

Supplementary Online Content

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

eTable 1. *Helicobacter pylori* therapy containing clarithromycin with appropriate doses and distributions of drug regimens for composite neuropsychiatric outcome^a

Co-prescription of two antibiotics and one of the proton pump inhibitors:				(%)
1.	Clarithromycin, 500 mg bd	Amoxicillin, 1000 mg bd	Esomeprazole, 20 mg bd	25.7
			Lansoprazole, 30 mg bd	9.2
			Omeprazole, 20 mg bd	1.2
			Pantoprazole, 40 mg bd	40.5
			Rabeprazole, 20 mg bd	19.6
2.	Clarithromycin, 250 mg bd	Metronidazole, 400 mg bd	Esomeprazole, 20 mg bd	1.2
			Lansoprazole, 30 mg bd	0.9
			Omeprazole, 20 mg bd	0.1
			Pantoprazole, 40 mg bd	0.8
			Rabeprazole, 20 mg bd	0.9

^aAll values are corrected to 1 decimal place.

eTable 2: ICD-9 for outcomes identification

	ICD-9 Codes
Composite neuropsychiatric events	290.11, 290.3, 290.41, 292.11, 292.12, 292.2, 292.81, 292.84, 292.85, 292.89, 292.9, 293.0, 293.1, 293.81, 293.82, 293.83, 293.89, 293.9, 294.0, 295.13, 295.14, 295.33, 295.34, 295.43, 295.44, 295.63, 295.64, 295.73, 295.74, 295.83, 295.84, 295.93, 295.94, 296.01, 296.02, 296.03, 296.04, 296.20, 296.21, 296.22, 296.23, 296.24, 296.40, 296.41, 296.42, 296.43, 296.44, 296.50, 296.51, 296.52, 296.53, 296.54, 296.60, 296.61, 296.62, 296.63, 296.64, 296.90, 296.99, 297.8, 297.9, 298.0, 298.1, 298.2, 298.3, 298.8, 298.9, 300.00, 300.09, 308.0, 308.1, 308.2, 309.82, 309.83, 309.89, 309.9, 311, 327.00, 327.01, 327.02, 327.09, 327.10, 327.11, 327.12, 327.14, 327.19, 780.01, 780.02, 780.09, 780.1, 780.50, 780.52, 780.54, 780.55, 780.56, 780.58, 780.59, 780.93, 780.97, 781.1, E930.3, E930.8, E930.9, E941.9, E947.8, E947.9, V40.0, V40.1, V40.2, V40.31, V40.39, V40.9
Psychotic events	292.11, 292.12, 292.2, 293.81, 293.82, 295.13, 295.14, 295.33, 295.34, 295.43, 295.44, 295.63, 295.64, 295.73, 295.74, 295.83, 295.84, 295.93, 295.94, 297.8, 297.9, 298.0, 298.1, 298.3, 298.8, 298.9, 780.1
Sensitivity analysis for psychotic events	292.11, 292.12, 292.2, 293.81, 293.82, 295.13, 295.14, 295.33, 295.34, 295.43, 295.44, 295.63, 295.64, 295.73, 295.74, 295.83, 295.84, 295.93, 295.94, 297.8, 297.9, 298.0, 298.1, 298.3, 298.8, 298.9, 308.1 , 780.1, 780.09
Cognitive impairment	298.2, 308.1, 780.02, 780.09, 780.93

eTable 3. The top three most frequently reported diagnostic codes for each outcome

<i>Composite neuropsychiatric events</i>	ICD-9 Code	Number of events	(%)
1	780.09	591	32.4
2	298.9	239	13.1
3	300.00	175	9.6
<i>Psychotic events</i>			
1	298.9	303	85.6
2	780.1	29	8.2
3	297.9	6	1.7
3	298.8	6	1.7
<i>Cognitive impairment</i>			
1	780.09	687	94.6
2	293.0	23	3.2
3	290.11	8	1.1

eTable 4. Incidence rate ratios for all outcomes after removing the first day of *Helicobacter pylori* therapy in sensitivity analysis

	No of events	Age adjusted incidence rate ratio (95% CI)
<i>Composite neuropsychiatric events</i>		
Baseline	1766	NA
14 days before prescription	14	1.63 (0.96-2.77)
Days 2-14	33	4.19 (2.96-5.92)
Days 15-30	9	0.95 (0.49-1.83)
<i>Psychotic events</i>		
Baseline	340	NA
14 days before prescription	3	1.73 (0.55-5.43)
Days 2-14	8	5.10 (2.51-10.36)
Days 15-30	2	1.07 (0.27-4.31)
<i>Cognitive impairment</i>		
Baseline	705	NA
14 days before prescription	6	1.63 (0.73-3.66)
Days 2-14	9	2.72 (1.40-5.26)
Days 15-30	6	1.50 (0.67-3.35)

eTable 5. Incidence rate ratios for all outcomes after including the first day of *Helicobacter pylori* therapy in preexposure risk period in sensitivity analysis

	No of events	Age adjusted incidence rate ratio (95% CI)
<i>Composite neuropsychiatric events (n=1824)</i>		
Baseline	1766	NA
15 days on and before prescription	16	1.74 (1.06-2.85)
Days 2-14 since prescription start date	33	4.19 (2.96-5.92)
Days 15-30 since prescription start date	9	0.95 (0.49-1.83)
<i>Psychotic events (n=354)</i>		
Baseline	340	NA
15 days on and before prescription	4	2.15 (0.80-5.81)
Days 2-14 since prescription start date	8	5.10 (2.51-10.36)
Days 15-30 since prescription start date	2	1.07 (0.27-4.31)
<i>Cognitive impairment (n=726)</i>		
Baseline	705	NA
15 days on and before prescription	6	1.52 (0.68-3.41)
Days 2-14 since prescription start date	9	2.72 (1.40-5.26)
Days 15-30 since prescription start date	6	1.50 (0.67-3.35)

eTable 6. Incidence rate ratios for all outcomes dividing the period of current use in sensitivity analysis

	No of events	Age adjusted incidence rate ratio (95% CI)
<i>Composite neuropsychiatric events (n=1824)</i>		
Baseline	1766	NA
14 days before prescription	14	1.63 (0.96-2.77)
Days 1-7 since prescription start date	19	4.41 (2.80-6.94)
Days 8-14 since prescription start date	16	3.82 (2.33-6.26)
Days 15-30 since prescription start date	9	0.95 (0.49-1.83)
<i>Psychotic events (n=354)</i>		
Baseline	340	NA
14 days before prescription	3	1.77 (0.57-5.56)
Days 1-7 since prescription start date	4	4.72 (1.75-12.73)
Days 8-14 since prescription start date	5	6.14 (2.52-14.93)
Days 15-30 since prescription start date	2	1.09 (0.27-4.40)
<i>Cognitive impairment (n=726)</i>		
Baseline	705	NA
14 days before prescription	6	1.70 (0.76-3.82)
Days 1-7 since prescription start date	4	2.29 (0.85-6.13)
Days 8-14 since prescription start date	5	2.97 (1.23-7.18)
Days 15-30 since prescription start date	6	1.56 (0.70-3.50)

eTable 7. Incidence rate ratios for psychotic events after including nonspecific ICD-9 descriptions^a

	No of events	Age adjusted incidence rate ratio (95% CI)
<i>Psychotic events (n=1005)</i>		
Baseline	974	NA
14 days before prescription	9	1.84 (0.95-3.55)
Days 1-14 since prescription start date	16	3.34 (2.03-5.49)
Days 15-30 since prescription start date	6	1.12 (0.50-2.51)

^aThe non-specific ICD-9 codes included 308.1 (predominant disturbance of consciousness) and 780.09 (other alteration of consciousness).

eTable 8. Incidence rate ratios for all outcomes among patients on *Helicobacter pylori* therapy containing clarithromycin, amoxicillin, and proton pump inhibitors only

	No of events	Age-adjusted incidence rate ratios (95% CI)
Composite neuropsychiatric events (n=1755)		
Baseline	1701	NA
14 days before prescription	14	1.71 (1.01-2.90)
Days 1-14 since prescription date	32	3.95 (2.78-5.61)
Days 15-30 since prescription date	8	0.88 (0.44-1.77)
Psychotic events (n=347)		
Baseline	333	NA
14 days before prescription	3	1.75 (0.56-5.50)
Days 1-14 since prescription date	9	5.41 (2.77-10.57)
Days 15-30 since prescription date	2	1.08 (0.27-4.37)
Cognitive impairment (n=697)		
Baseline	678	NA
14 days before prescription	6	1.72 (0.77-3.85)
Days 1-14 since prescription date	8	2.36 (1.17-4.75)
Days 15-30 since prescription date	5	1.31 (0.54-3.18)

eTable 9. Crude and adjusted odds ratios (ORs) for composite neuropsychiatric events in nested case-control analysis

	Case	Control
N	1061	4241
Mean age at event date (years)*	62.7	62.7
Male sex, (%)	497 (46.8)	1985 (46.8)
	Crude OR (95% CI)	Adjusted OR (95% CI)^a
Days 1-14 on or prior to index date (current use) ^b	3.55 (2.28-5.52)	3.45 (2.16-5.50)
Days 15-30 prior to index date (recent use)	1.40 (0.73-2.71)	1.46 (0.74-2.88)

^aOdds ratios adjusted for the use of psychiatric services in public sector and the use of other drugs prior to the event including cardiovascular drugs (i.e. diuretics and/or calcium channel blockers), bronchodilators, psychotropic drugs, antiepileptic drugs, antiparkinsonian drugs, antiretroviral drugs, oral corticosteroids and nonsteroidal anti-inflammatory drugs in the previous 365 days.

eTable 10. Adjusted estimates in nested case-control analysis

	Adjusted odds ratio (95% CI)
Use of <i>H pylori</i> therapy containing clarithromycin days 1-14 on or prior to index date (current use)	3.45 (2.16-5.50)
Use of psychiatric services in public sector in the previous 365 days prior to index date	1.94 (1.26-3.00)
Use of other drugs in public sector in the previous 365 days prior to index date	
Diuretics and/or calcium channel blockers	1.53 (1.30-1.82)
Bronchodilators	0.92 (0.70-1.20)
Psychotropic drugs	1.94 (1.66-2.26)
Antiepileptic drugs	2.53 (1.94-3.30)
Antiparkinsonian drugs	2.24 (1.41-3.57)
Antiretroviral drugs	0.72 (0.31-1.68)
Oral corticosteroids	1.24 (0.92-1.67)
Nonsteroidal anti-inflammatory drugs	1.14 (0.95-1.35)
Use of <i>H pylori</i> therapy containing clarithromycin days 15-30 prior to index date (recent use)	1.46 (0.74-2.88)
Use of psychiatric services in public sector in the previous 365 days prior to index date	2.01 (1.29-3.13)
Use of other drugs in public sector in the previous 365 days prior to index date	
Diuretics and/or calcium channel blockers	1.49 (1.25-1.77)
Bronchodilators	0.89 (0.68-1.17)
Psychotropic drugs	1.96 (1.67-2.29)
Antiepileptic drugs	2.49 (1.90-3.27)
Antiparkinsonian drugs	2.47 (1.54-3.97)
Antiretroviral drugs	0.74 (0.31-1.74)
Oral corticosteroids	1.22 (0.90-1.64)
Nonsteroidal anti-inflammatory drugs	1.12 (0.94-1.34)

eFigure. Flowchart of the patient inclusion for primary outcome in self-controlled case series analysis

