

# Use of systemic fluoroquinolones in primary care and hospital settings in the UK: a drug utilisation study

### Background



- Fluoroquinolone antibiotics have been approved decades ago
- They are commonly prescribed in primary care and hospitals to treat different types of infections, e.g. respiratory and urinary tract infections.
- More recently, they have been associated with an increased risk of severe adverse events
- MHRA issued Risk Minimisation Measures in March 2019
  - no fluoroquinolone prescriptions for self-limiting, mild or moderate infections
  - avoid use in patients who have previously had serious adverse reactions
  - special caution for people ≥60 years, renal impairment or solid-organ transplants
  - avoid use of a corticosteroid with a fluoroquinolone

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Fluoroquinolone antibiotics: new restrictions and precautions for use due to very rare reports of disabling and potentially long-lasting or irreversible side effects

Disabling, long-lasting or potentially irreversible adverse reactions affecting musculoskeletal and nervous systems have been reported very rarely with fluoroquinolone antibiotics. Fluoroquinolone treatment should be discontinued at the first signs of a serious adverse reaction, including tendon pain or inflammation.

From: Medicines and Healthcare products Regulatory Agency Published 21 March 2019

# **Research question and Objectives**

#### Objectives

#### Population-level drug utilisation:

To estimate the **incidence** and **prevalence** of use of fluoroquinolones in the UK stratified by setting, calendar term/year, and age for the period 2012-2022.

Additional analysis: Interrupted time series analyses

#### Patient-level drug utilisation

To characterise new users and calculate the duration, indication and dose of fluoroquinolone use in the UK, stratified by setting, calendar term/year, and age.

Additional stratifications for characterisation:

- before/after RMM intervention
- age groups 18-59, >60
- Comorbidities/comedication as suggested as by MHRA
- Previous use of other antibiotics





# Methods

### Study population

#### Population-level drug utilisation

All people in database

- recorded between 01/01/2012 and 31/12/2022
- at least 30 days of previous database visibility.

#### Patient-level drug utilisation

New users of any fluoroquinolone

- not using the same index medicine for 30 days
- between 01/01/2012 and 31/12/2022
- at least 30 days of visibility prior to therapy initiation







# Methods

# Diagnostics and Study Code

#### **Feasibility checks**

- DrugExposureDiagnostics
- CohortDiagnostics



#### **R-Packages used for study**





# **Population-level drug utilisation before/after RMM**





Primary care databases (CPRD GOLD + AURUM) + Primary/secondary care data from Scotland (HIC)

### **Interrupted time series analyses**







# **Population-level drug utilisation before/after RMM**



Hospital databases (Barts Health) 2013-2021 [Great Ormond Street Hospital and Lancashire data 2019 onwards]



### New user characterisation



		Primary care databases		Primary/Secondary care	Hospital databases			
Variable	Format	CPRD Aurum	CPRD GOLD	HIC Dundee	Barts Health	Lancashire	GOSH	
Number of subjects	N	1,044,142	384,744	67,394	7,007	2,287	46	
Number of records	Ν	1,621,106	606,683	113,740	8,680	2,527	192	
Age	median [IQR]	58 [39 - 73]	59 [41 - 73]	58 [41 - 72]	57 [37 - 71]	70 [55 - 80]	6 [1 - 10]	
Sex: Female	N (%)	807,037 (50%)	305,647 (50%)	55,397 (49%)	4,000 (46%)	1,236 (49%)	96 (50%)	
Comedication								
Antibiotics 30 days prior	N (%)	512,815 (32%)	205,629 (34%)	NA	2,528 (29%)	NA	NA	
Glucocorticoids 1 year prior	N (%)	256,745 (16%)	100,620 (17%)	NA	NA	NA	NA	
Comorbidities								
Chronic Kidney Disease	N (%)	190,944 (12%)	73,448 (12%)	NA	1,632 (19%)	NA	NA	
Solid organ transplant	N (%)	6,128 (0%)	2,297 (0%)	NA	275 (3%)	NA	NA	
Trauma	N (%)	405,076 (25%)	132,508 (22%)	NA	252 (3%)	NA	NA	
Stroke ischemic hemorrhagic	N (%)	21,187 (1%)	7,362 (1%)	NA	538 (6%)	NA	NA	
COPD	N (%)	140,878 (9%)	52,072 (9%)	NA	1,649 (19%)	NA	NA	
Heart valve disorder	N (%)	140,878 (9%)	52,072 (9%)	NA	1,649 (19%)	NA	NA	
Hypertension	N (%)	441,640 (27%)	121,405 (20%)	NA	3,869 (45%)	NA	NA	
Hyperlipidemia	N (%)	139,987 (9%)	46,181 (8%)	NA	2,339 (27%)	NA	NA	
Ischemic heart disease	N (%)	128,943 (8%)	44,761 (7%)	NA	1,595 (18%)	NA	NA	

# Indication for fluoroquinolones before/after RMM

Conditions recorded within 7 days before treatment start was used as proxy for indication

Barts Health

After RMM (age group ≥60 years) Before RMM (age group ≥60 years)



**CPRD** Aurum

CPRD GOLD



# **Drug utilisation: DrugExposure Diagnostics**



#### DrugExposureDiagnostics

Menu	≡									
Background	Database Ir	ngredient								
Databases 🗸	5 items selected 🔹	ciprofloxacin 🔹								
Study diagnostics	Concepts in database	Drug record durations	Drug source concepts	Drug record missing	values					
≫ Drug exposure diagnostics										
➤ Cohort diagnostics	Overall per ingredient By concept									
Study results 🔇										
	Show 10 V entries Search:									
	cdm_name 🔶 in	gredient_concept_id 🔶	ingredient 🔶 n_records	n_negative_days	minimum_drug_exposure_days	q25_drug_expo	sure_days 🔶 median_drug	g_exposure_days 🔶 q75_drug_exposure_days	xposure_days 🔶 maximu	um_drug_exposure_days 🔶
	project_3619	1797513	ciprofloxacin 1000	D 0		1	1	1	1	1
	CPRDAurumFull	1797513	ciprofloxacin 1000	D 0		1	5	7	28	1130
	CPRD GOLD	1797513	ciprofloxacin 1000	0 0		1	5	5	7	90
	lthtr	1797513	ciprofloxacin 1000	0 0		1	1	1	1	1
	sqldb-gosh-CDM- dev	1797513	ciprofloxacin 370	3 0		1	1	1	1	1
	Showing 1 to 5 of 5 entries									Previous 1 Next

		CPRD AURUM	CPRD GOLD
Duration	Median [IQR]	7 days [5 -10]	5 days [5-7]
Initial dose	Median [IQR]	1000mg [1000 – 1000mg]	1000mg [1000 – 1400mg]
Cumulative dose	Median [IQR]	7000mg [5000 – 1000mg]	7000mg [5000mg – 1000mg]



- ✓ **RMM was effective** in reducing population-level incidence of fluoroquinolones prescriptions
- ✓ Slightly stronger effect in people ≥60 years
- ✓ Substantial proportion of new users received different antibiotic the immediate time before "second-line" use
- Proportion of prescriptions for urinary tract infections and respiratory tract infections decreased after RMM relative to the time before



### Thank you very much!



Katherine, Helen, Stephanie, John, Patrick, Allison Ed and Dani OHDSI UK Data Partners Oxford team

It's been a great week!