

## **Supplementary appendix**

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Table S1. Korea Drug Codes for oral fluoroquinolones and cefixime

Medications	Korea Drug Codes
Ciprofloxacin	134101ATB,134103ATB, 134105ATB, 134105ATR, 134108ATR, 134109ATB
Levofloxacin	183201ATB, 183202ATB, 183203ATB
Ofloxacin	203901ATB, 203904ATB
Moxifloxacin	380301ATB
Cefixime	126301ACH

Table S2. Korea Drug Codes for medications used in the exclusion criteria that are associated with prolonged QT intervals or an increased risk of developing torsades de pointes

Medications	Korea Drug Codes
Amiodarone	107401ATB
Sotalol	230401ATB, 230402ATB
Quinidine	222001ATB, 222002ATB
Digoxin	144801ATB
Flecainide	159302ATB
Propafenone	219501ATB, 219502ATB
Erythromycin	153501ACH, 153801ATB, 154001ACH
Clarithromycin	134901ATB, 134904ATB
Telithromycin	455901ATB
Chloroquine	171602ATB, 171701ATB, 171702ATB, 171703ATB, 171704ATB,
Ketoconazole	179601ATB,
Itraconazole	179101ACH, 179104ATB
Voriconazole	456501ATB
Sunitinib	487701ACH, 487702ACH, 487703ACH
Domperidone	148402ATB, 148501ATB
Dolasetron	414602ATB
Ondansetron	204601ATB, 204601ATD, 204603ATB
Granisetron	167301ATB, 167301ATD
Sumatriptan	233802ATB, 233803ATB
Zolmitriptan	415601ATB
Naratriptan	415501ATB
Chlorpromazine	131901ATB, 131905ATB, 131908ATB
Haloperidol	167903ATB, 167904ATB, 167905ATB, 167906ATB, 167908ATB,
Pimozide	212401ATB, 212402ATB
Clozapine	137501ATB, 137502ATB
Quetiapine	378601ATB, 378602ATB, 378603ATB, 378604ATB, 378605ATR, 378606ATR, 378607ATR, 378608ATR, 378609ATR,
Risperidone	224201ATB, 224201ATD, 224202ATB, 224203ATB, 224204ATB, 224207ATB,
Imipramine	173701ATB,
Paroxetine	209301ATB, 209302ATB, 209304ATR, 209305ATR, 209306ATR,
Sertraline	227001ATB, 227002ATB
Venlafaxine	247502ATR, 247504ATR
Fluoxetine	161501ACH, 161502ACH, 161502ATD, 161504ACR
Fluvoxamine	162501ATB, 162502ATB

Table S3. ICD-10 covariate codes

<i>Comorbidities</i>	
Hypertension	I10-I13.x, I15.x
Diabetes mellitus	E10.x-E14.x
Acute myocardial infarction	I21.x, I22.x, I23.x
Ischaemic heart disease	I20.x, I24.x, I25.x
Cardiomyopathy	I42.x, I43.x
Valve disorder	I34.x-37.x
Arrhythmia	I44.x, I45.x, I47.0, I47.1, I47.9, I49.1-9
Congestive heart failure	I11.0, I13.0, I13.2, I50.x, J81.x
Congenital heart disease	Q20.x-26.x
Cancer	C00.x–C99.x
Cerebrovascular disease	G45.x, G46.x, I60.x–I69.x
Renal disease	N00.x-N08.x, N17.x-19.x, N25.x, Z49.x, Z94.0, Z99.2
Arterial disease	I70.x-I79.x
Venous thromboembolism	I26.x, I80.x
Dementia	F00.x–F03.x, G30.x
Rheumatic disease (connective tissue disease)	M05.x, M06.x, M32.x–M34.x
Peptic ulcer disease	K25.x–K28.x
Chronic lung disease	J40.x-47.x, J60.x-70.x
<i>Indications for antibiotics</i>	
Upper respiratory infection	J01.x-J06.x
Pneumonia	J13.x-J18.x
Other respiratory infection	J20.x-J22.x
Gastrointestinal infection	A00.x-A09.x
Urinary tract infection	N10.x-N12.x, N30.x, N39.0, N41.x
Genitourinary infection	N34.x, N45.x, N70.x-77.x
Skin/wound infection	L00.x-L08.x

ICD-10=International Classification of Diseases, Tenth Revision

Table S4. Baseline characteristics of patients using cefixime or ciprofloxacin and the standardized difference before and after IPTW

	Cefixime	Ciprofloxacin	Standardized difference	
			Before IPTW	After IPTW
No. of subjects	402930	1466133		
Age, mean $\pm$ SD	49.3 $\pm$ 17.7	48.5 $\pm$ 17.3	0.041	0.046
No. of females (%)	238329 (59.1)	951813 (64.9)	0.119	0.042
<i>No. of Comorbidities (%)</i>				
Hypertension	121529 (30.2)	410360 (28.0)	0.048	0.044
Diabetes mellitus	97779 (24.3)	321483 (21.9)	0.056	0.042
Acute myocardial infarction	6536 (1.6)	17451 (1.2)	0.037	0.008
Ischaemic heart disease	45810 (11.4)	137303 (9.4)	0.066	0.019
Cardiomyopathy	1450 (0.4)	3668 (0.3)	0.020	0.003
Valve disorder	1826 (0.5)	4971 (0.3)	0.018	0.005
Arrhythmia	14387 (3.6)	45727 (3.1)	0.025	0.008
Congestive heart failure	21753 (5.4)	59507 (4.1)	0.063	0.019
Congenital heart disease	550 (0.1)	1599 (0.1)	0.008	0.002
Cancer	43336 (10.8)	128612 (8.8)	0.067	0.015
Cerebrovascular disease	42741 (10.6)	127394 (8.7)	0.065	0.030
Renal disease	27440 (6.8)	93946 (6.4)	0.016	0.027
Arterial disease	58202 (14.4)	201275 (13.7)	0.021	0.021
Venous thromboembolism	5613 (1.4)	15375 (1.0)	0.031	0.005
Dementia	17245 (4.3)	48445 (3.3)	0.051	0.037
Rheumatic disease	29610 (7.3)	97980 (6.7)	0.026	0.009
Peptic ulcer disease	148247 (36.8)	527527(36.0)	0.017	0.038
Chronic lung disease	215194 (53.4)	633215 (43.2)	0.206	0.026
<i>No. of Antibiotic Indications (%)</i>				
Upper respiratory infection	41000 (10.2)	34919 (2.4)	0.326	0.002
Pneumonia	17362 (4.3)	13792 (0.9)	0.212	0.002
Other respiratory infection	31943 (7.9)	49097 (3.3)	0.200	0.003
Gastrointestinal infection	10997 (2.7)	258359 (17.6)	0.508	0.001
Urinary tract infection	24497 (6.1)	477439 (32.6)	0.712	0.014
Genitourinary infection	10357 (2.6)	103874 (7.1)	0.212	0.003
Skin/Wound infection	15212 (3.8)	13240 (0.9)	0.191	0.002
<i>Month, No (%)</i>				
1	51082 (12.7)	198022 (13.5)	0.122	0.028
2	41252 (10.2)	139390 (9.5)		
3	43687 (10.8)	136164 (9.3)		
4	39505 (9.8)	123691 (8.4)		
5	32150 (8.0)	107959 (7.4)		
6	28567 (7.1)	110219 (7.5)		
7	25587 (6.4)	121446 (8.3)		
8	26722 (6.6)	118711 (8.1)		
9	27912 (6.9)	104986 (7.2)		
10	29177 (7.2)	97368 (6.6)		
11	26293 (6.5)	97704 (6.7)		
12	30966 (7.7)	110473 (7.5)		

Table S5. Baseline characteristics of patients using cefixime or levofloxacin and the standardized difference before and after IPTW

	Cefixime	Levofloxacin	Standardized difference	
			Before IPTW	After IPTW
No. of subjects	402930	1141961		
Age, mean $\pm$ SD	49.3 $\pm$ 17.7	50.4 $\pm$ 16.7	0.068	0.042
No. of females (%)	238329 (59.1)	643076 (56.3)	0.057	0.064
<i>No. of Comorbidities (%)</i>				
Hypertension	121529 (30.2)	346918 (30.4)	0.005	0.026
Diabetes mellitus	97779 (24.3)	268447 (23.5)	0.018	0.024
Acute myocardial infarction	6536 (1.6)	15209 (1.3)	0.024	0.005
Ischaemic heart disease	45810 (11.4)	122740 (10.7)	0.020	0.014
Cardiomyopathy	1450 (0.4)	3443 (0.3)	0.010	0.001
Valve disorder	1826 (0.5)	4643 (0.4)	0.007	0.003
Arrhythmia	14387 (3.6)	38751 (3.4)	0.010	0.007
Congestive heart failure	21753 (5.4)	55276 (4.8)	0.025	0.013
Congenital heart disease	550 (0.1)	1430 (0.1)	0.003	<0.001
Cancer	43336 (10.8)	118618 (10.4)	0.012	0.011
Cerebrovascular disease	42741 (10.6)	113241 (9.9)	0.023	0.021
Renal disease	27440 (6.8)	73935 (6.5)	0.013	0.016
Arterial disease	58202 (14.4)	173004 (15.1)	0.020	0.015
Venous thromboembolism	5613 (1.4)	14016 (1.2)	0.015	0.004
Dementia	17245 (4.3)	41097 (3.6)	0.035	0.022
Rheumatic disease	29610 (7.3)	77971 (6.8)	0.020	0.006
Peptic ulcer disease	148247 (36.8)	418871 (36.7)	0.002	0.027
Chronic lung disease	215194 (53.4)	586894 (51.4)	0.040	0.019
<i>No. of Antibiotic Indications (%)</i>				
Upper respiratory infection	41000 (10.2)	71542 (6.3)	0.143	0.002
Pneumonia	17362 (4.3)	54016 (4.7)	0.020	0.007
Other respiratory infection	31943 (7.9)	118629 (10.4)	0.085	0.001
Gastrointestinal infection	10997 (2.7)	26806 (2.3)	0.024	<0.001
Urinary tract infection	24497 (6.1)	255878 (22.4)	0.480	0.003
Genitourinary infection	10357 (2.6)	104759 (9.2)	0.284	0.012
Skin/Wound infection	15212 (3.8)	20509 (1.8)	0.121	0.001
<i>Month, No (%)</i>				
1	51082 (12.7)	186297 (16.3)	0.161	0.020
2	41252 (10.2)	128738 (11.3)		
3	43687 (10.8)	128601 (11.3)		
4	39505 (9.8)	113718 (10.0)		
5	32150 (8.0)	89592 (7.8)		
6	28567 (7.1)	83536 (7.3)		
7	25587 (6.4)	76140 (6.7)		
8	26722 (6.6)	74130 (6.5)		
9	27912 (6.9)	72417 (6.3)		
10	29177 (7.2)	72734 (6.4)		
11	26293 (6.5)	55296 (4.8)		
12	30966 (7.7)	60762 (5.3)		

Table S6. Baseline characteristics of patients using cefixime or ofloxacin and the standardized difference before and after IPTW

			Standardized difference	
	Cefixime	Ofloxacin	Before IPTW	After IPTW
No. of subjects	402930	1830786		
Age, mean $\pm$ SD	49.3 $\pm$ 17.7	50.3 $\pm$ 16.9	0.061	0.009
No. of females (%)	238329 (59.1)	1120119 (61.2)	0.042	0.006
<i>No. of Comorbidities (%)</i>				
Hypertension	121529 (30.2)	540934 (29.5)	0.013	0.005
Diabetes mellitus	97779 (24.3)	382877 (20.9)	0.080	0.001
Acute myocardial infarction	6536 (1.6)	11731 (1.0)	0.058	0.001
Ischaemic heart disease	45810 (11.4)	161602 (8.8)	0.084	0.004
Cardiomyopathy	1450 (0.4)	3924 (0.2)	0.027	<0.001
Valve disorder	1826 (0.5)	6219 (0.3)	0.018	0.001
Arrhythmia	14387 (3.6)	53536 (2.9)	0.036	0.001
Congestive heart failure	21753 (5.4)	68471 (3.7)	0.079	0.003
Congenital heart disease	550 (0.1)	1894 (0.1)	0.010	<0.001
Cancer	43336 (10.8)	122116 (6.7)	0.145	0.008
Cerebrovascular disease	42741 (10.6)	155453 (8.5)	0.072	0.001
Renal disease	27440 (6.8)	83202 (4.5)	0.098	0.005
Arterial disease	58202 (14.4)	268362 (14.7)	0.006	0.003
Venous thromboembolism	5613 (1.4)	16571 (0.9)	0.046	0.004
Dementia	17245 (4.3)	46626 (2.5)	0.096	0.005
Rheumatic disease	29610 (7.3)	112629 (6.2)	0.048	0.001
Peptic ulcer disease	148247 (36.8)	636452 (34.8)	0.042	0.004
Chronic lung disease	215194 (53.4)	810357 (44.3)	0.184	0.004
<i>No. of Antibiotic Indications (%)</i>				
Upper respiratory infection	41000 (10.2)	200376 (10.9)	0.025	0.006
Pneumonia	17362 (4.3)	10048 (0.5)	0.246	0.001
Other respiratory infection	31943 (7.9)	266793 (14.6)	0.211	0.005
Gastrointestinal infection	10997 (2.7)	116001 (6.3)	0.174	0.002
Urinary tract infection	24497 (6.1)	204458 (11.2)	0.182	0.006
Genitourinary infection	10357 (2.6)	75822 (4.1)	0.087	0.004
Skin/Wound infection	15212 (3.8)	47573 (2.6)	0.067	0.004
<i>Month, No (%)</i>				
1	51082 (12.7)	255833 (14.0)	0.058	0.009
2	41252 (10.2)	200347 (10.9)		
3	43687 (10.8)	207332 (11.3)		
4	39505 (9.8)	177080 (9.7)		
5	32150 (8.0)	141413 (7.7)		
6	28567 (7.1)	127462 (7.0)		
7	25587 (6.4)	117053 (6.4)		
8	26722 (6.6)	115864 (6.3)		
9	27912 (6.9)	117031 (6.4)		
10	29177 (7.2)	124597 (6.8)		
11	26293 (6.5)	116492 (6.4)		
12	30966 (7.7)	130282 (7.1)		

Table S7. Baseline characteristics of patients using cefixime or moxifloxacin and the standardized difference before and after IPTW

	Cefixime	Moxifloxacin	Standardized difference	
			Before IPTW	After IPTW
No. of subjects	402930	47080		
Age, mean $\pm$ SD	49.3 $\pm$ 17.7	58.4 $\pm$ 17.4	0.521	0.007
No. of females (%)	238329 (59.1)	23586 (50.1)	0.183	0.024
<i>No. of Comorbidities (%)</i>				
Hypertension	121529 (30.2)	21690 (46.1)	0.332	0.031
Diabetes mellitus	97779 (24.3)	17977 (38.2)	0.304	0.027
Acute myocardial infarction	6536 (1.6)	1292 (2.7)	0.077	0.011
Ischaemic heart disease	45810 (11.4)	9408 (20)	0.239	0.024
Cardiomyopathy	1450 (0.4)	438 (0.9)	0.071	0.005
Valve disorder	1826 (0.5)	513 (1.1)	0.073	0.002
Arrhythmia	14387 (3.6)	2761 (5.9)	0.108	0.012
Congestive heart failure	21753 (5.4)	5724 (12.2)	0.241	0.013
Congenital heart disease	550 (0.1)	110 (0.2)	0.023	0.004
Cancer	43336 (10.8)	10285 (21.8)	0.304	0.010
Cerebrovascular disease	42741 (10.6)	8389 (17.8)	0.208	0.018
Renal disease	27440 (6.8)	5657 (12)	0.179	0.025
Arterial disease	58202 (14.4)	9298 (19.7)	0.141	0.019
Venous thromboembolism	5613 (1.4)	1704 (3.6)	0.143	0.002
Dementia	17245 (4.3)	4046 (8.6)	0.176	0.023
Rheumatic disease	29610 (7.3)	4453 (9.5)	0.076	0.012
Peptic ulcer disease	148247 (36.8)	21304 (45.3)	0.173	0.024
Chronic lung disease	215194 (53.4)	36096 (76.7)	0.503	0.003
<i>No. of Antibiotic Indications (%)</i>				
Upper respiratory infection	41000 (10.2)	2024 (4.3)	0.228	0.019
Pneumonia	17362 (4.3)	10567 (22.4)	0.553	0.018
Other respiratory infection	31943 (7.9)	2898 (6.2)	0.069	0.017
Gastrointestinal infection	10997 (2.7)	142 (0.3)	0.200	<0.001
Urinary tract infection	24497 (6.1)	396 (0.8)	0.290	0.015
Genitourinary infection	10357 (2.6)	806 (1.7)	0.059	0.060
Skin/Wound infection	15212 (3.8)	589 (1.3)	0.162	0.040
<i>Month, No (%)</i>				
1	51082 (12.7)	8179 (17.4)	0.201	0.046
2	41252 (10.2)	5913 (12.6)		
3	43687 (10.8)	5674 (12.1)		
4	39505 (9.8)	4736 (10.1)		
5	32150 (8.0)	3549 (7.5)		
6	28567 (7.1)	3132 (6.7)		
7	25587 (6.4)	2486 (5.3)		
8	26722 (6.6)	2323 (4.9)		
9	27912 (6.9)	2383 (5.1)		
10	29177 (7.2)	2791 (5.9)		
11	26293 (6.5)	2412 (5.1)		
12	30966 (7.7)	3502 (7.4)		