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Supplementary Material

Article Title: Antibiotic Exposure and the Risk for Depression, Anxiety, or Psychosis: A Nested Case-Control Study

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This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary eTable 1. Risk for Depressive Disorders as a Function of Time from Last Prescription of Specific Antibiotic Courses

Antibiotic type	Time from last antibiotic prescription (years)	Cases	Controls	Crude OR	Adjusted OR ^{a,b}
Penicillins	0	125,654 (61.91%)	550,056 (68.42%)	Reference	Reference
	1-5	67,960 (33.48%)	215,007 (26.74%)	1.54 (1.51-1.57)	1.38 (1.33-1.43)
	5-10	8,502 (4.19%)	34,913 (4.34%)	1.23 (1.19-1.28)	1.15 (1.08-1.22)
	>10	858 (0.42%)	3,985 (0.50%)	1.11 (0.99-1.23)	1.04 (0.92-1.18)
Cephalosporines	0	186,925 (92.09%)	755,390 (93.96%)	Reference	Reference
	1-5	12,460 (6.14%)	36,289 (4.51%)	1.44 (1.39-1.48)	1.31 (1.23-1.39)
	5-10	3,081 (1.52%)	10,311 (1.28%)	1.26 (1.19-1.34)	1.19 (1.09-1.30)
	>10	508 (0.25%)	1,971 (0.25%)	1.09 (0.94-1.26)	1.09 (0.93-1.28)
Macrolides	0	177,485 (87.44%)	725,383 (90.23%)	Reference	Reference
	1-5	20,352 (10.03%)	60,247 (7.49%)	1.42 (1.38-1.45)	1.29 (1.24-1.35)
	5-10	4,401 (2.17%)	15,598 (1.94%)	1.2 (1.14-1.26)	1.13 (1.05-1.22)
	>10	736 (0.36%)	2,733 (0.34%)	1.16 (1.03-1.31)	1.13 (0.99-1.30)
Quinolones	0	196,297 (96.71%)	784,315 (97.56%)	Reference	Reference
	1-5	5,320 (2.62%)	15,028 (1.87%)	1.42 (1.36-1.49)	1.31 (1.21-1.42)
	5-10	1,204 (0.59%)	4,135 (0.51%)	1.18 (1.07-1.29)	1.06 (0.94-1.21)
	>10	153 (0.08%)	483 (0.06%)	1.29 (1.00-1.67)	1.18 (0.87-1.61)
Sulfonamides	0	183,752 (90.53%)	744,652 (92.62%)	Reference	Reference
	1-5	15,662 (7.72%)	46,394 (5.77%)	1.41 (1.37-1.45)	1.33 (1.26-1.40)
	5-10	3,088 (1.52%)	11,356 (1.41%)	1.15 (1.08-1.21)	1.07 (0.98-1.16)
	>10	472 (0.23%)	1,559 (0.19%)	1.28 (1.10-1.49)	1.22 (1.03-1.45)
Tetracyclines	0	186,184 (91.73%)	750,775 (93.38%)	Reference	Reference
	1-5	13,457 (6.63%)	41,243 (5.13%)	1.33 (1.30-1.37)	1.24 (1.17-1.30)
	5-10	2,947 (1.45%)	10,576 (1.32%)	1.15 (1.08-1.22)	1.09 (1.00-1.19)
	>10	386 (0.19%)	1,367 (0.17%)	1.18 (1.00-1.39)	1.19 (0.99-1.43)
Imidazole	0	193,497 (95.33%)	777,161 (96.67%)	Reference	Reference
	1-5	7,569 (3.73%)	20,518 (2.55%)	1.51 (1.45-1.57)	1.34 (1.25-1.44)
	5-10	1,680 (0.83%)	5,522 (0.69%)	1.26	1.12

	>10	228 (0.11%)	760 (0.1%)	(1.17-1.37) 1.26 (1.02-1.55)	(0.99-1.25) 1.17 (0.92-1.49)
Antifungals	0	193,341 (95.25%)	773,078 (96.16%)	Reference	Reference
	1-5	7,808 (3.85%)	24,261 (3.02%)	1.3 (1.25-1.35)	1.18 (1.10-1.26)
	5-10	1,625 (0.80%)	5,912 (0.74%)	1.11 (1.03-1.20)	1.04 (0.93-1.17)
	>10	200 (0.10%)	710 (0.09%)	1.15 (0.92-1.44)	1.12 (0.87-1.44)
Antivirals	0	200,136 (98.60%)	794,854 (98.87%)	Reference	Reference
	1-5	2,307 (1.14%)	7,233 (0.90%)	1.27 (1.18-1.35)	1.12 (1.04-1.27)
	5-10	481 (0.24%)	1,684 (0.21%)	1.14 (0.99-1.31)	1.09 (0.90-1.32)
	>10	50 (0.02%)	190 (0.02%)	1.05 (0.68-1.63)	1.00 (0.60-1.65)

^a Adjusted for obesity (body mass index > 30), smoking (ever/never), alcohol consumption, Townsend quantiles, number of urinary tract, and upper and lower respiratory infections before index date.

^b After the Bonferroni correction, the *P* value needed to show statistical significance was .006.

Abbreviation: OR = odds ratio.

Supplementary eTable 2. Risk for Anxiety Disorder as a Function of Time from Last Prescription of Specific Antibiotic Courses

Antibiotic type	Time from last antibiotic prescription (years)	Cases	Controls	Crude OR	Adjusted OR ^{a,b}
Penicillins	0	8,487 (58.25%)	36,598 (63.25%)	Reference	Reference
	1-5	5,160 (35.42%)	17,581 (30.38%)	1.37 (1.29-1.47)	1.3 (1.15-1.47)
	5-10	818 (5.61%)	3,215 (5.56%)	1.23 (1.08-1.39)	1.18 (0.98-1.43)
	>10	105 (0.72%)	468 (0.81%)	1.09 (0.79-1.49)	1.09 (0.76-1.57)
Cephalosporines	0	13,127 (90.10%)	53,215 (91.97%)	Reference	Reference
	1-5	1,048 (7.19%)	3,260 (5.63%)	1.35 (1.21-1.50)	1.33 (1.09-1.62)
	5-10	329 (2.26%)	1,140 (1.97%)	1.22 (1.02-1.47)	1.13 (0.87-1.47)
	>10	66 (0.45%)	247 (0.43%)	1.13 (0.75-1.70)	1.18 (0.75-1.87)
Macrolides	0	12,390 (85.04%)	50,693 (87.61%)	Reference	Reference
	1-5	1,613 (11.07%)	5,168 (8.93%)	1.30 (1.20-1.42)	1.18 (1.01-1.38)
	5-10	487 (3.34%)	1,659 (2.87%)	1.24 (1.07-1.45)	1.14 (0.91-1.43)
	>10	80 (0.55%)	342 (0.59%)	1.00 (0.70-1.42)	0.99 (0.67-1.48)
Quinolones	0	13,935 (95.64%)	55,982 (96.75%)	Reference	Reference
	1-5	461 (3.16%)	1,362 (2.35%)	1.37 (1.18-1.60)	1.50 (1.16-1.94)
	5-10	146 (1.00%)	459 (0.79%)	1.31 (1.00-1.71)	1.13 (0.76-1.68)
	>10	28 (0.19%)	28 (0.19%)	1.99 (1.03-3.85)	1.90 (0.88-4.10)
Sulfonamides	0	12,771 (87.65%)	52,247 (90.30%)	Reference	Reference
	1-5	1,356 (9.31%)	4,148 (7.17%)	1.39 (1.26-1.53)	1.46 (1.24-1.73)
	5-10	373 (2.56%)	1,205 (2.08%)	1.33 (1.12-1.59)	1.30 (1.00-1.68)
	>10	70 (0.48%)	262 (0.45%)	1.16 (0.79-1.70)	1.16 (0.75-1.80)
Tetracyclines	0	12,991 (89.16%)	53,025 (91.64%)	Reference	Reference
	1-5	1,185 (8.13%)	3,521 (6.09%)	1.40 (1.27-1.55)	1.39 (1.17-1.66)
	5-10	343 (2.35%)	1,125 (1.94%)	1.28 (1.07-1.53)	1.32 (1.01-1.73)
	>10	51 (0.35%)	191 (0.33%)	1.12 (0.71-1.75)	1.33 (0.80-2.21)
Imidazole	0	13,660 (93.75%)	55,108 (95.24%)	Reference	Reference
	1-5	631 (4.33%)	1,918 (3.31%)	1.37 (1.20-1.56)	1.50 (1.19-1.89)
	5-10	244 (1.67%)	719 (1.24%)	1.43	1.30

				(1.16-1.78)	(0.95-1.80)
	>10	35 (0.24%)	117 (0.2%)	1.25	1.21
				(0.73-2.16)	(0.64-2.27)
Antifungals	0	13,689 (93.95%)	54,972 (95.01%)	Reference	Reference
	1-5	639 (4.39%)	2,182 (3.77%)	1.19	1.24
				(1.05-1.36)	(0.99-1.55)
	5-10	216 (1.48%)	605 (1.05%)	1.47	1.57
				(1.18-1.85)	(1.15-2.16)
	>10	26 (0.18%)	103 (0.18%)	1.04	1.24
				(0.56-1.93)	(0.64-2.40)
Antivirals	0	14,317 (98.26%)	56,999 (98.51%)	Reference	Reference
	1-5	191 (1.31%)	676 (1.17%)	1.12	1.13
				(0.89-1.40)	(0.82-1.55)
	5-10	53 (0.36%)	166 (0.29%)	1.28	1.36
				(0.82-1.97)	(0.76-2.41)
	>10	9 (0.06%)	21 (0.04%)	1.71	1.53
				(0.57-5.10)	(0.44-5.29)

^a Adjusted for obesity (body mass index > 30), smoking (ever/never), alcohol consumption, Townsend quantiles, number of urinary tract, and upper and lower respiratory infections before index date.

^b After the Bonferroni correction, the *P* value needed to show statistical significance was .006.

Abbreviation: OR = odds ratio.

Supplementary eTable 3. Risk for Psychotic Disorder as a Function of Time from Last Prescription of Specific Antibiotic Courses

Antibiotic type	Time from last antibiotic prescription (years)	Cases	Controls	Crude OR	Adjusted OR ^{a,b}
Penicillins	0	1,828 (67.96%)	7,316 (68.73%)	Reference	Reference
	1-5	723 (26.88%)	2,780 (26.12%)	1.05 (0.90-1.23)	0.95 (0.71-1.28)
	5-10	134 (4.98%)	483 (4.54%)	1.11 (0.81-1.51)	1.05 (0.67-1.65)
	>10	5 (0.19%)	65 (0.61%)	0.30 (0.08-1.10)	0.22 (0.04-1.17)
Cephalosporines	0	2,540 (94.42%)	10,046 (94.38%)	Reference	Reference
	1-5	99 (3.68%)	412 (3.87%)	0.96 (0.69-1.32)	0.87 (0.49-1.55)
	5-10	40 (1.49%)	155 (1.46%)	1.04 (0.62-1.74)	0.99 (0.48-2.05)
	>10	11 (0.41%)	31 (0.29%)	1.47 (0.53-4.07)	1.09 (0.33-3.60)
Macrolides	0	2,405 (89.41%)	9,543 (89.66%)	Reference	Reference
	1-5	214 (7.96%)	804 (7.55%)	1.06 (0.84-1.33)	0.89 (0.59-1.36)
	5-10	63 (2.34%)	237 (2.23%)	1.05 (0.69-1.60)	0.98 (0.54-1.80)
	>10	8 (0.30%)	60 (0.6%)	0.51 (0.17-1.48)	0.61 (0.18-2.05)
Quinolones	0	2,621 (97.43%)	10,362 (96.59%)	Reference	Reference
	1-5	50 (1.86%)	207 (1.94%)	0.96 (0.62-1.49)	0.96 (0.45-2.08)
	5-10	17 (0.63%)	63 (0.59%)	1.06 (0.50-2.28)	1.25 (0.48-3.21)
	>10	2 (0.07%)	12 (0.11%)	0.66 (0.08-5.54)	0.71 (0.04-14.10)
Sulfonamides	0	2,515 (93.49%)	9,933 (93.32%)	Reference	Reference
	1-5	134 (4.98%)	522 (4.90%)	1.01 (0.76-1.35)	0.76 (0.46-1.28)
	5-10	35 (1.30%)	161 (1.51%)	0.85 (0.50-1.46)	0.58 (0.26-1.31)
	>10	6 (0.22%)	28 (0.26%)	0.82 (0.21-3.14)	0.64 (0.13-3.10)
Tetracyclines	0	2,508 (93.23%)	9,916 (93.16%)	Reference	Reference
	1-5	132 (4.91%)	554 (5.20%)	0.94 (0.71-1.25)	1.18 (0.74-1.86)
	5-10	45 (1.67%)	142 (1.33%)	1.25 (0.76-2.04)	0.97 (0.46-2.05)
	>10	5 (0.19%)	32 (0.30%)	0.60 (0.16-2.32)	0.56 (0.12-2.57)
Imidazole	0	2,596 (96.51%)	10,329 (97.04%)	Reference	Reference
	1-5	72 (2.68%)	235 (2.21%)	1.24 (0.84-1.82)	1.25 (0.67-2.33)
	5-10	17 (0.63%)	61 (0.57%)	1.13	1.47

	>10	5 (0.19%)	19 (0.18%)	(0.53-2.43) 1.04	(0.57-3.75) 0.96
	0	2,582 (95.99%)	10,259 (96.38%)	(0.26-4.20) Reference	(0.19-4.83) Reference
Antifungals	1-5	82 (3.05%)	298 (2.80%)	1.10 (0.77-1.57)	0.97 (0.53-1.75)
	5-10	26 (0.97%)	75 (0.70%)	1.36 (0.71-2.59)	1.15 (0.45-2.96)
	>10	-	12 (0.11%)	NA	NA
Antivirals	0	2,658 (98.81%)	10,517 (98.81%)	Reference	Reference
	1-5	27 (1.00%)	86 (0.81%)	1.24 (0.67-2.28)	1.03 (0.40-2.64)
	5-10	5 (0.19%)	36 (0.34%)	0.55 (0.14-2.07)	0.43 (0.08-2.35)
	>10	-	5 (0.05%)	NA	NA

^a Adjusted for obesity (body mass index > 30), smoking (ever/never), alcohol consumption, Townsend quantiles, number of urinary tract, and upper and lower respiratory infections before index date.

^b After the Bonferroni correction, the *P* value needed to show statistical significance was .006.

Abbreviations: NA = not applicable, OR = odds ratio.

Supplementary eAppendix: List of Read codes according to the three psychiatric diagnoses (depression, anxiety, and psychosis)

Depression

1465; 212S.00; E112.00; E112.11; E112.12 ; E112.13; E112.14; E112000 ; E112100;
E112200; E112300; E112400; E112500; E112600; E112z00; E113.00; E113.11;
E113000; E113100; E113200; E113300; E113400; E113500; E113600; E113700;
E113z00; E11y200; E130.11; E135.00; E204.00; E290.00; E290z00; E291.00;
E2B..00; E2B0.00; E2B1.00; Eu32.00; Eu32.11; Eu32.12; Eu32.13; Eu32000;
Eu32100; Eu32200; Eu32211; Eu32212; Eu32213; Eu32300; Eu32311; Eu32312;
Eu32313; Eu32314; Eu32400 ; Eu32500; Eu32600; Eu32700; Eu32800; Eu32y00;
Eu32y11; Eu32y12; Eu32z00; Eu32z11; Eu32z12; Eu32z13; Eu32z14; Eu33.00;
Eu33.11; Eu33.12; Eu33.13; Eu33.14; Eu33000; Eu33100; Eu33211; Eu33212;
Eu33214; Eu33311; Eu33313; Eu33314; Eu33315; Eu33316; Eu33400; Eu33y00
Eu33z00; Eu33z11; Eu34113; Eu3y111.

Anxiety

1465; E200400; E200500; E202.12; Eu05400; Eu40.00; Eu40y00; Eu40z00; Eu41.00;
Eu41000; Eu41100; Eu41y00 ; Eu41z00; Eu41z11; Eu05400.

Psychosis

212 ;1464W.00; E100.00; E100.11; E100000; E100100; E100300; E100400;
E100500; E100z00; E101.00; E101000; E101100; E101200; E101300; E101400;
E101500; E101z00; E102.00; E102000; E102100; E102200 ; E102300; E102400;
E102500; E102z00; E103.00; E103000; E103100; E103200 ; E103300; E103400;
E103500; E103z00; E105.00; E105000; E105100; E105200 ; E105300; E105400;
E105500; E105z00; E106.00; E107.00; E107.11; E107000; E107100; E107200;

E107300; E107400; E107500; E107z00; E10y.00; E10y.11; E10y000; E10y100;
E10yz00; E10z.00; E13z.11; Eu20.00; Eu20000; Eu20011; Eu20100; Eu20111;
Eu20200; Eu20300; Eu20311; Eu20500; Eu20511; Eu20600; Eu20y00; Eu20y11;
Eu20z00; Eu21.13; Eu23.00; Eu23111; Eu23112; Eu23200; Eu23300; Eu23y00;
Eu23z00; Eu24.13; Eu25100; Eu25111; Eu25112; Eu25211; Eu2y.00; Eu2y.00;
ZV11000; Eu05200.