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Introduction

The threat of antimicrobial resistance has been recognised as one of the preeminent concerns for the future treatment of infections. However, the relationship between antimicrobial consumption and resistance is complex. Community use represents the bulk, approximately 80%, of antimicrobial prescriptions within the UK, with many of these antibiotics being prescribed for the treatment of UTIs. Approximately 5 antibiotics make up 70%-80% of the antibiotics prescribed for the treatment of UTIs. We know that in some cases over 40% of the bacteria that cause UTIs are resistant to some of the antibiotics used, yet we do not know how the patient outcome is affected in terms of relapse, treatment failure, progression onto more serious illness and hospitalisation and ultimately death. The majority of cases of antimicrobial therapy for UTI are initiated empirically before culture results are available².

Aim

1. What is the epidemiology of community prescribing for UTIs in terms of patient characteristics and length and number of prescriptions by the five main antibiotic types (Amoxicillin, Ciprofloxacin, Co-amoxiclav, Nitrofurantoin and Trimethoprim).
2. To identify long-term users of antibiotics.
3. What proportion of initial antibiotic prescriptions required a subsequent different antibiotic (a surrogate for treatment failure) and what was the pattern of antibiotic use in these cases?

Method

The Prescribing Information System which holds all community dispensed prescriptions in NHS Scotland was examined to identify a cohort of patients who had been dispensed a sentinel antibiotic (Amoxicillin, Ciprofloxacin, Co-amoxiclav, Nitrofurantoin and Trimethoprim) at any point from 2009 to 2012. The entry point into the study cohort was the month of first dispensing of one of the 5 sentinel antibiotics. Then patients were followed up to the end of 2012.

For the cohort of patients identified we conducted analysis using an anonymised linked data extract containing:

All PIS prescriptions from the date of the sentinel antibiotic.

Patient history of acute & geriatric long stay hospital admissions (from SMR01).

Patient history from ECOSS of positive laboratory samples with antimicrobial sensitivities results

NRS death records where a patient has subsequently died

Number (%) of patients with at least one prescription dispensed overall, by year of first prescription, by gender, by age group, by Scottish Index of Multiple Deprivation (SIMD) quintile and by long-term user status for the following groups of prescriptions:

Any (Amoxicillin, Ciprofloxacin, Co-Amoxiclav, Nitrofurantoin or Trimethoprim)

Excl.Amox (Ciprofloxacin, Co-Amoxiclav, Nitrofurantoin or Trimethoprim)

UTI-Specific (Nitrofurantoin or Trimethoprim)

	Sentinel Antibiotic Group		
	Any	Excl.Amox	UTI-Specific
Any	1093227 (100.0%)	1092151 (99.9%)	752225 (68.8%)
Not Dispensed	0 (0.0%)	1076 (0.1%)	341002 (31.2%)

By Year of First Prescription

Year	Any	Excl.Amox	UTI-Specific
2009	399761 (36.6%)	387772 (35.5%)	219877 (29.2%)
2010	267543 (24.5%)	268986 (24.6%)	187680 (24.9%)
2011	230054 (21.0%)	231342 (21.2%)	178386 (23.7%)
2012	195869 (17.9%)	204051 (18.7%)	166282 (22.1%)

By Gender

Gender	Any	Excl.Amox	UTI-Specific
Male	310974 (28.4%)	310405 (28.4%)	137198 (18.2%)
Female	782253 (71.6%)	781746 (71.6%)	615027 (81.8%)

By Age at the First Prescription

Age Group	Any	Excl.Amox	UTI-Specific
16-34	268896 (24.6%)	268318 (24.6%)	184476 (24.5%)
35-49	242173 (22.2%)	241717 (22.1%)	152857 (20.3%)
50-64	247287 (22.6%)	246841 (22.6%)	160108 (21.3%)
>65	334871 (30.6%)	335275 (30.7%)	254784 (33.9%)

By SIMD Quintile (Q1=Most Deprived, Q5=Least Deprived)

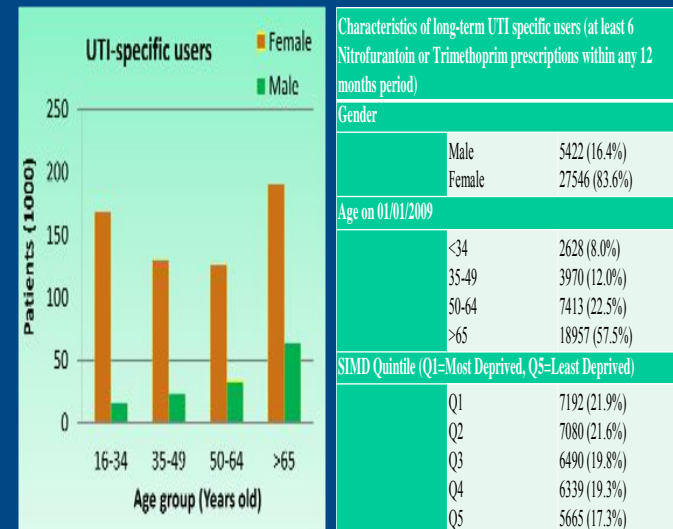
Quintile	Any	Excl.Amox	UTI-Specific
Q1	247671 (22.8%)	247405 (22.8%)	169301 (22.7%)
Q2	232451 (21.4%)	232289 (21.4%)	159286 (21.4%)
Q3	215015 (19.8%)	214788 (19.8%)	147401 (19.8%)
Q4	198832 (18.3%)	198625 (18.3%)	138783 (18.6%)
Q5	190210 (17.5%)	189983 (17.5%)	131272 (17.6%)

By Long-Term user Status (maximum number of prescriptions dispensed within any 12 month period)

User Status	Any	Excl.Amox	UTI-Specific
1	463267 (42.4%)	659867 (60.4%)	467429 (62.1%)
2	276247 (25.3%)	222737 (20.4%)	150940 (20.1%)
3	146397 (13.4%)	91810 (8.4%)	59181 (7.9%)
4	78780 (7.2%)	43303 (4.0%)	27307 (3.6%)
5	43500 (4.0%)	23109 (2.1%)	14400 (1.9%)
≥6	85036 (7.8%)	51325 (4.7%)	32968 (4.4%)

Number of different antibiotics dispensed

Number of antibiotics	Any	Excl.Amox	UTI-Specific
0	0 (0.0%)	1076 (0.1%)	341002 (31.2%)
1	491315 (44.9%)	770210 (70.5%)	590438 (54.0%)
2	402731 (36.8%)	239930 (21.9%)	161787 (14.8%)
3	144671 (13.2%)	68052 (6.2%)	0 (0.0%)
4	44179 (4.0%)	13959 (1.3%)	0 (0.0%)
5	10331 (0.9%)	0 (0.0%)	0 (0.0%)



Results

There were 1,093,227 patients aged 16-100 identified as receiving at least one prescription for the 5 sentinel antibiotics (Amoxicillin, Ciprofloxacin, Co-amoxiclav, Nitrofurantoin and Trimethoprim). There were 71.6% females in the cohort, with 30.6% of all patients are >65 years old. In this group of patients, 44.9% were prescribed with one type of antibiotic, and 36.8% with two different antibiotics from the original treatment antibiotics. Deprivation and prescribing rates were not associated.

68.8% of the patients had at least one of the UTI specific antibiotics (Trimethoprim, Nitrofurantoin). For the UTI specific antibiotics, 4.4% were long-term users (had more than 6 prescriptions in any 12 month period). The majority of recurrent prescriptions were for trimethoprim (59%). For the UTI specific antibiotics recurrent use was higher in females (83.6%) over the age of 65 years (57.5%). Deprivation was almost equally distributed among the UTI-specific long term users.

11.2% of patients prescribed Trimethoprim had a treatment failure (defined as a different antibiotic prescribed within 60 days) and 16.7% of initial nitrofurantoin use had a treatment failure as defined.

There were a total of 121,716 patients, aged 16-100, who had an organism isolated and had sensitivity testing performed. Of these, 7477 had an *E.coli* isolated and blood tested for resistance to one of the 5 sentinel antibiotics. Resistance to any of the 5 sentinel antibiotics in *E.coli* was found in 5285 (70.7%) patients. Of those who were first tested as sensitive, 355 (16.2%) switched to being resistant to at least one of the sentinel antibiotics. Of patients initially sensitive to Trimethoprim, 4.0% (143) were subsequently found to be resistant.

Conclusion

This is the first study in the UK using a national linked patient level data set that describes the population receiving at least one antibiotic used for the treatment of UTIs. It confirms that most treatment for UTI occurs within the elderly female population. UTI specific antibiotic (trimethoprim / nitrofurantoin) long-term users are approximately 4.4% of the study population. The assumption is that this is long term suppressive therapy for recurrent UTIs.

There is a treatment failure rate of between 11-16% in the patient group being treated with long term antibiotics for presumed recurrent UTI.

This data set will be used for future appropriate regression modelling.

References

1. Scottish antimicrobial prescribing group report on antimicrobial use and resistance in humans 2014. <http://www.hps.scot.nhs.uk/haic/amr/spotlightdetail.aspx?id=21191>
2. Scottish Intercollegiate Guidelines Network (SIGN). Management of suspected bacterial urinary tract infection in adults. Edinburgh: SIGN; 2012. (SIGN publication no. 88). [July 2012]. <http://www.sign.ac.uk>