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
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

- **CodelistGenerator**
  - CRAN - Package CodelistGenerator (r-project.org)
- **IncidencePrevalence**
  - CRAN - Package IncidencePrevalence (r-project.org)
- **PatientProfiles**
  - CRAN - Package PatientProfiles (r-project.org)
- **DrugUtilisation**
  - CRAN - Package DrugUtilisation (r-project.org)
Population-level drug utilisation before/after RMM

Primary care databases (CPRD GOLD + AURUM) + Primary/secondary care data from Scotland (HIC)
Interrupted time series analyses

\[ Y_t = \alpha + \beta_1 \cdot \text{time} + \beta_2 \cdot \text{intervention} + \beta_3 \cdot \text{time since intervention} + \epsilon \]
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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Format</th>
<th>Primary care databases</th>
<th>Primary/Secondary care</th>
<th>Hospital databases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>CPRD Aurum</td>
<td>CPRD GOLD</td>
<td>HIC Dundee</td>
</tr>
<tr>
<td>Number of subjects</td>
<td>N</td>
<td>1,044,142</td>
<td>384,744</td>
<td>67,394</td>
</tr>
<tr>
<td>Number of records</td>
<td>N</td>
<td>1,621,106</td>
<td>606,683</td>
<td>113,740</td>
</tr>
<tr>
<td>Sex: Female</td>
<td>N (%)</td>
<td>807,037 (50%)</td>
<td>305,647 (50%)</td>
<td>55,397 (49%)</td>
</tr>
<tr>
<td>Comedication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics 30 days prior</td>
<td>N (%)</td>
<td>512,815 (32%)</td>
<td>205,629 (34%)</td>
<td>NA</td>
</tr>
<tr>
<td>Glucocorticoids 1 year prior</td>
<td>N (%)</td>
<td>256,745 (16%)</td>
<td>100,620 (17%)</td>
<td>NA</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>N (%)</td>
<td>190,944 (12%)</td>
<td>73,448 (12%)</td>
<td>NA</td>
</tr>
<tr>
<td>Solid organ transplant</td>
<td>N (%)</td>
<td>6,128 (0%)</td>
<td>2,297 (0%)</td>
<td>NA</td>
</tr>
<tr>
<td>Trauma</td>
<td>N (%)</td>
<td>405,076 (25%)</td>
<td>132,508 (22%)</td>
<td>NA</td>
</tr>
<tr>
<td>Stroke ischemic hemorrhagic</td>
<td>N (%)</td>
<td>21,187 (1%)</td>
<td>7,362 (1%)</td>
<td>NA</td>
</tr>
<tr>
<td>COPD</td>
<td>N (%)</td>
<td>140,878 (9%)</td>
<td>52,072 (9%)</td>
<td>NA</td>
</tr>
<tr>
<td>Heart valve disorder</td>
<td>N (%)</td>
<td>140,878 (9%)</td>
<td>52,072 (9%)</td>
<td>NA</td>
</tr>
<tr>
<td>Hypertension</td>
<td>N (%)</td>
<td>441,640 (27%)</td>
<td>121,405 (20%)</td>
<td>NA</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>N (%)</td>
<td>139,987 (9%)</td>
<td>46,181 (8%)</td>
<td>NA</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>N (%)</td>
<td>128,943 (8%)</td>
<td>44,761 (7%)</td>
<td>NA</td>
</tr>
</tbody>
</table>
Indication for fluoroquinolones before/after RMM

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

- UTI
- Skin infection
- Respiratory infection
- Infection (unspecified)
- Implant infection
- GI tract infection
- Genital infection
- Fever
- ENT infection
- Bone/joint infection
- Bloodstream infection

Percentage

- After RMM (age group ≥60 years)
- Before RMM (age group ≥60 years)
Drug utilisation: DrugExposure Diagnostics

### DrugExperienceDiagnostics

<table>
<thead>
<tr>
<th>Database</th>
<th>Median [IQR]</th>
<th>5th</th>
<th>10th</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPRD AURUM</td>
<td>7 days [5-10]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPRD GOLD</td>
<td>5 days [5-7]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Value Type</th>
<th>Median [IQR]</th>
<th>5th</th>
<th>10th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial dose</td>
<td>1000mg [1000 – 1400mg]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cumulative dose</td>
<td>7000mg [5000 – 10000mg]</td>
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</tr>
</tbody>
</table>
Conclusion

✓ **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!