Patterns of recurring dispensing of guideline antibiotics for uncomplicated urinary tract infection in women over a 5-year period: longitudinal patterns of recurring dispensings of Dutch guideline UTI antibiotics

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Epidemiology

Patterns of recurring dispensing of guideline antibiotics for uncomplicated urinary tract infection in women over a 5-year period: Longitudinal patterns of recurring dispensings of Dutch guideline UTI antibiotics

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Abstract

Background. Urinary tract infection (UTI) is one of the most prevalent medical conditions among women seeking primary care. About 20–40% of the women have a UTI recurrence during their lifetime.

Objective. To provide insight in the patterns of recurring annual dispensing for antibiotics commonly used for UTI treatment in women, aged 18 years or older, during a 5-year follow-up period in the Netherlands.

Methods. The Dutch Foundation of Pharmaceutical statistics collects dispensing data from more than 90% of all community pharmacies. Pharmacies with complete data between years 2011 and 2017 were included. Women of age 18 years or older with a first dispensing of nitrofurantoin, fosfomycin, or trimethoprim in 2012 and a dispensing of any medication in 2017 were selected. For each year between 2013 and 2017, the proportions of women with recurring dispensing of nitrofurantoin, fosfomycin or trimethoprim were calculated and stratified for age categories.

Results. Within 1517 eligible community pharmacies, 463 821 women, aged 18 years or older, were dispensed one of the antibiotics in 2012, and 239 292 women still visited the same pharmacy in 2017. About 56% of them received at least one recurring dispensing during 5 years of follow-up. Each year, ~20% of the source population had at least one recurring dispensing. Approximately 2% of the source population had at least one recurring dispensing in each year of follow-up.

Conclusions. Over the 5-year study period, more than 50% of the source population had at least one recurring dispensing for uncomplicated UTI, most of them with at least 1 year without UTI dispensing in between.

Key words: Antibacterial agents, cystitis, pharmacies, primary health care, recurrence, urinary tract infections.

Key Messages

- About 56% of the source population had at least one recurring UTI dispensing 2013–2017
- Most of these women had at least 1 year without a UTI dispensing
- Each year 20% of the source population had at least one recurring UTI dispensing
- Nearly 2% of the source population had UTI dispensing(s) each year of follow-up

Background

Urinary tract infection (UTI) is one of the most prevalent medical conditions among women in primary care. Approximately 60% of women experience symptomatic acute bacterial cystitis in their lifetime (1). An estimated 20–40% of women who have had one previous uncomplicated UTI episode are likely to experience recurring UTI (2–4). Commonly, recurrent UTI is defined as a recurring UTI with a frequency of three or more episodes in the last 12 months or two or more episodes in the last 6 months (5,6). It was shown that the prevalence of UTI (at least one physician-diagnosed UTI per year) increased with age, and in women over 65 years was ~20%, compared with ~11% in the overall population (7).

Risk factors for recurring UTI can be classified into four categories, (i) factors that decrease normal urogenital flora, e.g. frequent antibiotic use, personal hygiene, spermicide use, diaphragm/pessary use and menopause; (ii) factors that facilitate bacterial entry into the bladder, e.g. sexual intercourse, frequent catheterization and menopause; (iii) factors that decrease bacterial removal, e.g. decreased fluid intake, delayed voiding, incomplete bladder emptying and pelvic organ prolapse and; (iv) factors that impair the immune response, e.g. diabetes, steroid use, tobacco use and HIV/AIDS (8). A US study among women aged 18–49 years showed that UTI histories in first-degree female relatives were a strong and consistent risk factor with an increased risk for each type of relative and higher risk with greater number of infections (9). This study has also showed that the risk in women with combined exposures of a family UTI history and sexual intercourse frequency was considerably higher than with either exposure category alone.

The burden of recurring UTI has both personal and societal aspects (10–15). The societal burden includes the clinical and economic burden of illness. The personal burden comprises social and psychological effects which have a negative impact on the quality of life. Costs may be both direct and indirect: work absenteeism, for example, can impact both the economy and a patient's sense of wellbeing (10). Education about behavioural risk factors is advised for women with recurrent infections (16–19), but this may be relevant also for women with a recurrence of UTI after an interval of one or more years without UTI.

At present no large population-based studies have determined what proportions of women with uncomplicated UTI develop patterns of recurrences. This paper aims to provide insight in patterns of recurring dispensing of guideline antibiotics for treatment of uncomplicated UTI over a 5-year period in community dwelling women.

Methods

An observational descriptive study with routinely collected dispensing data was performed during 5 years of follow-up for women, with a first dispensing in 2012 of nitrofurantoin, fosfomycin, or trimethoprim.

Setting

In the Netherlands, the Dutch Foundation of Pharmaceutical statistics (SFK) collects dispensing data from more than 90% of all community pharmacies (20). The majority of patients visit one community pharmacy, which ensures completeness of the medication record and facilitates clinical risk management (21). In the database of the SFK, individuals are registered within a community pharmacy by a unique code generated by the pharmacy software system. By this unique encrypted code, patients can be tracked if they visit the same pharmacy. In the SFK database, information was available on patients' sex and year of birth, by which their age in 2012 could be calculated. Drug dispensing was coded by the Anatomic Therapeutic Chemical (ATC) system (22). No information on the reason of prescribing (indication) or loss to follow up from the database was available.

Pharmacy inclusion

Community pharmacies were included that had provided complete dispensing data for the period between 1 January 2011 and 31 December 2017 to the SFK.

Patient inclusion

All women, of age 18 years or older, were selected with a first dispensing in 2012 of one of the Dutch GP guideline recommended antibiotics for treatment of uncomplicated UTI. The recommended antibiotics were nitrofurantoin, fosfomycin and trimethoprim. We defined a first dispensing as the absence of a dispensing of an uncomplicated UTI antibiotic during the preceding 12 months, and the presence of an automatically generated code which states that a first dispensing fee was charged. We included only those women with any medication or medical device in their medication record in the same pharmacy in 2017, as this suggested that a woman was still registered at this pharmacy at the end of the 5-year study period. We reasoned that all dispensing including uncomplicated UTI antibiotics would have been covered for those women throughout the 5-year study period.

Data collection

We retrieved annual information on recurring dispensing of nitrofurantoin, fosfomycin and trimethoprim. Nitrofurantoin and trimethoprim can be used in different dosages and treatment durations, as well as for UTI prophylaxis. The Dutch GP UTI guideline, recommends for an uncomplicated UTI treatment, first nitrofurantoin (ATC (22) code: J01XE01) as a dose of 200 mg/day for 5 days, either 100 mg in a controlled release tablet twice daily for 5 days or 50 mg in a regular tablet four times per day, second, fosfomycin (J01XX01) as a one-off dose of 3 g, and third, trimethoprim (J01EA01) as a dose of 300 mg once daily for 3 days.

Data analysis

The number of women with dispensing of nitrofurantoin, fosfomycin and trimethoprim in each year of follow-up was divided by the total number of included women with a first dispensing in 2012. The number of women with dispensing in 2012 and in the follow-up years was stratified for age categories. We used descriptive statistics to analyse the data with SPSS 23.0 (SPSS Inc., Chicago, IL).

Results

Complete data were available from 1517 community pharmacies (77% of all community pharmacies in the Netherlands in 2012). In 2012, these pharmacies delivered a first dispensing of nitrofurantoin, fosfomycin or trimethoprim to 463 821 women, aged 18 years or older (on an average, 300 women per pharmacy per year). From these women, 239 292 (51.6%) still visited the same pharmacy in 2017 (Table 1) and were taken as the source population. About 224 529 women with a first dispensing of the UTI antibiotics in 2012 did not have any dispensing in 2017 within the same pharmacy, and thus were lost to follow-up. Compared with the source population, the proportions of women lost to follow-up were higher in the youngest and the oldest age categories, whereas the proportion of women 31–70 years was lower in the lost to follow-up population (Table 1). The mean age of the women in the source population was 54 years (±18.4 years) and ages varied between 18 and 103 years. The median age of women lost to follow up was 47 years and ages varied between 19 and 112 years.

In 2012, 84.4% of the women of the source population received nitrofurantoin, 6.1% of the women received fosfomycin and 18.5% received trimethoprim. The proportions of women using these antibiotics for those lost to follow up were comparable to the source population. The proportions of women treated with fosfomycin and trimethoprim in 2017 differed significantly from the proportions of women treated with these antibiotics in 2012. Of the women in the source population, 9.5% (n = 22 693) received more than one type of antibiotics in 2012.

From the women of the source population, 55.7% had at least one recurring dispensing of an UTI antibiotic in one of the 5 years of follow up. Consequently, 44.3% from those women still visiting the same pharmacy in 2017 did not return for a recurring dispensing of any of these antibiotics during the follow-up period. Figure 1 shows that in each year, from 2013 to 2017, one in five women of the source population returned to the pharmacy for at least one recurring dispensing of nitrofurantoin, fosfomycin or trimethoprim. From the 52 272 women with a recurring dispensing in 2014, about 56.6% did not have a dispensing in the preceding year 2013 (data not shown). After 2014, the proportion of women without any dispensing in the preceding years gradually decreased from 39.4% in 2015 to 25.7% in 2017. Figure 2 shows for each year of follow-up, the number of women with at least one recurring dispensing of nitrofurantoin, fosfomycin or trimethoprim during the corresponding and previous study years. Among these women with recurring dispensing, the proportions of younger women (aged between 19–30 and 31–50 years) were lower than the proportions of older women.

Table 2 shows that the proportion of women without any recurring dispensing during follow-up was highest in the youngest age group (50.5%) and lowest in the oldest age group (36.6%). From the women of the source population, 25.7% (n = 61 517) had at least one recurring dispensing in one year of follow-up, whereas 1.8% (n = 4393) had at least one recurring dispensing in each year of follow-up.

Table 1. Characteristics of included women and of women lost to follow up with a first dispensing of a guideline antibiotic recommended for uncomplicated urinary tract infection in 2012; included women also with at least one recurring dispensing of a guideline antibiotic recommended for uncomplicated urinary tract infection in 2017[a]

	Women still visiting the same pharmacy at the end of follow-up: Source population	Women not visiting the same pharmacy at the end of follow up: Lost to follow up
Number of women ≥18 years, first prescription[b] of nitrofurantoin, fosfomycin, or trimethoprim in 2012	239 292 (100%)	224 529 (100%)
Number of women included/ lost to follow up within age categories[c]		
18–30 years (% of women included/ lost to follow up)	34 118 (14.3%)	62 523 (27.8%)
31–50 years (% of women included/ lost to follow up)	69 436 (29.0%)	58 811 (26.2%)
51–70 year (% of women included/ lost to follow up)	86 117 (36.0%)	45 794 (20.4%)
≥ 71 years (% of women included/ lost to follow up)	49 621 (20.7%)	57 400 (25.6%)
Number of women[d] with a first prescription in 2012 of		
Nitrofurantoin (% of women included / lost to follow up)	202 062 (84.4%)	189 834 (84.5%)
Fosfomycin (% of women included/ lost to follow up)	14 658 (6.1%)	11 535 (5.1%)
Trimethoprim (% of women included/ lost to follow up)	44 248 (18.5%)	38 033 (16.9%)
Number of women[d] with a recurring UTI prescription in 2017 of		
Nitrofurantoin (% of all women with prescription in 2017)	38 796 (74.2%)	
Fosfomycin (% of all women with prescription in 2017)	19 084 (36.5%)	
Trimethoprim (% of all women with prescription in 2017)	3306 (6.3%)	

[a]Data from 1517 community pharmacies (77% of all community pharmacies in the Netherlands in 2012).

[b]Women ≥18 years with a first dispensing in 2012, defined as no dispensing of the same antibiotic drug in the previous 12 months and a registration for a first dispensing consultation in the pharmacy system with at least one dispensing in the same pharmacy in 2017.

[c]Age categories applied to women's age in 2012.

[d]Number of separate users of uncomplicated UTI antibiotics can add up to more than the women included and proportions can add up to more than 100%, due to women that had first dispensing of more than one type of antibiotic for uncomplicated urinary tract infection in 2012 and 2017.

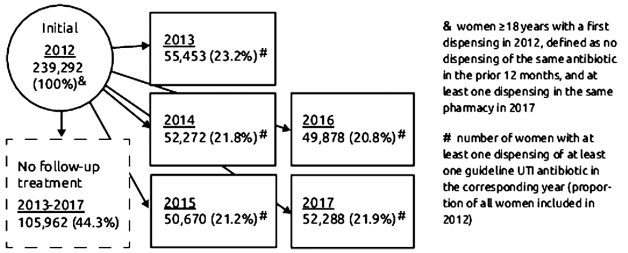

Figure 1. Return of women with a first dispensing of a guideline antibiotic for uncomplicated urinary tract infection in 2012& to the pharmacy between years 2013 and 2017, for at least one recurring dispensing or no recurring dispensing in any year of follow-up

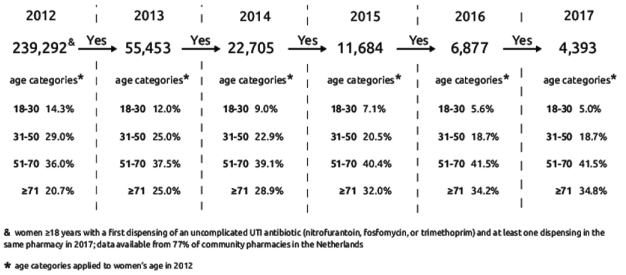

Figure 2. Recurring dispensing during 5 years of follow-up in women with a first dispensing of a guideline antibiotic for uncomplicated urinary tract infection in 2012&

Discussion

Our results show that more than half of the women still visiting the same pharmacy at the end of the study period had at least one recurring dispensing of a guideline antibiotic for uncomplicated UTI during 5 years of follow-up. Within a subsequent year the proportions of another UTI dispensing were between 20% and 23%. This proportion is within the range of 20–40% that was reported earlier for recurrent UTI (2,4).A Finnish study among women aged 17–82 years reported 44% UTI recurrence within one year (23). In these studies recurrent UTIs were defined as three or more episodes in 12 months. Our definition of recurring UTIs was less strict, counting at least one recurring prescription of an UTI antibiotic.

About 2% of the women included in our study received at least one recurring dispensing during every year in five years of follow-up. Most of these women belonged to the age category 51–70 years. In this age category most women are menopausal, and menopause was reported as one of the risk factors for UTI (8).

As UTI is one of the most prevalent medical conditions among women in primary care and ~60% of women experience symptomatic acute bacterial cystitis in their lifetime (1), UTI provides a high workload for primary care. In recent years, there have been increasing concerns in several countries about the rising workload in general practice, amongst others caused by the increase of multimorbidity and chronic diseases, an aging population, and the pressure to reduce access to secondary care (24). Moreover, the increasing costs of the healthcare system demand changes in the organisation of care (25). Stimulating patients' self-management to prevent recurring episodes of uncomplicated UTI seems to be a logical approach. There is of course always concern on overuse of antibiotics resulting in increasing antimicrobial resistance (26).

Women with recurring UTI may need additional care to improve self-management, aimed at prevention of uncomplicated UTI in the future. The GP or another health care provider can provide this additional care for women with recurring UTI (27,28). However, it may be preferable to educate women on preventive measures or discuss with them delay of antibiotic treatment with increased fluid intake and painkillers (29), before starting patient-initiated treatment (30). A study showed that UTI symptoms recovered spontaneously within one week in about 50% of symptomatic women not taking antibiotics (31). Other studies showed that more than one third of women with UTI symptoms were willing to delay antibiotic treatment when asked by their GP (32). Women preferred not to take antibiotics and were open to alternative management approaches (33).

This study provides insight in the patterns of recurring dispensing for guideline antibiotics for uncomplicated UTI and an indication of the size of the problem. Further work needs to be done to identify predictors of recurring prescribing and to study the effect of education about risk factors on recurring prescribing.

Strengths and limitations

A strength of our study was that we used routinely collected dispensing data from a majority of community pharmacies in the Netherlands, which enabled us to follow nearly 250 000 female users of guideline recommended antibiotics for uncomplicated UTI for 5 years. In the Netherlands all antibiotics for UTI treatment are only available through prescription and 90% of patients visit the same pharmacy (21).Because of this the medication was almost completely covered by the database. Another strength is that, although we lacked the reason for prescribing, uncomplicated UTI is the only indication for nitrofurantoin, fosfomycin and trimethoprim in the electronic GP prescription module. On the other hand, nitrofurantoin and trimethoprim may also be used for UTI prophylaxis at different dosages and durations of use. In our study, only dispensings for women with a guideline recommended dosage and duration were counted as recurring dispensings. By doing so, we also excluded slightly different dosage regimens for pregnant women and other risk groups (for instance, diabetes comorbidity).

A limitation in our study was that women were coded within the community pharmacies and could not be followed for dispensing from another pharmacy. Therefore we included only those women who still had any dispensing within the same pharmacy at follow-up after 5 years. This, however, led to the exclusion of almost half of all women with a first dispensing in 2012. The youngest and oldest age groups were relatively more present in those women that could not be followed until the end of the study (Table 1). This may be due to moving or death. Statline, the National Statistics Database in the Netherlands provided yearly data on the proportions of people moving within municipalities and entering other municipalities per 1000 inhabitants, and the relative number of deceased (34). From these data 43% of the population moved within a municipality or into another municipality or died between 2012 and 2017. This proportion is comparable to the 48% lost to follow up in our study. Therefore, we conclude that the loss of follow-up is not related to our research question and thus is not likely to create bias to our results on the prevalence of recurring UTI dispensing in women.

Another limitation was that we did not analyse what proportion of the source population had recurrent UTI. We did not do this because our aim was to analyse recurrence of UTI in all women over a 5-year period.

Table 2. Number of women with a first dispensing for uncomplicated urinary tract infection in 2012[a,b] with total number of years of follow-up, every year with at least one recurring dispensing, stratified for age categories[c]

	18–30 years	31–50 years	51–70 years	≥71 years	Sum
No recurring dispensing during follow-up (% within age category)	17 240 (50.5%)	33 872 (48.8%)	36 672 (42.6%)	18 178 (36.6%)	105 962 (44.3%)
Recurring dispensing during 1 year of follow-up (% within age category)	9429 (27.6%)	17 981 (25.9%)	21 648 (25.1%)	12 459 (25.1%)	61 517 (25.7%)
Recurring dispensing during 2 years of follow-up (% within age category)	4548 (13.3%)	9614 (13.8%)	13 438 15.6%)	8389 (16.9%)	35 989 (15.0%)
Recurring dispensing during 3 years of follow-up (% within age category)	1944 (5.7%)	4889 (7.0%)	8094 (9.4%)	5696 (11.5%)	20 623 (8.6%)
Recurring dispensing during 4 years of follow-up (% within age category)	738 (2.2%)	2260 (3.3%)	4441 (5.1%)	3369 (6.8%)	10 808 (4.5%)
Recurring dispensing during 5 years of follow-up (% within age category)	219 (0.6%)	820 (1.2%)	1824 2.1%)	1530 (3.1%)	4393 (1.8%)
Sum of all women included per age category	34 118 (100%)	69 436 (100%)	86 117 100%)	49 621 (100%)	239 292 (100%)

[a]Data from 1517 community pharmacies (77% of all community pharmacies in the Netherlands in 2012).

[b]Women aged ≥18 years with a first dispensing in 2012, defined as no dispensing of the same antibiotic in the previous 12 months, and at least one dispensing in the same pharmacy in 2017.

[c]Age categories applied to women's age in 2012.

We also may have missed some recurring dispensing in women who incidentally visited another pharmacy for out-of-hours services. This would lead to under-estimation of the proportion of women with recurring dispensing.

Conclusion

This study shows that over the 5-year study period, more than 50% of the women had at least one recurring antibiotic dispensing to treat uncomplicated UTI. Patient empowerment is needed to prevent recurrence of UTI and antibiotic treatment, and health care providers can play an important role in this. They can discuss risk factors for UTI with women and educate them on preventive measures. Also, GPs can discuss with women delay of antibiotic treatment with increased fluid intake and painkillers.

Declaration

Funding: No sources of funding were used to assist in the conduct of this study or the preparation of this article.

Ethical approval: The independent advisory board of SFK approved the use of their anonymised and encrypted data for this study. Use of anonymous observational data in the Netherlands is not considered as subject to ethical approval from an independent medical ethical committee.

Conflict of interest: none.

Data availability

The datasets that were analysed during the current study are available from the corresponding author on reasonable request.

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