Supplementary Online Content

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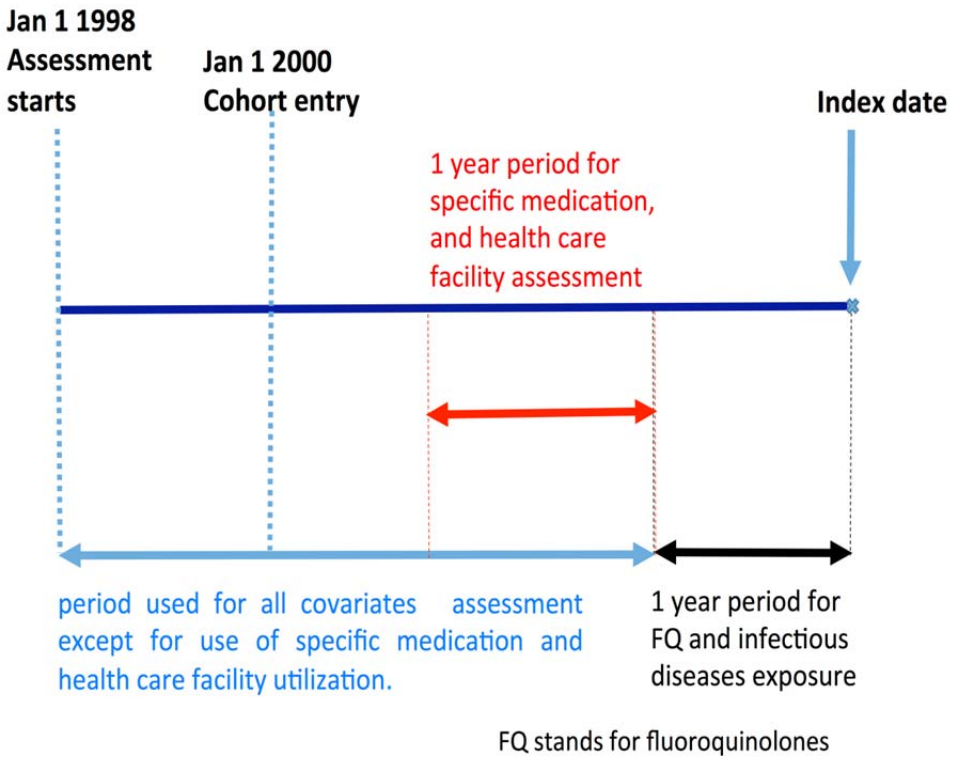
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure. Graphical timeline of the study design



eTable 1. ICD-9-CM Codes for infectious disease

Disease	ICD-9-CM Codes
Infectious colitis, enteritis, and gastroenteritis	009.0
Infectious diarrhea	009.2
Tuberculosis of meninges and central nervous system	013
Tuberculosis peritonitis	014
Tuberculosis of bones and joints	015
Tuberculosis of genitourinary system	016
Tuberculosis of other organs	017
Miliary tuberculosis	018
Bacterial meningitis	320
Acute and subacute bacterial endocarditis	421.0
Acute and subacute infective endocarditis in diseases classified elsewhere	421.1
Acute sinusitis	461
Acute bronchitis and bronchiolitis	466
Pneumococcal pneumonia	481
Other bacterial pneumonia	482
Pneumonia due to other specified organism	483
Pneumonia in infectious diseases classified elsewhere	484
Bronchopneumonia, organism unspecified	485
Pneumonia, organism unspecified	486
Bronchitis, not specified as acute or chronic	490
Chronic bronchitis	491
Bronchiectasis	494
Peritonitis and retroperitoneal infections	567
Acute cholecystitis	575.0
Other cholecystitis	575.1
Cholangitis	576.1
Infections of kidney	590
Urinary tract infection, site not specified	599.0
Carbuncle and furuncle	680
Cellulitis and abscess of finger and toe	681
Other cellulitis and abscess	682
Acute lymphadenitis	683
Impetigo	684

Pilonidal cyst	685
Other local infections of skin and subcutaneous tissue	686
Osteomyelitis periostitis and other infections involving bone	730
Fever and other physiologic disturbances of temperature regulation	780.6

eTable 2. Propensity score model for use of fluoroquinolones

Characteristics	IRR (95%CI) for use of Fluoroquinolone
AUC	**0.78**
Demographics	
Age	1.01 (1.00 - 1.01)
Age square	1.00 (1.00 - 1.00)
Gender : male (female as reference)	0.93 (0.87 - 0.99)
Area : mid-size central city (large central city as reference)	1.03 (0.96 - 1.11)
Area : suburban area (large central city as reference)	1.09 (0.98 - 1.22)
Area : countryside area (large central city as reference)	1.10 (0.87 - 1.39)
Premium rate : 1 – 19,999 New Taiwan Dollars (dependent as reference)	1.00 (0.89 - 1.14)
Premium rate : 20,000 – 39,999 New Taiwan Dollars (dependent as reference)	0.89 (0.79 - 1.01)
Premium rate : >40,000 New Taiwan Dollars (dependent as reference)	0.83 (0.72 - 0.95)
Calendar year 2001 (year 2000 as reference)	0.79 (0.69 - 0.91)
Calendar year 2002 (year 2000 as reference)	0.88 (0.76 - 1.01)
Calendar year 2003 (year 2000 as reference)	1.03 (0.89 - 1.18)
Calendar year 2004 (year 2000 as reference)	1.11 (0.97 - 1.27)
Calendar year 2005 (year 2000 as reference)	0.83 (0.71 - 0.96)
Calendar year 2006 (year 2000 as reference)	0.84 (0.72 - 0.98)
Calendar year 2007 (year 2000 as reference)	0.94 (0.81 - 1.09)
Calendar year 2008 (year 2000 as reference)	0.96 (0.82 - 1.11)
Calendar year 2009 (year 2000 as reference)	1.02 (0.88 - 1.19)
Calendar year 2010 (year 2000 as reference)	1.22 (1.06 - 1.41)
Calendar year 2011 (year 2000 as reference)	1.16 (0.99 - 1.34)
Charlson index score	
Charlson comorbidity index	1.08 (1.03 - 1.14)
Charlson comorbidity index : quadratic	0.99 (0.99 - 1.00)
Cardiovascular disease related	
Congestive heart failure	0.98 (0.87 - 1.11)
Cerebrovascular disease	1.06 (0.94 - 1.19)
Myocardial infarction/acute coronary syndromes	1.04 (0.84 - 1.27)
Stroke or transient ischemic attack	1.25 (1.08 - 1.43)
Peripheral arterial disease	0.94 (0.78 - 1.12)
Angina	0.96 (0.85 - 1.08)
Other ischemic heart disease	0.98 (0.86 - 1.13)
Cerebral atherosclerosis	0.96 (0.78 - 1.19)

Percutaneous coronary/coronary artery bypass graft intervention	1.08 (0.77 - 1.52)
bed-ridden status	1.09 (0.95 - 1.25)
Risk factors	
Diabetes	1.01 (0.92 - 1.12)
Amphetamines abuse	0.59 (0.08 - 4.60)
Tobacco	1.09 (0.75 - 1.58)
Hypertension	1.05 (0.96 - 1.15)
Lipid disorder	0.92 (0.85 - 1.01)
Marfan syndrome	12.2 (2.72 - 54.8)
Bicuspid aortic value	<.0001
Coarctation of the aortic	<.0001
Giant cell arteritis	1.58 (0.20 - 12.4)
Takayasu disease	<.0001
Cardio vascular syphilis	1.92 (0.25 - 14.9)
Turner syndrome	<.0001
Trauma(motor vehicle traffic accident)	0.90 (0.60 - 1.34)
Aortic valve disorders	1.13 (0.90 - 1.42)
Obstructive sleep apnea	1.00 (0.92 - 1.10)
Chronic obstructive pulmonary disease	1.02 (0.94 - 1.12)
Ischemic heart disease	0.88 (0.75 - 1.02)
Chronic kidney disease	1.18 (1.03 - 1.36)
Asthma	0.94 (0.86 - 1.04)
Cardiac valve disease	0.95 (0.81 - 1.11)
Conduction disorder	1.09 (0.81 - 1.45)
Atrial fibrillation	1.20 (0.99 - 1.46)
Obesity	0.93 (0.68 - 1.27)
Malignant hypertension	0.92 (0.73 - 1.15)
Schizophrenia	0.69 (0.49 - 0.97)
Opioid poisoning	2.87 (0.85 - 9.67)
Psychotropic poisoning	0.90 (0.37 - 2.21)
Seizure disorder(epilepsy)	1.04 (0.84 - 1.30)
Decubitus ulcer	1.68 (1.32 - 2.13)
Amputation	0.81 (0.57 - 1.13)
Any infection disease past 365 days	2.08 (1.94 - 2.24)
Outpatient visits	1.04 (1.03 - 1.04)
Outpatient visits : quadratic	1.00 (1.00 - 1.00)
Emergency department visits	1.07 (1.04 - 1.09)
Emergency department visits : quadratic	1.00 (1.00 - 1.00)
The number of hospitalization	1.58 (1.51 - 1.65)
The number of hospitalization : quadratic	0.97 (0.97 - 0.98)
Drugs use	
NSAIDs	1.14 (1.06 - 1.22)
Aspirin	1.01 (0.92 - 1.11)

Systemic immunosuppressive agents and biologics	1.05 (0.71 - 1.57)
Systemic corticosteroids	1.19 (1.10 - 1.29)
DMARDs	1.25 (1.02 - 1.54)
Statin	0.93 (0.81 - 1.06)
ACE inhibitors	0.91 (0.82 - 1.01)
Beta agonist	1.22 (1.11 - 1.33)
Angiotensin receptor blocker	0.87 (0.78 - 0.98)
Anticoagulant(antithrombotic agents)	1.04 (0.91 - 1.18)
Antiarrhythmic	1.11 (0.90 - 1.37)
Beta blocker(selective + non-selective)	0.93 (0.85 - 1.02)
Calcium channel blockers	1.00 (0.91 - 1.09)
Digoxin	0.99 (0.83 - 1.20)
Loop diuretics	1.24 (1.11 - 1.39)
Insulin	1.24 (0.97 - 1.59)
Oral hypoglycemic	1.12 (1.00 - 1.25)
Fibrate lipid-lowering agent	0.98 (0.81 - 1.18)
Nitrate anti-anginal	1.00 (0.87 - 1.14)
Peripheral vasodilators	0.85 (0.74 - 0.98)
Antidepressants	0.96 (0.86 - 1.06)
Benzodiazepine	0.96 (0.89 - 1.04)
Parkinson’s medication	1.01 (0.89 - 1.16)
Antipsychotics	1.04 (0.75 - 1.46)
Lithium	1.33 (0.62 - 2.87)
Hydroxyzine	1.09 (0.85 - 1.40)
Anticonvulsants	0.80 (0.65 - 0.98)

eTable 3. Annual population prevalence of fluoroquinolone use in Taiwan

Year	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Percentage	0.021	0.019	0.020	0.022	0.024	0.022	0.020	0.024	0.026	0.027	0.033	0.038

Note: Fluoroquinolone user is defined as having a ≥ 3 days prescription of fluoroquinolone, and within 30 days of the index episode of infection. Values are obtained from the NHIRD database.

eEquations. Population Attributable Risk (PAR)

$PAR = P_e (RR_e-1) \ / \ [1 + P_e (RR_e-1)]$
In 2011, $P_e = 0.038$ PS adjusted RR = 2.43 PS matched RR= 1.75

PAR (using PS adjusted RR) = 0.038(2.43-1)/[1+0.038(2.43-1)] = 0.052
PAR (using PS matched RR) = 0.038(1.75-1)/[1+0.038(1.75-1)] = 0.028