients. We have used the default distributions for these in the stan_glmer function. We used similar models for the other analyses.

The following is a selection of our raw data and explanation of how it relates to the components to equations above (refer to Table A).

Table A. Extract from data used in the main analysis

	Column no.						
	1	2	3	4	5	6	7
Row no.	SSRI treatment (0/1)	CNS drug ATC group	CNS drug-SSRI combination	Person-years	Female (0/1)	Age category (years)	No. events
1	0	N02Apre	0-N02AA01pre	166,3655	0	06-17	4
2	0	N02Apre	0-N02AA05pre	781,1116	0	06-17	21
3	0	N02Apos	0-N02AA01pos	164,0767	0	06-17	3
4	0	N02Apos	0-N02AA05pos	778,4504	0	06-17	13
5	1	N02Apre	1-N02AA01pre	1,232033	0	06-17	1
6	1	N02Apre	1-N02AA05pre	4,032854	0	06-17	0
7	1	N02Apos	1-N02AA01pos	0,977413	0	06-17	1
8	1	N02Apos	1-N02AA05pos	3,811088	0	06-17	0

In Table A, the third column ("CNS drug-SSRI combination") represents X. The comparison of interest is the rate of events in periods after ("pos") versus before ("pre") initiation of a specific CNS drug during either any or no SSRI treatment. For example, to investigate the impact of initiating N02AA01 during SSRI treatment, we compare the number of events by person-years in 1-N02AA01pos (row 7) to the number of events by person-years in 1-N02AA01pre (row 5). In order to account for the biological similarity across initiating drugs, we use information on the CNS drug ATC group (column 2), which represents Z, to improve the estimation of β. For example, we get the effect of initiating any CNS drug from the group "N02A" by comparing the events by person-years in any row marked "N02Apos" to the events by person-years in any row marked "N02Apre". We can then use these estimates to "shrink" the estimates of initiating any specific CNS drug during an SSRI treatment towards each other within the CNS drug ATC groupings (in this case, within the "N02A" group). The analysis is adjusted for SSRI treatment (column 1), sex (column 5), and age category (column 6), which together represent W.

References in supplementary text:

1. Sjölander A, Vansteelandt S. Frequentist versus Bayesian approaches to multiple testing. *European journal of epidemiology* 2019;34(9):809-21.
2. Witte JS, Greenland S, Kim L-L, et al. Multilevel modeling in epidemiology with GLIMMIX. *Epidemiology* 2000;11(6):684-88.

Figure S1. IRRs and credible intervals of suicidal behavior from CNS drug initiation during treatment with any SSRI, by sex.

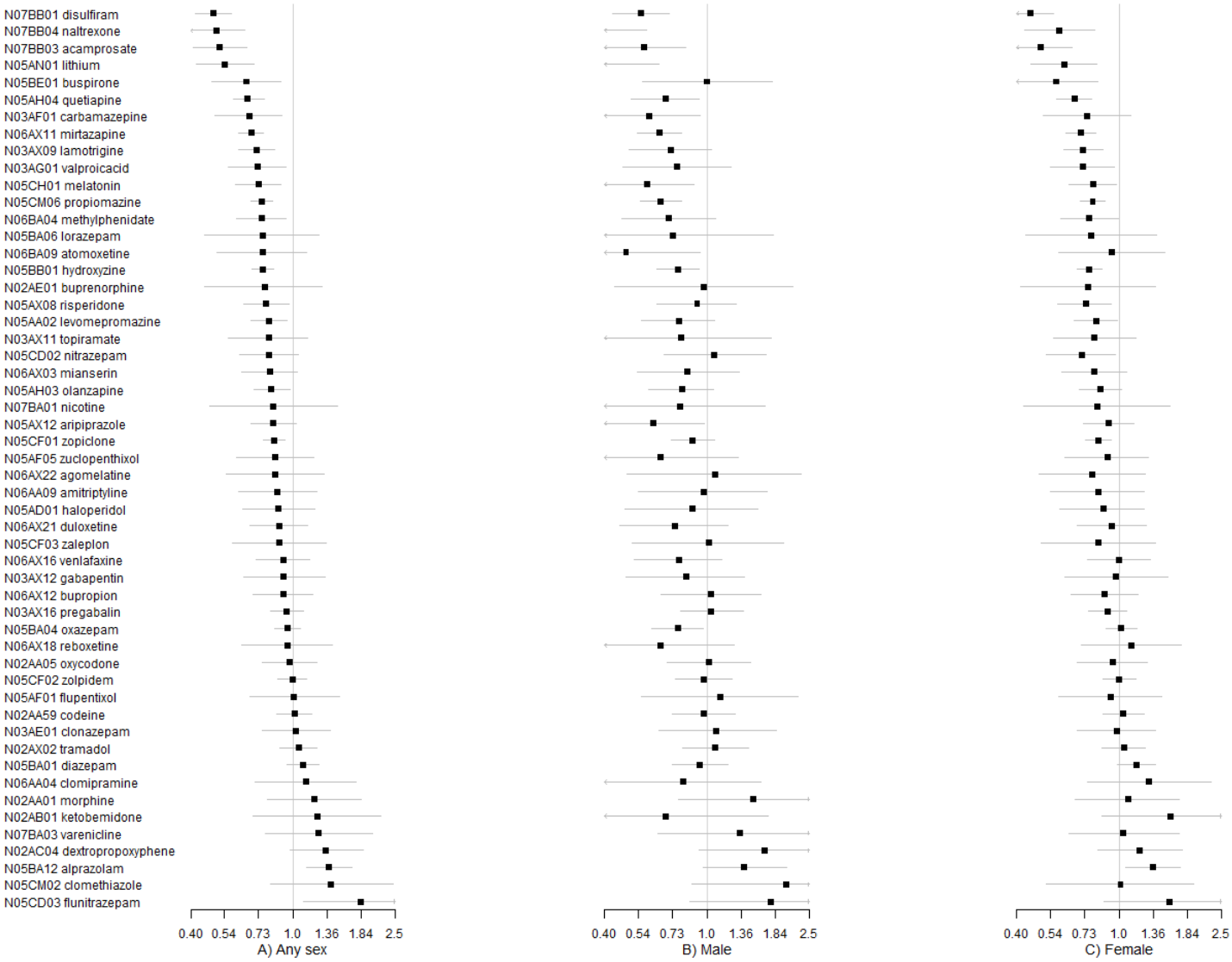

Figure S2. IRRs and credible intervals of suicidal behavior from CNS drug initiation during treatment with any SSRI and outside of SSRI treatment among individuals aged >17 years.

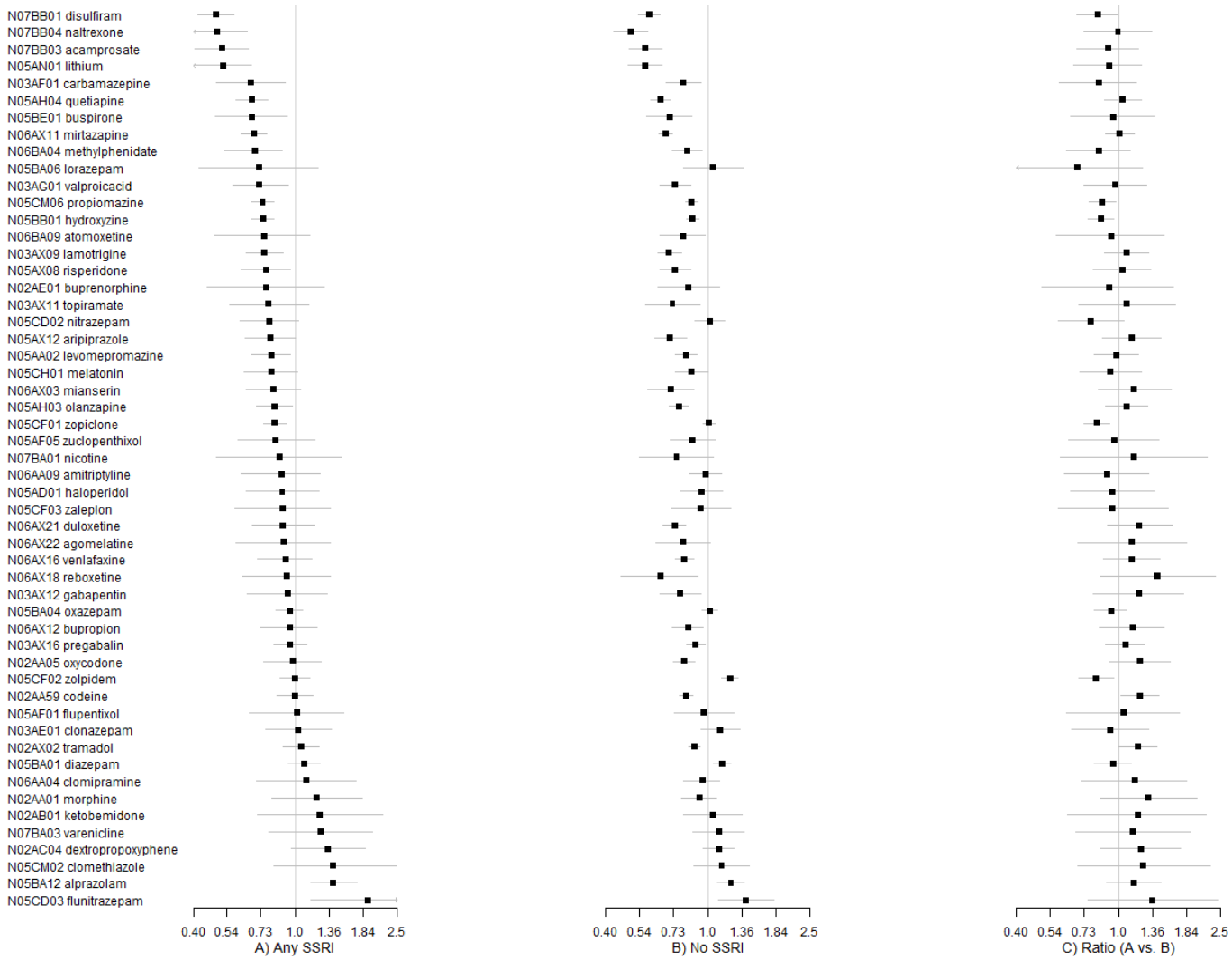

Figure S3. IRRs and credible intervals of suicidal behavior from CNS drug initiation during treatment with any SSRI and outside of SSRI treatment, considering only suicidal behavior of known intent as the outcome

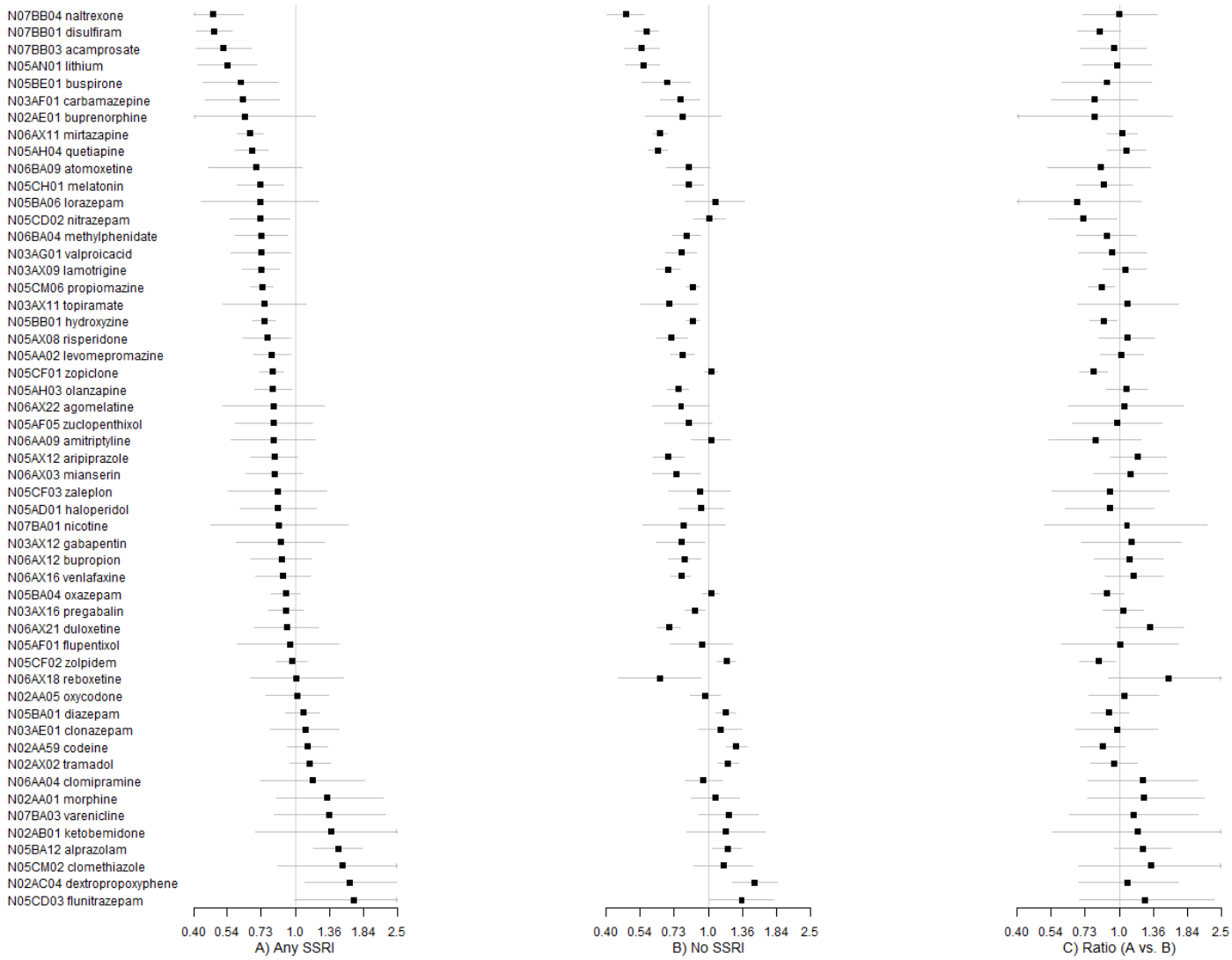

Figure S4. IRRs and credible intervals of suicidal attempts from CNS drug initiation during treatment with any SSRI and outside of SSRI treatment, when only suicide attempts are included in the outcome definition.

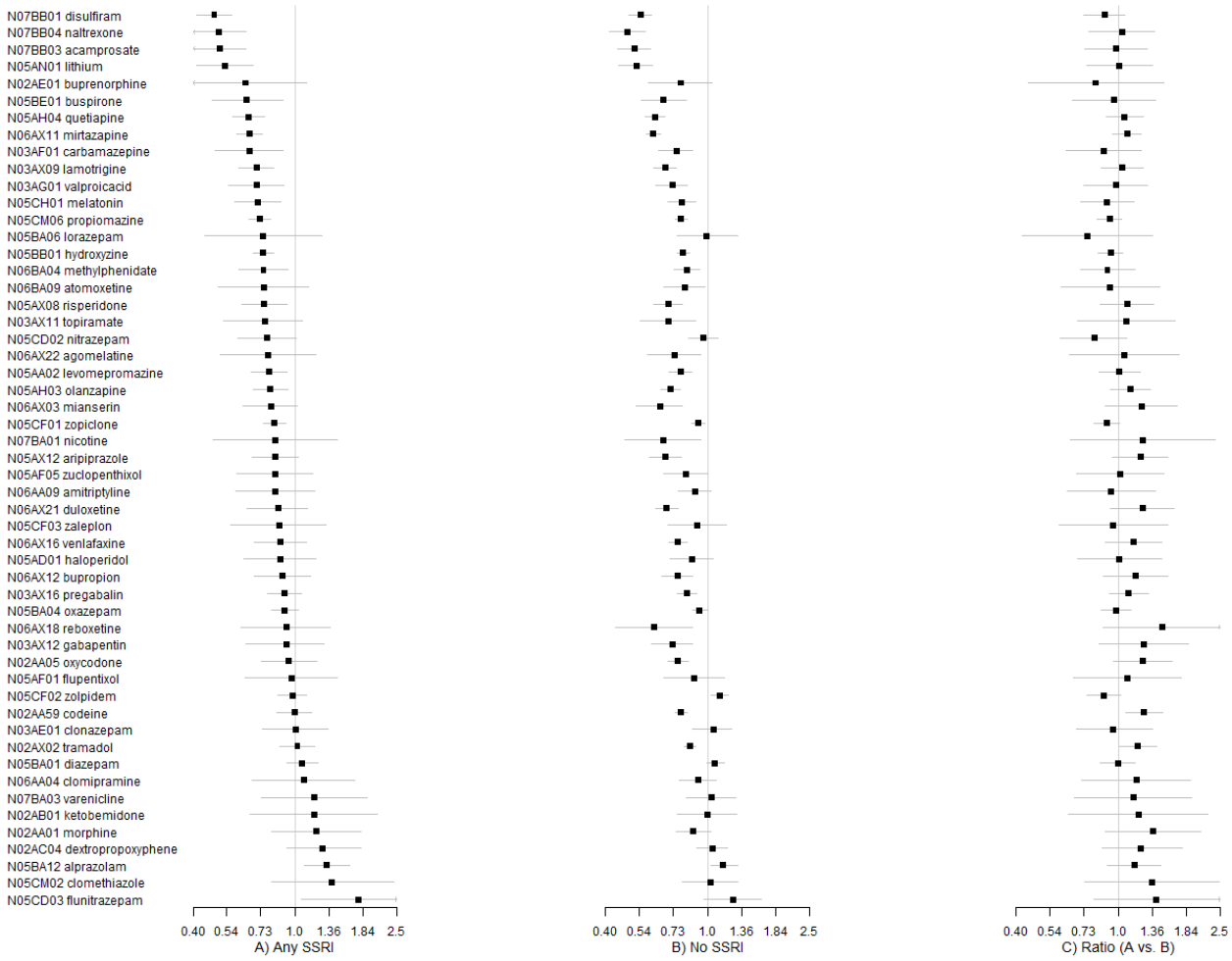

Figure S5. IRRs and credible intervals of suicidal behavior from CNS drug initiation during treatment with any SSRI and outside of SSRI treatment, excluding the date on which the additional CNS drug was initiated

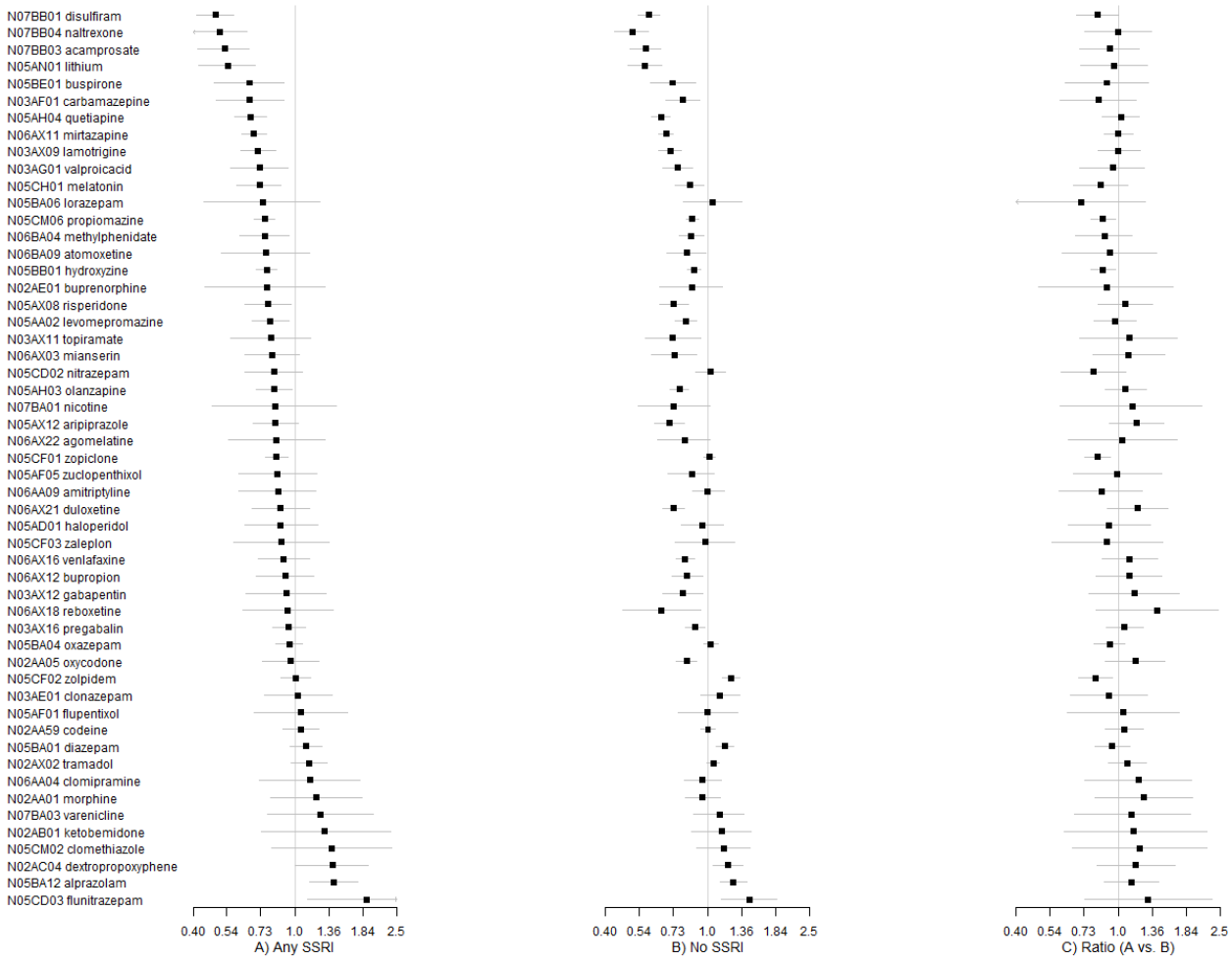

Figure S6. IRRs and credible intervals of suicidal behavior from CNS drug initiation during treatment with any SSRI and outside of SSRI treatment in the main analysis when using a frequentist Poisson regression model.