Supplementary Online Content

Sun S, Kuja-Halkola R, Faraone SV, et al. Association of psychiatric comorbidity with the risk of premature death among children and adults with attention-deficit/hyperactivity disorder. *JAMA Psychiatry.* Published online August 7, 2019. doi:10.1001/jamapsychiatry.2019.1944

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Definition and Diagnosis Age of Psychiatric Disorders

Psychiatric and behavior disorders	ICD-10 codes	Diagnosis age (years old)			Category for analysis
		25% quartile	Median	75% quartile	
ADHD	F90, PDR medication use	9.9	13.8	17.7	Main Exposure
Autism spectrum disorders (ASD)	F84	9.7	13.7	17.9	Early-onset disorder
Intellectual disability (ID)	F7x	8.3	12.3	16.3	Early-onset disorder
Conduct disorders (CD/ODD)	F90.1, F91	9.7	13.0	15.6	Early-onset disorder
Eating disorders (ED)	F50.0-F50.3, F50.9	15.3	17.5	20.4	Later-onset disorder
Substance use disorders (SUD)	F10-F16, F18-F19	16.7	19.0	21.6	Later-onset disorder
Depressive disorders (Dep)	F32-F34	15.7	18.3	21.4	Later-onset disorder
Bipolar disorders (Bip)	F30-F31	17.5	20.2	23.5	Later-onset disorder
Anxiety disorders (Anx)	F40-F41	16.1	18.8	21.9	Later-onset disorder
Schizophrenia (SCZ)	F2x	18.4	20.8	23.5	Later-onset disorder
Personality disorder (PD)	F60-F62, F69	19.2	21.2	23.7	Later-onset disorder

eTable 2. Psychiatric Disorders in Individuals With and Without ADHD by Sex[a]

	Total	ADHD, No. (%)	Non-ADHD, No. (%)
Male	1 374 790 (100.0)	57 919 (100.0)	1 316 871 (100.0)
Autism spectrum disorders	24 229 (1.8)	11 149 (19.3)	13 080 (1.0)
Intellectual disorder	12 568 (0.9)	6 107 (7.1)	8 461 (0.6)
Conduct disorders	5 929 (0.4)	4 202 (7.3)	1 727 (0.1)
Eating disorders	1 482 (0.1)	230 (0.4)	1 252 (0.1)
Substance use disorder	37 009 (2.7)	6 786 (11.7)	30 223 (2.3)
Depression	29 678 (2.16)	7 630 (13.2)	22 048 (1.7)
Bipolar disorder	3 279 (0.2)	1 197 (2.1)	2 082 (0.2)
Anxiety disorder	29 687 (2.2)	7 338 (12.7)	22 349 (1.7)
Schizophrenia	4 089 (0.3)	972 (1.7)	3 117 (0.2)
Personality disorder	3 625 (0.3)	1 279 (2.2)	2 346 (0.2)
Female	1 300 825 (100.0)	28 751 (100.0)	1 272 074 (100.0)
Autism spectrum disorders	10 739 (0.8)	4 606 (16.0)	6 133 (0.5)
Intellectual disorder	8 326 (0.6)	1 908 (6.6)	6 418 (0.5)
Conduct disorders	3 054 (0.2)	1 698 (5.9)	1 356 (0.1)
Eating disorders	18 514 (1.4)	1 627 (5.7)	16 887 (1.3)
Substance use disorder	31 178 (2.4)	4 732 (16.5)	26 446 (2.1)
Depression	50 913 (3.9)	8 483 (29.5)	42 430 (3.3)
Bipolar disorder	7 036 (0.5)	2 047 (7.1)	4 989 (0.4)
Anxiety disorder	53 224 (4.1)	9 031 (31.4)	44 193 (3.5)
Schizophrenia	2 848 (0.2)	604 (2.1)	2 444 (0.2)
Personality disorder	10 012 (0.8)	2 635 (9.2)	7 377 (0.6)

[a] All variables were statistically different between ADHD and non-ADHD group, with p-values<0.0001 by two-sided χ^2 test.

eTable 3. All-Cause Mortality Rates by Levels of Covariates and Psychiatric Disorders

	Deaths	Person-years at risk	Mortality rate
Overall	6655	29 237 993	2.28
ADHD			
Yes	424	366 332	11.57
No	6 231	28 871 661	2.16
Sex			
Male	4378	15 033 655	2.91
Female	2277	14 204 338	1.60
Age			
Childhood	2475	19 659 410	1.26
Adulthood	4180	9 578 583	4.36
Year of birth#			
1983-1992	4635	13 188 501	3.51
1993-2002	1450	11 524 829	1.26
2003-2009	570	4 524 663	1.26
Birth weight			
<2500	483	1 195 009	4.04
2500-3999	4931	22 482 143	2.19
≥4000	1241	5 560 841	2.23
Maternal age at birth[a]			
<20	304	696 192	4.37
20-29	3930	15 870 827	2.48
30-39	2270	12 014 862	1.89
≥40	151	656 112	2.30
Parental education level			
Primary and lower-secondary	344	964 663	3.57
Upper-secondary	2914	12 237 350	2.38
Post-secondary	2300	13 520 237	1.70
Postgraduate	1097	2 515 743	4.36
Parental employment status			
Employed	5918	27 603 463	2.14
Not employed	737	1 634 530	4.51
Autism spectrum disorders	196	154 717	12.67
Intellectual disorder	336	135 413	24.81
Conduct disorders	64	44 023	14.54
Eating disorders	93	97 704	9.52
Substance use disorder	1056	330 228	31.98
Depression	732	340 511	21.50
Bipolar disorder	124	35 571	34.86
Anxiety disorder	726	311 910	23.28
Schizophrenia	168	29 397	57.15
Personality disorder	250	55 441	45.09

[a] Year of birth and maternal age at birth were analyzed with 1-year intervals in adjusted Cox regression models.

eTable 4. Age at First Diagnosis of ADHD and All-Cause Mortality

	Age at first ADHD diagnosis [a]	Deaths	Mortality rate (/10 000 person-years)	Model 1[b] HR (95% CI)	Model 2 HR (95% CI)
Overall	<=12	39	2.48	1.50 (1.04-2.17)	1.33 (0.92-1.92)
	13-17	124	8.45	2.69 (2.20-3.31)	2.41 (1.97-2.96)
	>=18	261	42.06	10.34 (8.94-11.96)	9.12 (7.88-10.55)
	Non-ADHD	6231	2.16	1.0 (reference)	1.0 (reference)
Male	<=12	29	2.32	1.62 (1.12-2.34)	1.43 (0.99-2.07)
	13-17	95	9.36	2.60 (2.11-3.19)	2.32 (1.89-2.85)
	>=18	200	58.53	9.18 (7.93-10.62)	8.10 (7.00-9.38)
	Non-ADHD	4 054	2.74	1.0 (reference)	1.0 (reference)
Female	<=12	10	3.10	3.24 (1.74-6.06)	2.86 (1.53-5.33)
	13-17	29	6.41	3.50 (2.42-5.08)	3.17 (2.19-4.59)
	>=18	61	21.88	9.13 (7.03-11.87)	8.24 (6.33-10.71)
	Non-ADHD	2 177	1.54	1.0 (reference)	1.0 (reference)

[a] ADHD treated as time-varying exposure while calculating death counts and mortality rates (per 10 000 person-years).

[b] Model 1 (crude model) adjusted for sex and year of birth; Model 2 (adjusted model) furtherly adjusted for sex and year of birth, birth weight, maternal age at birth, parental education level, and parental employment status. No psychiatric comorbidity adjusted here.

eTable 5. Association Between ADHD and Cause-Specific Mortality Risks in the Overall Cohort

Cause of Death[a]	Deaths (mortality rates)			Model 1[b] HR (95% CI)	Model 2 HR (95% CI)
	Total	Non-ADHD	ADHD		
Unnatural causes	3755 (1.28)	3409 (1.18)	346 (9.44)	7.32 (5.78-9.28)	6.48 (5.12-8.21)
Suicide	1301 (0.44)	1168 (0.40)	133 (3.63)	9.37 (6.81-12.88)	8.63 (6.27-11.88)
Accidents	1948 (0.67)	1796 (0.62)	152 (4.15)	4.50 (2.84-7.13)	3.94 (2.49-6.25)
Other external causes	486 (0.17)	425 (0.15)	61 (1.67)	8.47 (6.19-11.57)	6.52 (3.68-11.57)
Natural causes	2883 (0.99)	2805 (0.97)	78 (2.13)	2.71 (1.82-4.04)	2.47 (1.66-3.68)

[a] Among the 6 231 deaths in individuals without ADHD, information on death causes was missing for 17 (0.3%) and they were not included in this analysis. ADHD was time-varying exposures while calculating mortality rates (per 10 000 person-years).
[b] Model 1 (crude model) adjusted for year of birth and sex; Model 2 (adjusted model) furtherly adjusted for birth weight, maternal age at birth, parental educational level and parental employment status.

eTable 6. Psychiatric Comorbidity and Cause-Specific Mortality Risks Among Young Adults With ADHD

Death cause	Comorbidity[a]	Deaths N (%)	Mortality rate	Model 1[b] HR (95% CI)	Model 2 HR (95% CI)
Natural	Overall	58 (100.0)	3.44	--	--
	ADHD only	16 (27.6)	2.27	--	--
	ADHD +any	42 (72.4)	4.27	1.64 (0.84-3.19)	1.57 (0.80-3.05)
	ADHD + ASD	8 (13.8)	3.19	0.60 (0.21-1.67)	0.62 (0.22-1.74)
	ADHD + ID	7 (12.1)	5.34	1.52 (0.60-3.88)	1.49 (0.58-3.80)
	ADHD + CD/ODD	NA	3.56	1.65 (0.59-4.64)	1.48 (0.53-4.18)
	ADHD + ED	5 (8.6)	10.54	6.00 (0.82-43.67)	5.89 (0.81-42.94)
	ADHD + SUD	26 (44.8)	8.07	3.52 (1.89-6.59)	3.23 (1.72-6.07)
	ADHD + Dep	18 (31.0)	4.42	1.15 (0.56-2.36)	1.15 (0.56-2.36)
	ADHD + Bip	5 (8.6)	6.22	0.67 (0.09-4.91)	0.65 (0.09-4.76)
	ADHD + Anx	16 (27.6)	4.28	1.29 (0.62-2.68)	1.27 (0.61-2.64)
	ADHD + SCZ	8 (13.8)	17.60	3.51 (1.36-9.08)	3.39 (1.31-8.78)
	ADHD + PD	11 (19.0)	9.93	2.98 (1.22-7.28)	2.84 (1.16-6.95)
Suicide	Overall	120	7.11	--	--
	ADHD only	6 (5.0)	0.85	--	--
	ADHD +any	114 (95.0)	11.60	9.10 (3.95-20.98)	8.96 (3.89-20.66)
	ADHD + ASD	24 (20.0)	9.57	1.13 (0.63-2.00)	1.13 (0.64-2.01)
	ADHD + ID	NA	0.76	--	--
	ADHD + CD/ODD	12 (10.0)	10.68	1.52 (0.70-3.31)	1.47 (0.68-3.20)
	ADHD + ED	6 (5.0)	12.65	2.86 (0.40-20.56)	2.83 (0.39-20.33)
	ADHD + SUD	82 (68.3)	25.44	6.65 (4.16-10.62)	6.61 (4.13-10.57)
	ADHD + Dep	67 (55.8)	16.44	4.22 (2.71-6.55)	4.20 (2.71-6.53)
	ADHD + Bip	23 (19.2)	28.62	6.18 (3.55-10.77)	6.09 (3.49-10.61)
	ADHD + Anx	78 (65.0)	20.87	5.84 (3.71-9.17)	5.79 (3.68-9.10)
	ADHD + SCZ	18 (15.0)	39.60	3.59 (1.88-6.85)	3.50 (1.84-6.68)
	ADHD + PD	44 (36.7)	39.73	6.69 (4.03-11.10)	6.60 (3.97-10.96)
Accident	Overall	133	7.88	--	--
	ADHD only	15 (11.3)	2.13	--	--
	ADHD +any	118 (88.7)	12.01	4.90 (2.79-8.62)	4.87 (2.77-8.57)
	ADHD + ASD	15 (11.3)	5.98	0.69 (0.39-1.24)	0.72 (0.40-1.28)
	ADHD + ID	NA[c]	2.29	0.20 (0.05-0.83)	0.20 (0.05-0.80)
	ADHD + CD/ODD	15 (11.3)	13.35	2.14 (1.20-3.82)	2.08 (1.16-3.72)
	ADHD + ED	NA	4.22	--	--
	ADHD + SUD	99 (74.4)	30.71	9.98 (6.47-15.39)	10.02 (6.49-15.49)
	ADHD + Dep	48 (36.1)	11.78	2.04 (1.39-3.01)	2.07 (1.40-3.04)
	ADHD + Bip	10 (7.5)	12.44	1.64 (0.76-3.54)	1.64 (0.76-3.55)
	ADHD + Anx	65 (48.9)	17.39	3.97 (2.71-5.82)	3.97 (2.70-5.82)
	ADHD + SCZ	16 (12.0)	35.20	3.52 (2.02-6.12)	3.50 (2.01-6.09)
	ADHD + PD	27 (20.3)	24.38	3.62 (2.21-5.92)	3.61 (2.20-5.91)

[a] ADHD and comorbid disorders were time-varying exposures while calculating death counts and mortality rates (per 10 000 person-years). ADHD only: ADHD without any comorbidity; ADHD + any: ADHD with any comorbid disorder(s); CD/ODD: conduct disorders including oppositional defiant disorder; ASD: autism spectrum disorders; ID: intellectual disability; ED: eating disorders; SUD: substance use disorders; Dep: depressive disorders; Bip: bipolar disorders; Anx: anxiety disorders; SCZ: schizophrenia disorders; PD: personality disorders.
[b] Model 1 adjusted for year of birth and sex; Model 2 furtherly adjusted for birth weight, maternal age at birth, parental educational level and parental employment status.
[c] NA: Death counts less than 5 were presented as NA (Not Available) for ethical consideration.

eTable 7. Sensitivity Analysis: Association Between NPR-Diagnosed ADHD[a] and All-Cause Mortality Rates

Age band (year-old)	Groups	Deaths	Person-years	Mortality rate (/10 000 person-years)	Model 1[b] HR (95% CI)	Model 2 HR (95% CI)
Overall	ADHD	6292	299 878	12.10	4.47 (3.96-5.06)	3.95 (3.49-4.47)
	Non-ADHD	363	28 938 113	2.17	1.0 (reference)	1.0 (reference)
Childhood	ADHD	31	154 153	2.01	1.50 (0.98-2.29)	1.33 (0.87-2.03)
	Non-ADHD	2444	19 505 257	1.25	1.0 (reference)	1.0 (reference)
Adulthood	ADHD	332	145 727	22.78	5.21 (4.58-5.94)	4.60 (4.04-5.24)
	Non-ADHD	3848	9 432 855	4.08	1.0 (reference)	1.0 (reference)

[a] Definition of ADHD was first diagnosis recorded in National Patient Register, analyzed as time-varying exposure.
[b] Model 1 adjusted for year of birth and sex; Model 2 furtherly adjusted for birth weight, maternal age at birth, parental educational level and parental employment status

eTable 8. All-Cause Mortality Risks and Number of Psychiatric Comorbidities or Psychotropic Medication Use With ADHD in Young Adults

Groups	Deaths	Person-years	Mortality rate	Model 1[b] HR (95% CI)	Model 2 HR (95% CI)
Overall	3 821	16 206 949	2.36	--	--
ADHD only	16	74 154	2.16	1.01 (0.61-1.68)	0.92 (0.55-1.53)
ADHD + 1 comorbidity/ medication a	47	68 947	6.82	2.41 (1.78-3.28)	2.15 (1.58-2.92)
ADHD + 2	66	38 306	17.23	4.83 (3.64-6.42)	4.28 (3.22-5.68)
ADHD + 3	80	19 414	41.21	11.44 (8.85-14.80)	9.90 (7.65-12.81)
ADHD + 4 or more	160	14 175	112.88	34.41 (28.58-41.42)	29.48 (24.46-35.53)
No above	3 452	15 991 953	2.16	1.0 (reference)	1.0 (reference)

[a] Comorbidity was identified by the first clinical diagnosis in NPR; psychotropic medication use identified as the first prescription in PDR. Comorbidity: Among autism spectrum disorders, intellectual disability, conduct disorders, eating disorders, substance use disorder, depression, bipolar disorder, schizophrenia, anxiety disorder, and personality disorder. ADHD and comorbid disorders were time varying covariates when calculating death counts and mortality rates (per 10 000 person-years). Psychotropic medication: Among antipsychotics (N05A); anxiolytics, hypnotics, and sedatives (N05B or N05C); antidepressants (N06A); antiepileptic drugs (N03A); drugs used in addictive disorders (N07B) and opioid pain medications (N02A).
[b] Model 1 (crude model) adjusted for sex and year of birth; Model 2 (adjusted model) furtherly adjusted for sex and year of birth, birth weight, maternal age at birth, parental education level, and parental employment status.

eTable 9. Sensitivity Analysis: Association Between ADHD and Premature Death in Young Adult Men and Women

| | ADHD | | Non-ADHD | | Covariate adjustment[a] | | Comorbidity adjustment | |
| | | | | | Model 1 | Model 2 | Model 3 | Model 4 |
Death causes	Death	Mortality rate[b]	Deaths	Mortality rate	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Male								
All-cause	286	26.24	2 499	5.21	5.63 (4.97-6.38)	5.00 (4.40-5.67)	4.26 (3.70-4.90)	1.47 (1.27-1.70)
Unnatural	244	22.38	1 821	3.80	6.71 (5.85-7.69)	5.87 (5.11-6.74)	5.61 (4.82-6.53)	1.60 (1.37-1.87)
Accident	114	10.46	898	1.87	6.69 (5.47-8.17)	5.79 (4.73-7.08)	5.91 (4.757.35)	2.02 (1.61-2.55)
Suicide	83	7.61	681	1.42	5.79 (4.58-7.30)	5.26 (4.16-6.66)	4.46 (3.42-5.81)	1.19 (0.91-1.55)
Other	47	4.31	230	0.48	9.87 (7.15-13.63)	8.07 (5.81-11.19)	8.00 (5.61-11.42)	1.69 (1.17-2.43)
Natural	42	3.85	668	1.39	2.95 (2.15-4.05)	2.72 (1.98-3.74)	1.53 (1.08-2.18)	1.03 (0.72-1.47)
Female								
All-cause	83	13.91	953	2.09	7.19 (5.72-9.04))	6.46 (5.13-8.14)	3.85 (2.96-5.02)	1.25 (0.96-1.62)
Unnatural	67	11.22	567	1.25	10.43 (8.03-13.53)	9.28 (7.13-12.06)	6.59 (4.84-8.97)	1.38 (1.03-1.85)
Accident	19	3.18	207	0.45	9.11 (5.62-14.77)	8.06 (4.95-13.12)	6.84 (3.96-11.82)	2.68 (1.52-4.74)
Suicide	37	6.20	260	0.57	11.46 (8.04-16.35)	10.53 (7.36-15.06)	6.46 (4.24-10.11)	1.16 (0.78-1.70)
Other	11	1.84	98	0.22	10.03 (5.29-18.99)	8.16 (4.28-15.54)	6.20 (2.94-13.07)	1.16 (0.57-2.35)
Natural	16	2.68	384	0.84	3.13 (1.89-5.18)	2.86 (1.73-4.75)	1.26 (0.73-2.16)	1.03 (0.59-1.78)

[a] Model 1 adjusted for year of birth and sex; Model 2 furtherly adjusted for birth weight, maternal age at birth, parental educational level and parental employment status. In addition to Model 2, Model 3 furtherly adjusted for early-onset disorders including conduct disorders, ASD and intellectual disability disorders; and in addition to Model 3, Model 4 furtherly adjusted for later-onset disorders including substance use disorder, depressive disorders, bipolar disorders, anxiety disorders, schizophrenia, personality disorders and eating disorders.

[b] ADHD and comorbid disorders were time-varying exposures while calculating mortality rates (per 10 000 person-years).