Supplementary Material

Deliberate self-poisoning:

real-time characterization of suicidal habits and toxidromes in the Food and Drug Administration Adverse Event Reporting System.

Running Title: Deliberate self-poisoning in the FAERS

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Table S1 – Query Check. We checked the representativeness of our DSP query with a more specific query including only terms inherent in suicide. Main drugs involved contributed to similar proportions of reports between the two queries, thus supporting our choice.

	DSP		**Suicidal DSP**	
Substance	N	%	N	%
paracetamol	4235	10.06	1880	8.44
promethazine	1486	3.53	1402	6.29
amlodipine	1433	3.40	621	2.91
quetiapine	1340	3.18	701	3.15
metformin	1220	2.90	608	2.73
ibuprofen	1138	2.70	552	2.48
alprazolam	1031	2.45	540	2.42
varenicline	1002	2.38	968	4.34
tramadol	996	2.37	324	1.45
venlafaxine	939	2.26	525	2.36

Table S2 – Comparison DSP reports vs any other FAERS report. Chi-square test was performed for categorical values, and p-values were corrected for multiple comparison using the Holm-Bonferroni method.

VARIABLE	DSP Reports N = 42,103		Other Reports N = 11,685,995		p-value
	N	%	N	%	
Gender					0.089
Woman	22,819	61.20	6,470,256	60.76	
Man	14,469	38.30	4,177,794	39.24	
Unknown	4,815	-	1,037,945	-	
Submission					**0.003**
Direct	494	1.17	768,687	6.58	
Expedited	38,474	91.38	6,026,848	51.57	
Periodic	3,135	7.45	4,890,453	41.85	
Unknown	0	-	7	-	
Reporter					**0.003**
Consumer	6,761	17.04	5,172,334	46.76	
Healthcare practitioner	4,110	10.36	530,145	4.79	
Lawyer	1,042	2.63	242,629	2.19	
Other	12,082	30.46	1,641,445	14.84	
Pharmacist	3,142	7.92	811,842	7.34	
Physician	12,534	31.59	2,663,257	24.08	
Unknown	2,432	-	624,343	-	
Age category					**0.003**
Neonate (<28d)	19	0.06	27,070	0.35	
Infant (28d-<2y)	50	0.15	48,921	0.63	
Child (2y-<12y)	160	0.48	175,177	2.25	
Teenager (12y-<18y)	4,088	12.26	201,512	2.59	
Adult (18y-<30y)	7,937	23.81	586,176	7.54	
Adult (30y-<50y)	11,943	35.83	1,673,835	21.52	
Adult (50y-<65y)	6,140	18.42	2,325,587	29.91	
Elderly (65y-<75y)	1,746	5.24	1,493,709	19.21	
Elderly (75y-<85y)	949	2.85	946,745	12.71	
Elderly (85y-<100y)	304	0.91	295,284	3.80	
Elderly (≥100y)	0	0.00	2,305	0.03	
Unknown	8,767	-	3,909,674	-	
Outcome					**0.003**
Death	7,218	17.14	1,071,316	9.17	
Life Threatening	6,440	15.30	297,138	2.54	
Disability	304	0.72	212,779	1.82	
Required Intervention	105	0.25	53,806	0.46	
Hospitalization	18,727	44.48	2,357,583	20.17	
Congenital	9	0.02	31,797	0.27	
Other Serious	7,383	17.54	3,014,736	25.80	
Non Serious	1,917	4.55	4,646,840	39.76	
Continent					**0.003**
Africa	155	0.38	46,363	0.41	
Antarctica	0	0.00	5	0.00	
Asia	3,639	9.00	761,946	6.71	
Europe	19,269	47.67	1,681,862	14.81	
North America	16,248	40.19	8,490,693	74.78	
Oceania	763	1.89	112,317	0.99	
South America	350	0.87	261,500	2.30	
Unknown	1,679	-	331,309	-	
Concomitant Alcohol	2,201	5.23	22,393	0.19	**<0.001**
Psychiatric Comorbidity	6,026	14.31	701,518	6.08	**<0.001**
Weight (Kg)		70 (58-84)		73 (60.00-89)	**<0.001**
unknown		34,302		8,742,343	

Table S3 – Comparing fatal vs non-fatal DSP reports' demographics. Chi-square test was performed for categorical values, and p-values were corrected for multiple comparison using the Holm-Bonferroni method.

VARIABLE		Fatal DSP Reports N = 7,218		Other DSP Reports N = 34,885		p-value
Gender						<0.001
Woman		2,987	54.83	19,832	62.29	
Man		2,461	45.17	12,008	37.71	
Unknown		1,770	-	3,045	-	
Submission						0.002
Direct		36	0.50	458	1.31	
Expedited		6,982	96.73	31,492	90.27	
Periodic		200	2.77	2,935	8.41	
Reporter						0.002
Consumer		528	8.15	6,233	18.78	
Healthcare practitioner		501	7.73	3,609	10.87	
Lawyer		67	1.03	975	2.94	
Other		2,165	33.42	9,917	29.88	
Pharmacist		959	14.80	2,183	6.58	
Physician		2,259	34.87	10,275	30.96	
Unknown		739	-	1,693	-	
Age category						0.002
Neonate (<28d)		8	0.13	11	0.04	
Infant (28d-<2y)		20	0.32	30	0.11	
Child (2y-<12y)		31	0.50	129	0.47	
Teenager (12y-<18y)		263	4.27	3,825	14.08	
Adult (18y-<30y)		1,160	18.82	6,777	24.94	
Adult (30y-<50y)		2,560	41.54	9,383	34.53	
Adult (50y-<65y)		1,406	22.81	4,734	17.42	
Elderly (65y-<75y)		381	6.18	1,365	5.02	
Elderly (75y-<85y)		252	4.09	697	2.57	
Elderly (≥85y)		82	1.33	222	0.82	
Unknown		1,055	-	7,712	-	
Outcome						-
Death		7,218	100.00	0	0.00	
Life Threatening		0	0.00	6,440	18.46	
Disability		0	0.00	304	0.87	
Required Intervention		0	0.00	105	0.30	
Hospitalization		0	0.00	18,727	53.68	
Congenital		0	0.00	9	0.03	
Other Serious		0	0.00	7,383	21.16	
Non Specified As Serious		0	0.00	1,917	5.50	
Continent						0.002
North America		4,162	65.51	12,086	35.47	
Europe		1,577	24.82	17,692	51.93	
Asia		442	6.96	3,197	9.38	
South America		21	0.33	329	0.97	
Oceania		113	1.78	650	1.91	
Africa		38	0.60	117	0.34	
Unknown		865	-	814	-	
Concomitant Alcohol		643	8.91	1,558	4.47	<0.001
Psychiatric Comorbidity		693	9.60	5,333	15.29	<0.001
Weight (Kgs) [IQR]		74 [60-90]		70 [58-83]		<0.001
Primary Suspects						
1°	paracetamol 1028		14.24	paracetamol 3,207	9.19	
2°	oxycodone 426		5.90	promethazine 1,479	4.24	
3°	bupropion 274		3.80	amlodipine 1,1244	3.57	
4°	metformin 247		3.42	quetiapine 1,207	3.46	
5°	acetylsalicylic acid		3.10	metformin 973	2.79	
6°	224		3.10	varenicline 959	2.75	
7°	hydrocodone 224		2.74	ibuprofen 953	2.73	
8°	diphenhydramine 198		2.72	risperidone 854	2.45	
9°	tramadol 196		2.63	alprazolam 841	2.41	
10°	alprazolam 190		2.62	venlafaxine 823	2.36	
	amlodipine 189					

Table S4 – goodness of fit test for drug-specific DSP reports. Chi-square test was performed for categorical values against the entire DSP reports population. p-values were corrected for multiple comparisons using the Holm-Bonferroni method and reported in each column of drug-specific DSP reports, under the percentages.

VARIABLE	Paracetamol DSP Reports N = 4,235		Promethazine DSP Reports N = 1,486		Amlodipine DSP Reports N = 1,433		Quetiapine DSP Reports N = 1,340		Metformin DSP Reports N = 1,220		DSP Reports N = 42,103	
	N	%	N	%	N	%	N	%	N	%	N	%
Gender												
Woman	2,415	67.12	1,092	75.26	644	56.74	800	65.36	534	51.25	22,819	61.20
Man	1,183	32.88	359	24.74	491	43.26	424	34.64	508	48.75	14,469	38.80
Unknown	637	–	35	–	298	–	116	–	178	–	4,815	–
		P<0.001		P<0.001		P=0.003		P=0.009		P<0.001		
Age												
		31 (20–46)		24 (18–33)		47 (25–55)		37 (26–48)		42 (23–55)		37 (23–51)
		P<0.001		P<0.001		P<0.001		P=0.847		P<0.001		
Outcome												
Death	1,028	24.27	7	0.47	189	13.19	133	9.93	247	20.25	7,218	17.14
Life Threatening	399	9.42	4	0.27	575	40.13	395	29.48	397	32.54	6,440	15.30
Disability	8	0.19	0	0.00	3	0.21	4	0.30	4	0.33	304	0.72
Required Intervention	6	0.14	0	0.00	2	0.14	6	0.45	5	0.41	105	0.25
Hospitalization	1,743	41.16	1,464	98.52	569	39.71	563	42.01	485	39.75	18,727	44.48
Congenital	1	0.02	0	0.00	0	0.00	0	0.00	0	0.00	9	0.02
Other Serious	979	23.12	11	0.74	91	6.35	209	15.60	72	5.90	7,383	17.54
Non Serious	71	1.68	0	0.00	4	0.28	30	2.24	10	0.82	1,917	4.55
		P<0.001		P<0.001		P=0.001		P=0.002		P<0.001		
Continent												
North America	2,166	53.81	12	0.81	651	45.97	372	28.10	425	35.39	16,248	40.19
Europe	1,654	41.09	1,466	98.79	417	29.45	720	54.38	361	30.06	19,269	47.67
Asia	134	3.33	4	0.27	297	20.97	168	12.69	293	24.40	3,639	9.00
South America	14	0.35	1	0.07	21	1.48	9	0.68	6	0.50	350	0.87
Oceania	42	1.04	1	0.07	13	0.92	53	4.00	77	6.41	763	1.89
Africa	15	0.37	0	0.00	17	1.20	2	0.15	39	3.25	155	0.38
Unknown	210	–	2	–	17	–	16	–	19	–	1,679	–
		P<0.001		P<0.001		P=0.001		P=0.002		P<0.001		
Concomitant Alcohol	331	7.82	2	0.13	36	2.51	72	5.37	33	2.70	2,201	5.23
		P<0.001		P<0.001		P<0.001		P=0.847		P<0.001		
Psychiatric comorbidity	214	5.05	5	0.34	34	2.37	336	25.07	70	5.74	6,036	14.31
		P<0.001		P<0.001		P<0.001		P<0.001		P<0.001		

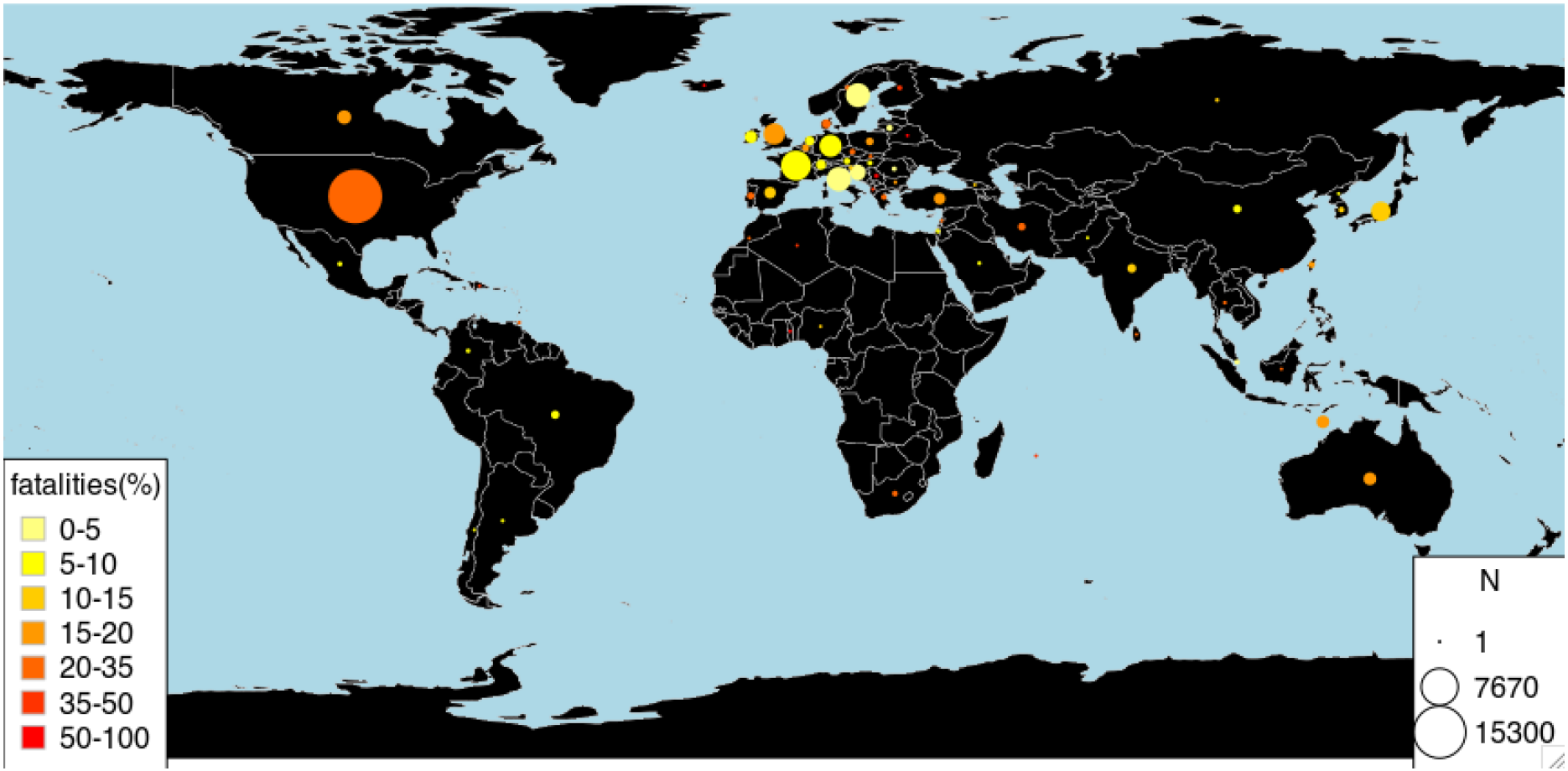

Figure S1– Geographical distribution of reports.

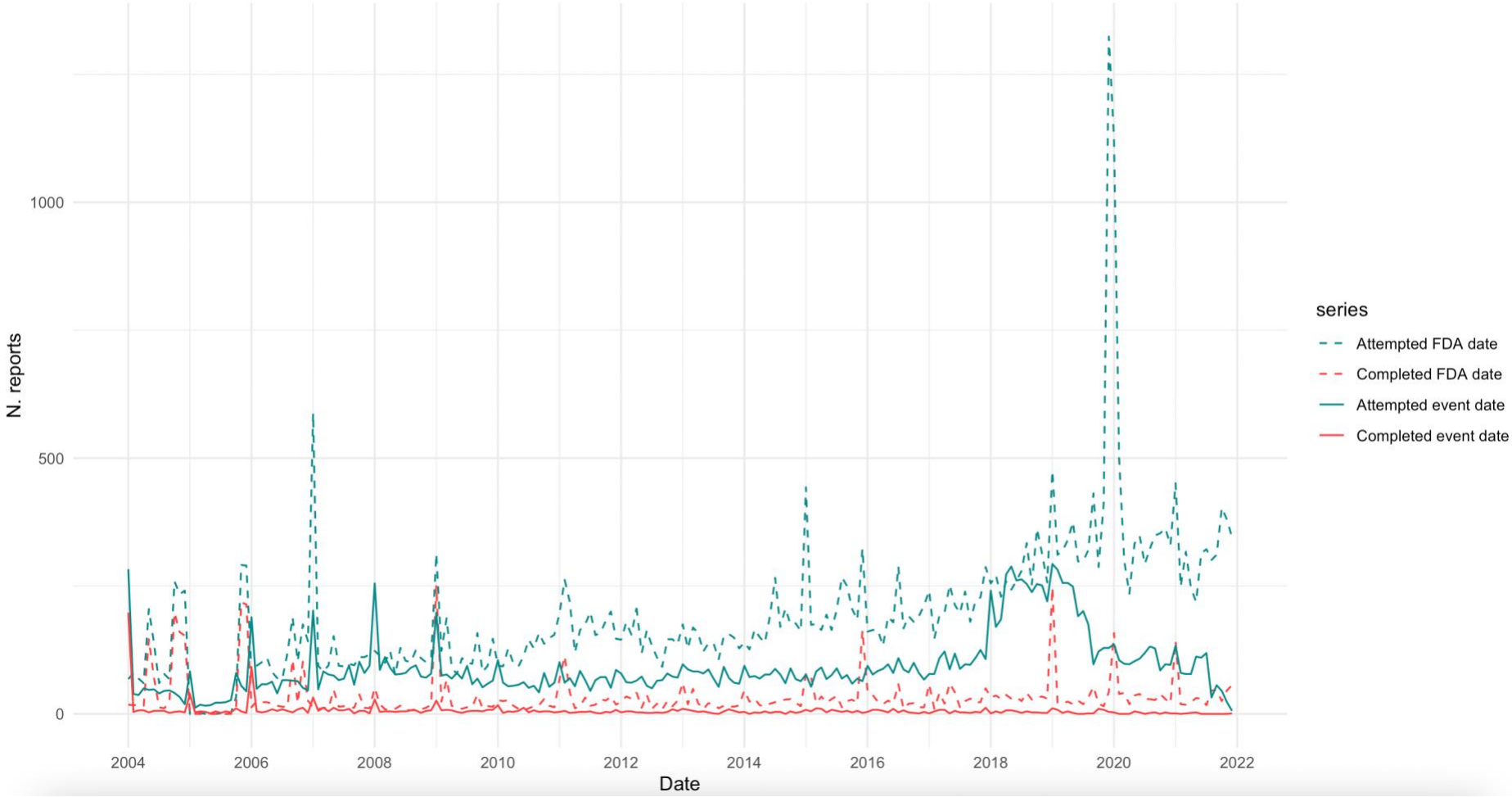

Figure S2– Time series. Monthly spaced time series of both attempted (in blue) and completed (in red) events, both referring to the submission date (dashed line) and to the event date (continuos line). The vertical lines, marking the January of every year, suggest a seasonal behavior of DSP reports.

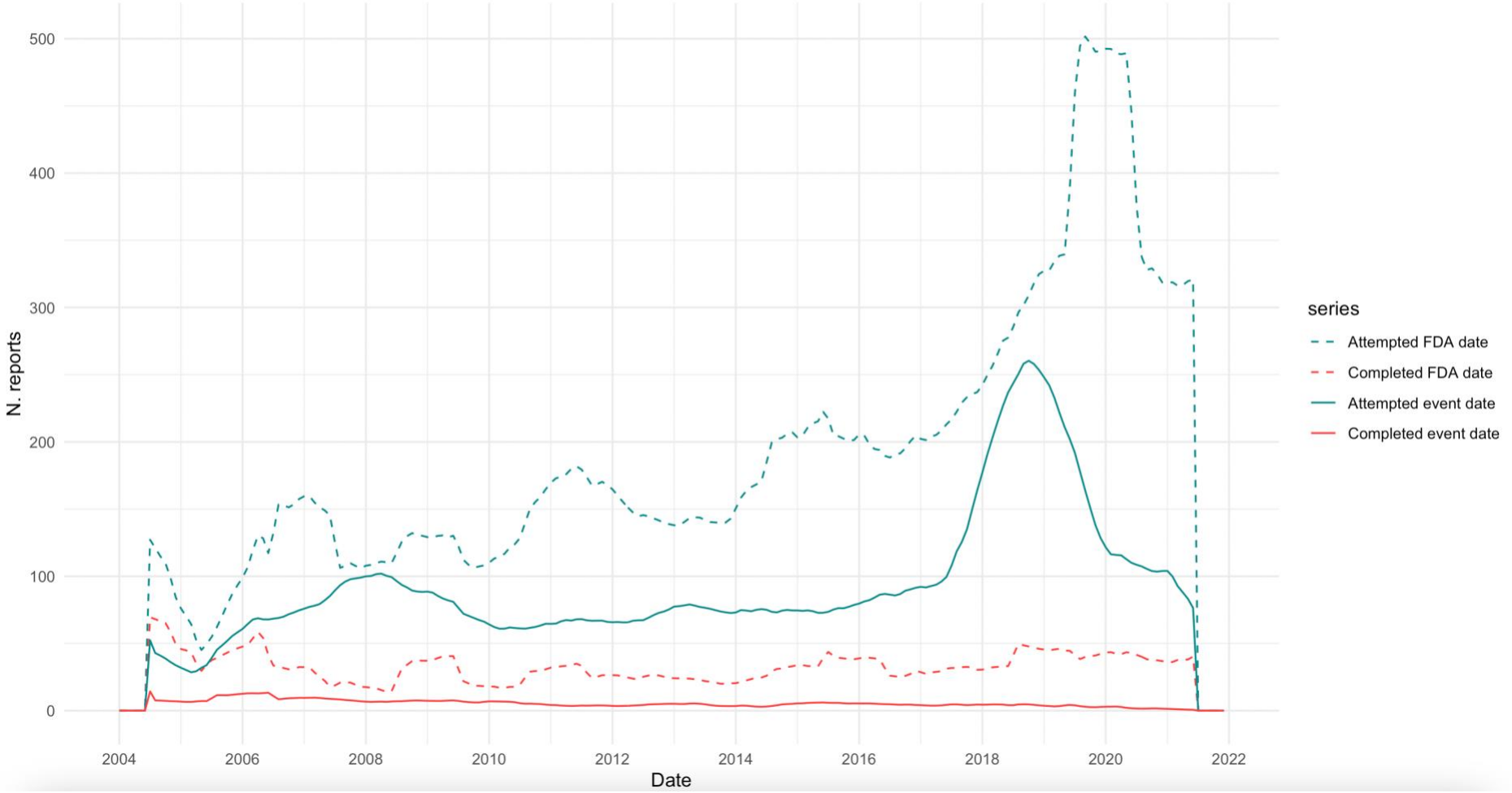

Figure S3– Temporal trends. Trend-cycle components, estimated through a 12-period MA process of both attempted (in blue) and completed (in red) events, both referring to the submission date (dashed line) and to the event date (continuous line).

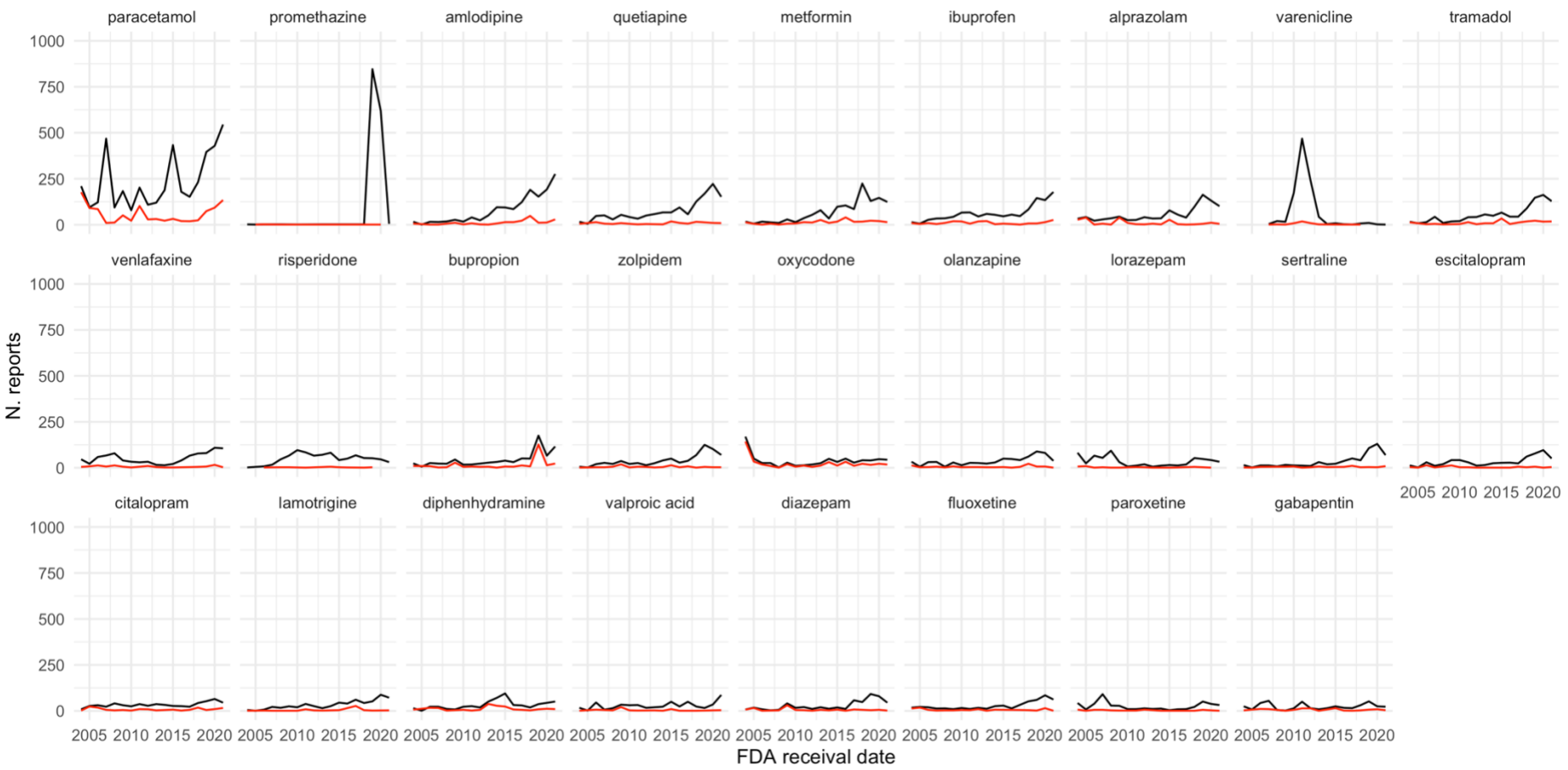

Figure S4 – Temporal trends. Temporal trends of suicidal acts (black) and completed suicides (red) are visualized by individual drug for the drugs contributing to more than 1% of the self-poisoning reports.

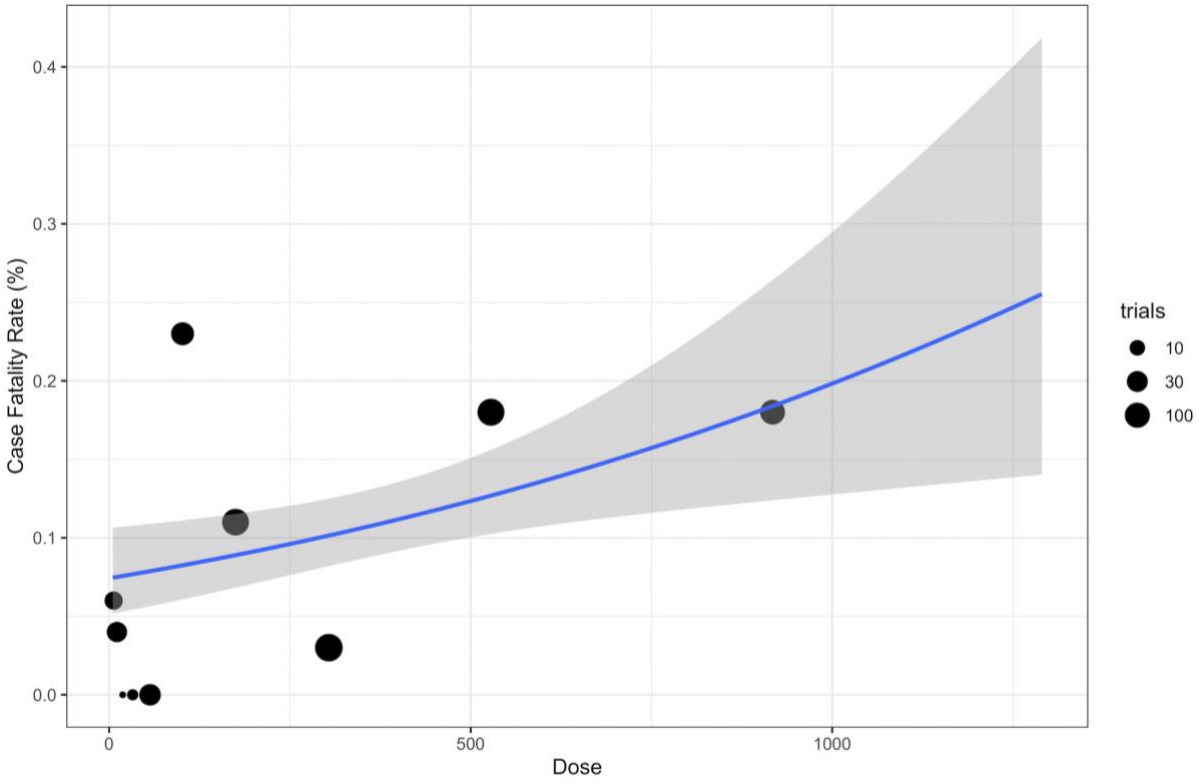

Figure S5 Lethal dose estimation for amlodipine. Observational data concerning doses (in milligrams) and fatality was fitted to a logistic model to estimate the lethal dose for different percentages. Reports were then grouped by dose (in logarithmic intervals – narrow near 0 and wider for higher doses – to account for the exposure distribution skewed to the right – i.e., many reports record lower doses, few higher doses–), and the case-fatality rate for each group was calculated. For each dose-interval, we plotted a point over the logistic, with x-coordinate the midpoint between dose limits, y-coordinate the estimated case-fatality rate, and size the logarithm of the number of reports. The pseudo-R^2 of the model was 0.66.

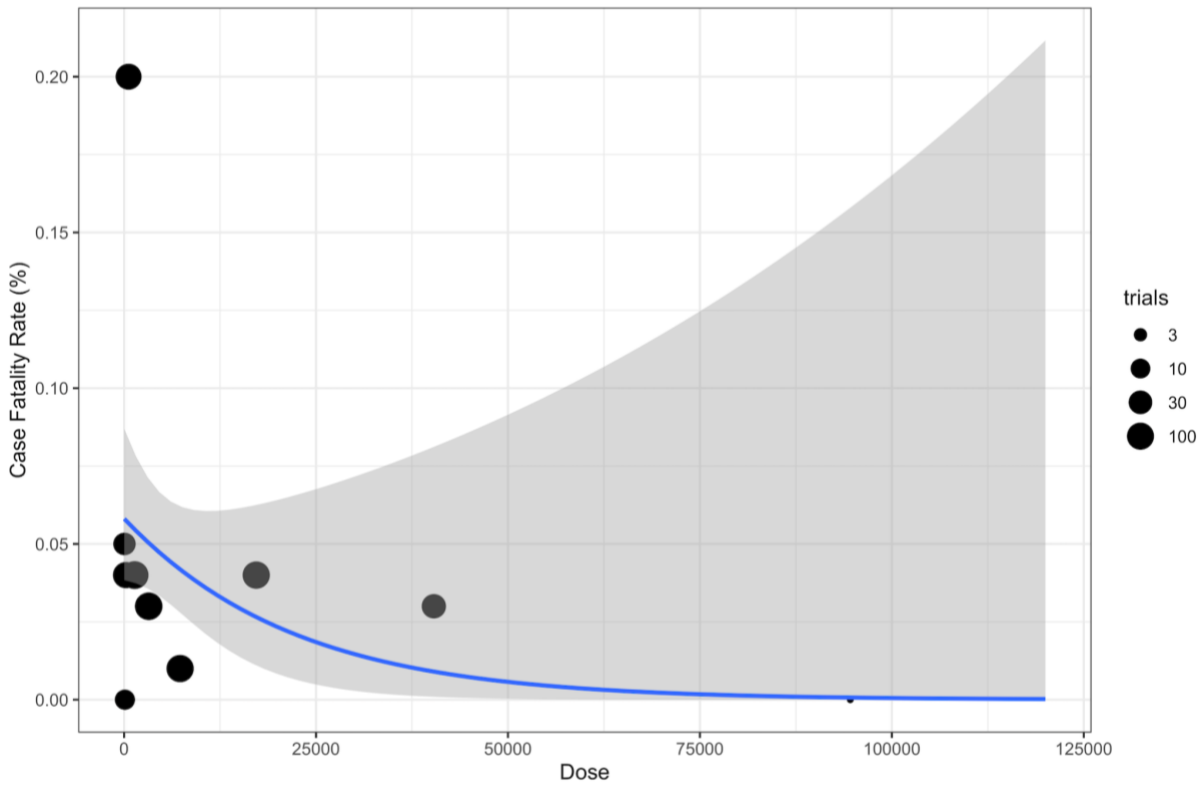

Figure S6 Lethal dose estimation for quetiapine. Observational data concerning doses (in milligrams) and fatality was fitted to a logistic model to estimate the lethal dose for different percentages. Reports were then grouped by dose (in logarithmic intervals – narrow near 0 and wider for higher doses – to account for the exposure distribution skewed to the right – i.e., many reports record lower doses, few higher doses–), and the case-fatality rate for each group was calculated. For each dose-interval, we plotted a point over the logistic, with x-coordinate the midpoint between dose limits, y-coordinate the estimated case-fatality rate, and size the logarithm of the number of reports. The pseudo-R^2 of the model was 0.07.

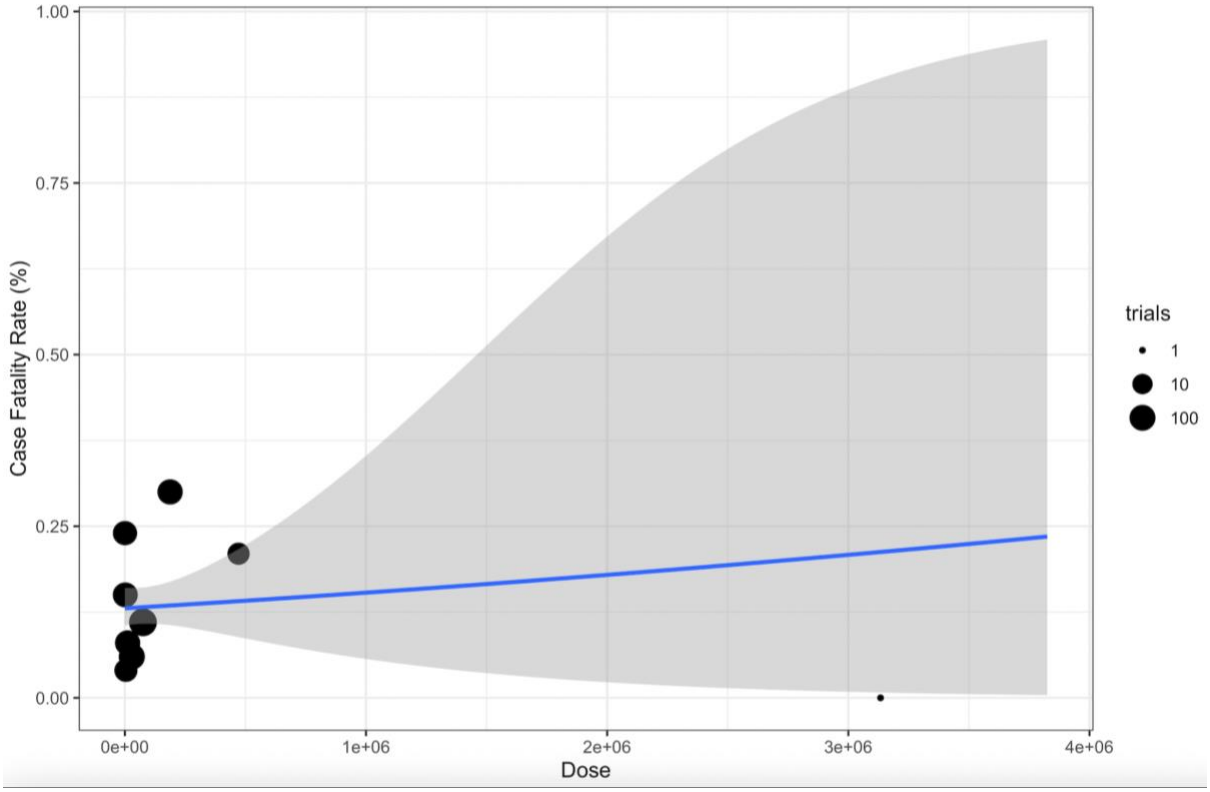

Figure S7 Lethal dose estimation for metformin. Observational data concerning doses (in milligrams) and fatality was fitted to a logistic model to estimate the lethal dose for different percentages. Reports were then grouped by dose (in logarithmic intervals – narrow near 0 and wider for higher doses – to account for the exposure distribution skewed to the right – i.e., many reports record lower doses, few higher doses–), and the case-fatality rate for each group was calculated. For each dose-interval, we plotted a point over the logistic, with x-coordinate the midpoint between dose limits, y-coordinate the estimated case-fatality rate, and size the logarithm of the number of reports. The pseudo-R^2 of the model was 0.00.