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# Office-based approach to urinary tract infections in 50 000 patients: results from the REWIND study

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ABSTRACT

*Objectives:* The REWIND study sought to describe the real-world clinical and prescribing practices for the management of urinary tract infection (UTI) in Italy, Belgium, Russia and Brazil in order to compare current practices with international, European and national guidelines.

*Methods:* An integrated mixed-methods approach was adopted that used information from primary care electronic medical records in longitudinal patient databases available in Italy and Belgium, and surveys of physicians in Russia (general practitioners) and Brazil (gynaecologists).

*Results:* In total, 49 548 female patients were included in the study. Antibiotics were the most common management option for UTI in Italy (71.1%, *n*=27 600), Belgium (92.4%, *n*=7703), Russia (81.9%, *n*=1231) and Brazil (82.4%, *n*=740). Fosfomycin trometamol was the first-choice antibiotic for the treatment of UTI in all countries. Ciprofloxacin was also commonly prescribed in Italy (24.6%, *n*=6796), Belgium (17.8%, *n*=1373), Russia (14.9%, *n*=184) and Brazil (9.6%, *n*=71), while prescription of nitrofurantoin was common in Belgium (24.5%, *n*=1890) alone.

*Conclusions:* Despite differences in study designs and data sources, fosfomycin trometamol was found to be the most commonly prescribed treatment for UTI in all participating countries. In Belgium, real-world prescribing practices for UTI adhered more closely to European guidelines than national guidelines. Although not recommended in international and European guidelines for lower UTI management, the use of fluoroquinolones was still widespread.



## 1. Introduction

Management of urinary tract infection (UTI) in healthy women typically relies on treatment with antibiotics. However, in recent years, antibiotics traditionally prescribed for uncomplicated UTI have become increasingly associated with antimicrobial resistance, and many are no longer recommended as first-line treatment [1–5]. At present, the guidelines of the European Association of Urology (EAU) recommend the following antibiotics as first-line treatment of acute uncomplicated cystitis: fosfomycin trometamol, pivmecillinam and nitrofurantoin [6]. Alternatively, co-trimoxazole or trimethoprim may be considered as treatment options for UTI in areas where the resistance rate of *Escherichia coli* is <20%. Due to concerns about antimicrobial resistance and adverse environmental effects, the EAU guidelines do not recommend the use of fluoroquinolones for the management of cystitis [6].

Despite EAU recommendations, local guidelines for the use of antibiotics for uncomplicated UTI vary considerably across Europe. For example, while current local guidelines for UTI management in Italy are aligned with EAU recommendations [7], this

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is not the case in Belgium [8]. It is also important to note that there are indications that clinical adherence to local guidance for UTI management is low in both countries [9,10], although evidence about current clinical practices in Europe, and elsewhere, is limited.

Differences in local UTI management guidelines across Europe are likely to be driven by a number of factors, including regional variability in antimicrobial resistance rates, availability of antibiotics in different countries, and local differences in clinical practices [11]. Given that these factors are not specific to Europe, a similar picture is also expected in other countries.

Due to discrepancies between international and national guidelines, potential low adherence to national guidelines [9,10], and a lack of published information on the current clinical management of UTI, this study was undertaken to investigate the real-world clinical and prescribing practices for the management of UTI in four countries – Italy, Belgium, Russia and Brazil – using primary and secondary care data.

## 2. Materials and methods

### 2.1. Study design

The multi-country REWIND (REal World INternational Database) study comprised a retrospective cohort study using primary care electronic medical record databases in Italy and Belgium (study period 1 January 2016 to 31 December 2017), and a primary market research (PMR) survey of physicians in Russia and Brazil (conducted in December 2018 and January 2019).

### 2.2. Data sources

In Italy and Belgium, IQVIA longitudinal patient databases (LPDs) of primary care medical records were used to collect information on UTI management. LPDs contain patient records on all signs and symptoms, diagnoses and prescribed medications. The information reported in LPDs allows patients and doctors to be monitored longitudinally. Data are recorded directly into LPDs from doctors' surgeries in real-time during patient consultations via a practice management software system. The panel of contributing physicians is maintained as a representative sample of the primary care physician population in Italy and Belgium according to three criteria known to influence prescribing: age, sex and geographical distribution. As such, results from LPD studies are generalizable to the entire populations of Italy and Belgium, and have been used to investigate a wide range of therapeutic areas in epidemiological and drug utilization studies [12–15].

PMR data were collected from physicians who manage patients with UTI in Russia [general practitioners (GPs)] and Brazil (gynaecologists) via a 30-min quantitative questionnaire, distributed using computer-assisted web interviewing or face-to-face methods. Physicians were sampled from global market research panels collaborating with IQVIA.

### 2.3. Study population and study period

In Italy and Belgium, female patients aged ≥18 years with a diagnosis of UTI during the recruitment period (1 January 2016–31 December 2016) were eligible for inclusion. The date of first UTI diagnosis during the recruitment period was defined as the index date. Patients with a diagnosis of UTI in the 12 months preceding the index date were excluded from the analysis. Patients were required to have at least 12 months of follow-up data from the index date. Patients diagnosed with radiation cystitis or chemo-/radiotherapy in the 12 months preceding the index date were excluded.

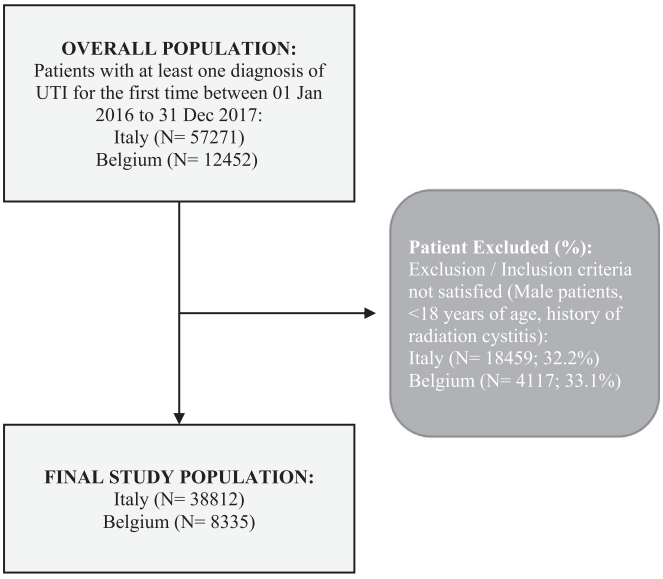


**Fig. 1.** Patient selection flowchart (Italy and Belgium).

In Russia and Brazil, physicians completed a structured screening questionnaire and were considered eligible to submit data if they had managed any female patient who presented with a UTI in the previous 12 months.

### 2.4. Outcomes

In Italy and Belgium, UTI diagnoses and concomitant conditions were identified using International Classification of Diseases (ICD) codes [ICD-9 (Italy) and ICD-10 (Belgium)] (Table S1, see online supplementary material). Any UTI-related interventions recorded within 14 days of UTI diagnosis were considered to be attributable to that diagnosis. Patients with recurrent UTI were defined as those who had three or more episodes of infection within 1 year or two episodes in 6 months [6,16,17]. Those not classified as recurrent UTI patients were classified as sporadic UTI patients. Medical treatments were identified using the Anatomical Therapeutic Chemical (ATC) Classification System. Table S2 (see online supplementary material) shows the ATC codes used to identify the antimicrobial, anti-inflammatory and supplementary therapies associated with a diagnosis of UTI. Pregnancy status was estimated at the index date.

In Russia and Brazil, each participating physician completed a patient record form (PRF) for the last five eligible patients they had treated. The PRFs collected information on patient characteristics and clinical information in relation to the presenting UTI, including age, diagnosis type (uncomplicated, complicated or recurrent UTI), pregnancy status, and UTI treatments received.

### 2.5. Statistical analysis

Qualitative variables were reported using frequencies ($n$) and percentages (%), and quantitative variables were reported using means and standard deviations. All analyses were performed using SAS Version 9.4 (SAS Institute, Cary, NC, USA).

## 3. Results

### 3.1. Patient population

In total, 49 548 patients were eligible for inclusion in the study. In Italy and Belgium, 38 812 and 8335 eligible patients, respectively, were identified in LPDs and included in the study (Fig. 1).

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**Table 1**
Patient demographics and clinical features measured at the index date (Italy and Belgium) or reported at questionnaire completion (Russia and Brazil), presented by country.

| | Italy | | Belgium | | Russia | | Brazil | |
|---|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | *n* | % |
| No. of patients | 38 812 | | 8335 | | 1503 | | 898 | |
| Age (years) | | | | | | | | |
| Mean (SD) | 57.3 (19.0) | | 52.4 (19.5) | | 41.5 (15.5) | | 36.5 (12.5) | |
| Age group (years) | | | | | | | | |
| 18–50 | 14 510 | 37.4 | 3875 | 46.5 | 1080 | 71.9 | 769 | 85.6 |
| >50 | 24 302 | 62.6 | 4460 | 53.5 | 423 | 28.1 | 129 | 14.4 |
| Concomitant conditions | | | | | | | | |
| Diabetes mellitus[a] | 4000 | 10.3 | 444 | 5.3 | 201 | 13.4 | 250 | 27.8 |
| Urological disorders[b] | 16 | 0.04 | 0 | 0.0 | 367 | 24.4 | 21 | 2.3 |
| Pregnancy | 2374 | 6.1 | 141 | 1.7 | 113 | 7.5 | 361 | 40.2 |
| Use of contraceptives | - | - | 988 | 11.9 | 150 | 10.0 | 140 | 15.6 |
| Patient subgroups | | | | | | | | |
| Sporadic UTI patients[c] | 27 055 | 69.7 | 7095 | 85.1 | 1131 | 75.2 | 706 | 78.6 |
| Assessed by physician as complicated UTI | - | - | - | - | 200 | 13.3 | 123 | 8.2 |
| Recurrent UTI patients[d] | 11 757 | 30.3 | 1240 | 14.9 | 372 | 24.8 | 192 | 21.4 |

UTI, urinary tract infection.
Percentages were calculated out of the total cohort of patients identified in each country.
[a] Controlled or uncontrolled.
[b] Including ureteral obstruction (i.e. stone, stricture), vesicoureteral reflux and incomplete voiding.
[c] Patients not classified as recurrent UTI patients.
[d] Measured after 1-year of follow-up and with no history of UTI for 12 months preceding the index date (Italy and Belgium). Defined as patients with three or more episodes of UTI in 1 year or two episodes in 6 months. In Russia and Brazil, recurrent UTI patients were identified by physician at questionnaire completion.

PRFs for 1503 patients were submitted from 301 GPs surveyed in Russia, and 898 PRFs were submitted from 183 gynaecologists in Brazil.

### 3.2. Patient characteristics

The characteristics of patients at the index date (Italy and Belgium) and survey completion (Russia and Brazil) are shown in Table 1. Patient age varied between the country cohorts; while most patients in Italy and Belgium were aged ≥50 years, those in Russia and Brazil were more likely to be younger. The proportions of patients identified as having recurrent UTI during the study period in the LPDs were 30.3% (*n*=11757) in Italy and 14.9% (*n*=1240) in Belgium. Similar proportions were reported by physicians in Russia and Brazil via the PMR surveys: 24.8% (*n*=372) and 21.4% (*n*=192), respectively. The prevalence of concomitant conditions varied widely across the four country cohorts (Table 1). For example, the proportion of pregnant patients seen by physicians (gynaecologists) in Brazil (40.2%, *n*=361) was considerably higher compared with the proportion of pregnant patients seen by physicians (GPs) in the other three countries (Table 1). A similar trend was observed for the proportion of patients with a diagnosis of diabetes. The number of urology-related cases reported in Russia was relatively high (24.4%, *n*=367) compared with Italy, Belgium and Brazil.

### 3.3. Treatment prescription

Considering the data reported in the LPDs, nearly all patients from Belgium were prescribed a treatment for their first episode of UTI (*n*=7913, 94.9%), while over one-quarter (26.0%) of patients from Italy received no treatment (Table 2). Overall, very low prescription rates for anti-inflammatories and supplements were reported in the Italian and Belgian LPDs. Antibiotics were the most commonly prescribed treatments for managing the first episode of UTI in patients from Italy and Belgium [71.1% (*n*=27 600) and 92.4% (*n*=7703), respectively], and in patients from Russia and Brazil [81.9% (*n*=1231) and 82.4% (*n*=740), respectively]. In Russia, this was associated with a very high prescription rate for supplements (85.4%) and anti-inflammatories (37.1%). Canephron was reported to be the most commonly prescribed herbal product in Russia (66.4% of the total sample, *n*=998). In Russia and Brazil, the proportion of patients who received no treatment at all was low (Table 2). When considering pregnant patients, the proportion treated with antibiotics was reduced compared with the overall study cohorts in Italy, Belgium and Russia, while the proportion treated with antibiotics was increased compared with the overall study cohort in Brazil.

### 3.4. Antibiotic choice

The most commonly prescribed antibiotics for managing the first episode of UTI are shown in Table 3 (grouped by type). Fosfomycin trometamol was the most commonly prescribed first-line antimicrobial in all country cohorts: 38.8% (*n*=10 715) in Italy, 35.7% (*n*=2750) in Belgium, 21.6% (*n*=266) in Russia and 39.7% (*n*=294) in Brazil. Ciprofloxacin was the next most commonly prescribed antibiotic in Italy (24.6%, *n*=6796), Russia (14.9%, *n*=184) and Brazil (9.6%, *n*=71), whereas the next most commonly prescribed antibiotic in Belgium was nitrofurantoin (24.5%, *n*=1890), an antimicrobial agent seldom prescribed in the other three countries (Table 3). Overall, fosfomycin trometamol, nitrofuran derivatives (29.9%, *n*=2306) and fluoroquinolones (24.6%, *n*=1893) represented >90% of the antibiotic types prescribed as first-line therapy in the Belgian cohort. Similarly, in Italy, fosfomycin trometamol and fluoroquinolones (*n*=10 683, 38.6%) represented over three-quarters of the antibiotic types prescribed as first-line treatment of UTI. In the Brazilian and Russian cohorts, antibiotic prescribing was more varied. For example, compared with Italy and Belgium, the use of penicillin (amoxicillin/clavulanic acid; 14.9%, *n*=183) and cephalosporins (cefixime; 7.8%, *n*=96) was relatively high in Russia, along with the use of cephalosporins (cefalexin; 8.1%, *n*=60) in Brazil (Table 3). The reported use of co-trimoxazole and macrolides was marginal in all four country cohorts, with the highest reported prescribing rates seen in Brazil: 3.2% and 3.9%, respectively (Table 3).

In pregnant patients, fosfomycin trometamol was the first-choice antibiotic in all four country cohorts, ranging from 36.5% to 48.8% (Fig. 2). The use of quinolones in pregnant patients (Fig. 2)

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**Table 2**
Number of patients and type of treatment prescribed for the first episode of urinary tract infection (UTI) at the index date (Italy and Belgium) or reported at questionnaire completion (Russia and Brazil). Focus on antibiotic use in the subgroups of pregnant and recurrent UTI patients, presented by country.

| | Italy | | Belgium | | Russia | | Brazil | |
|---|---|---|---|---|---|---|---|---|
| | *n* | % (*n*=38 812) | *n* | % (*n*=8335) | *n* | % (*n*=1503) | *n* | % (*n*=898) |
| Overall[a] | | | | | | | | |
| Prescription for antibiotics | 27 600 | 71.1 | 7703 | 92.4 | 1231 | 81.9 | 740 | 82.4 |
| Prescription for anti-inflammatories | 272 | 0.7 | 51 | 0.6 | 558 | 37.1 | 116 | 12.9 |
| Prescription for supplements | 806 | 2.1 | 0 | 0.0 | 1284 | 85.4 | 5 | 0.6 |
| Other treatments not classified | 663 | 1.7 | 191 | 2.3 | 0 | 0.0 | 0 | 0.0 |
| No treatment prescribed | 10 107 | 26.0 | 422 | 5.1 | 6 | 0.4 | 85 | 9.5 |
| Use of antibiotics[b] | | | | | | | | |
| Recurrent UTI patients[c] | 10 305 | 87.6 | 1174 | 94.7 | 328 | 88.2 | 114 | 59.4 |
| Pregnant patients | 1448 | 61.0 | 115 | 81.6 | 65 | 57.5 | 342 | 94.7 |

[a] Not mutually exclusive: the number of patients in each group may be more than the total cases (each patient could have been prescribed a combination of treatments).
[b] Percentages were calculated out of the number of patients identified in each subgroup.
[c] Measured after 1-year of follow-up and with no history of UTI for 12 months preceding the index date (Italy and Belgium). Defined as patients with three or more episodes of UTI in 1 year or two episodes in 6 months. In Russia and Brazil, recurrent UTI patients were identified by physician at questionnaire completion.

**Table 3**
Main antibiotics prescribed as first-line management of urinary tract infection at the index date (Italy and Belgium) or reported at questionnaire completion (Russia and Brazil), presented by country.

| | Italy | | Belgium | | Russia | | Brazil | |
|---|---|---|---|---|---|---|---|---|
| | *n* | % (*n*=27 600) | *n* | % (*n*=7703) | *n* | % (*n*=1231) | *n* | % (*n*=740) |
| **Fosfomycin** | 10 715 | 38.8 | 2750 | 35.7 | 266 | 21.6 | 294 | 39.7% |
| **Fluoroquinolones** | | | | | | | | |
| Ciprofloxacin | 6796 | 24.6 | 1373 | 17.8 | 184 | 14.9 | 71 | 9.6% |
| Levofloxacin | 2492 | 9.0 | 78 | 1.0 | 143 | 11.6 | 48 | 6.5% |
| Norfloxacin | 699 | 2.5 | 332 | 4.3 | 55 | 4.5 | 30 | 4.1% |
| Ofloxacin | 0 | 0.0 | 110 | 1.4 | 62 | 5.0 | 0 | 0.0% |
| Prulifloxacin | 698 | 2.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0% |
| **Nitrofuran derivatives** | | | | | | | | |
| Nitrofurantoin | 448 | 1.6 | 1890 | 24.5 | 35 | 2.8 | 43 | 5.8% |
| Nifurtoinol | 0 | 0.0 | 416 | 5.4 | 0 | 0.0 | 0 | 0.0% |
| Furazidin | 0 | 0.0 | 0 | 0.0 | 90 | 7.3 | 0 | 0.0% |
| **Trimethoprim/sulfamethoxazole** | 732 | 2.7 | 84 | 1.1 | 4 | 0.3 | 24 | 3.2% |
| **Penicillins** | | | | | | | | |
| Amoxicillin/clavulanic acid | 1165 | 4.2 | 92 | 1.2 | 183 | 14.9 | 48 | 6.5% |
| Amoxicillin | 224 | 0.8 | 78 | 1.0 | 0 | 0.0 | 19 | 2.6% |
| **Cephalosporins** | | | | | | | | |
| Cefalexin | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 60 | 8.1% |
| Cefixime | 732 | 2.7 | 0 | 0.0 | 96 | 7.8 | 0 | 0.0% |
| Cefotaxime | 0 | 0.0 | 0 | 0.0 | 14 | 1.1 | 0 | 0.0% |
| Ceftriaxone | 95 | 0.3 | 0 | 0.0 | 0 | 0.0 | 48 | 6.5% |
| Cefuroxime | 42 | 0.2 | 51 | 0.7 | 0 | 0.0 | 1 | 0.1% |
| **Macrolides** | | | | | | | | |
| Azithromycin | 89 | 0.3 | 0 | 0.0 | 0 | 0.0 | 29 | 3.9% |
| Other[a] | 2673 | 9.7 | 449 | 5.8 | 99 | 8.0 | 25 | 3.4% |

Percentages were calculated out of the total number of patients receiving antibiotic treatment.
[a] Antibiotics not specified/classified or combinations of different antibiotics.

was reduced compared with the general study cohorts (as described in Table 3). For example, in Italy, the percentage of patients prescribed fluoroquinolones at the first GP visit decreased from 38.7% in the general study cohort (Table 3) to 22.9% in pregnant patients (Fig. 2). Similar trends were reported in Belgium [24.6% (all patients) vs. 13.9% (pregnant patients)], Russia (36.1% vs. 9.2%) and Brazil (20.1% vs. 11.4%). The use of penicillin for management of the first UTI episode was higher in pregnant patients in Russia, Belgium and Italy compared with the general study cohorts (Tables 3 and Fig. 2). In pregnant patients, nitrofuran derivatives were primarily used in Belgium (34.8%, *n*=40), with lower levels reported in the other three countries, particularly Italy (0.6%, *n*=9).

In patients with recurrent UTI, fluoroquinolones were the most commonly prescribed first-line treatment in Russia (42.7%, *n*=140) and Brazil (28.1%, *n*=32), while prescription of fosfomycin trometamol was limited to 43 (13.1%) and 28 (24.6%) patients, respectively (Fig. 2).

## 4. Discussion

### 4.1. Main findings

This real-world, international study of nearly 50 000 female patients in primary and secondary care settings provides a representative description of current clinical practices for the management of UTI in Italy, Belgium, Russia and Brazil. In particular, this study provides clear indications of prescribing behaviour, including antibiotic choice, of physicians in these four countries when treating female patients generally, and in the subgroups of recurrent UTI and pregnancy.

Patients from the four country cohorts differed in terms of demographics and clinical features. In Brazil, most patients were young pregnant women, which is not surprising given that the participating physicians from Brazil were gynaecologists, who would be expected to manage more patients of childbearing age com-

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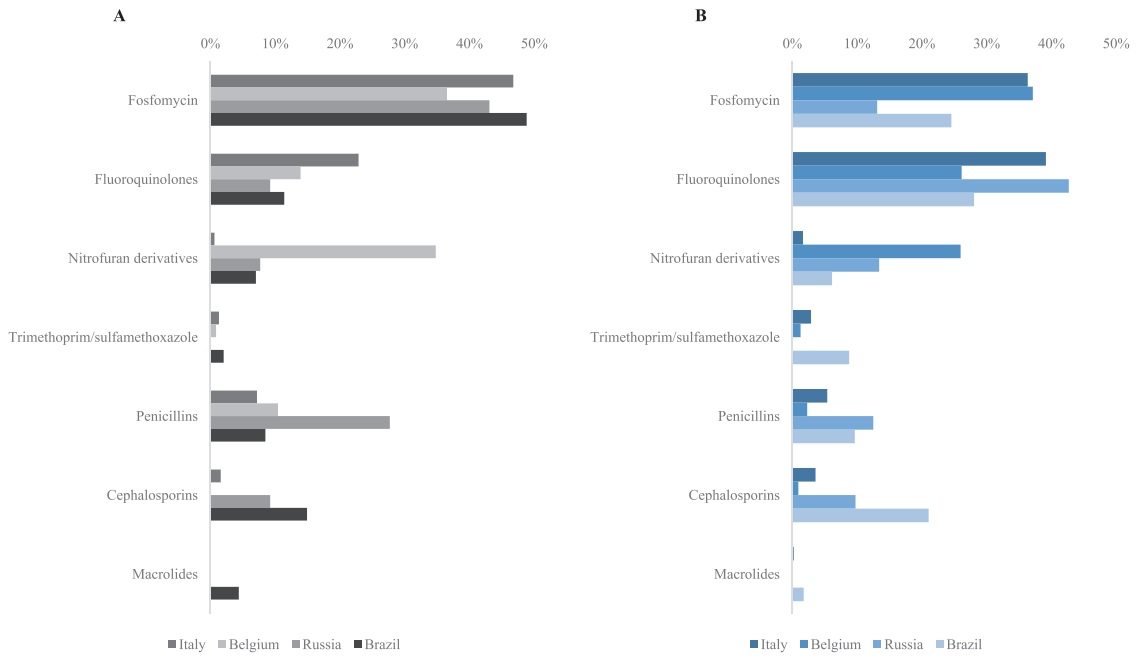


**Fig. 2.** Subgroups of pregnant (A) and recurrent (B) patients with urinary tract infection (UTI): main antibiotics prescribed for the first episode of UTI at the index date (Italy and Belgium) or reported at questionnaire completion (Russia and Brazil) for each country.

pared with GPs. In Italy and Belgium, the incidence of UTI was highest in patients aged >50 years. This is an important consideration because this cohort of patients would likely be postmenopausal – a known risk factor for complicated UTI [5,6]. Interestingly, despite the relatively high rates of pregnancy and diabetes reported in the Brazilian cohort, gynaecologists only reported a modest proportion of women with complicated UTI; this was mirrored in Russia, where relatively high levels of concomitant urological disorders were reported. These concomitant conditions are considered clear risk factors for complicated UTI, suggesting potential differences in physicians' perceptions of what defines complicated UTI, and indicates differences between international/EAU guidelines [5,6] and real-world clinical practices in Brazil and Russia.

### 4.2. Findings in the context of existing literature

There is some evidence to suggest that the proportion of patients who experience recurrent UTI is approximately 25%; however, this is largely estimated from cross-sectional surveys [16,17] and anecdotal information. In the LPD component of this study (Italy and Belgium), the robust longitudinal study design, large patient cohorts and sole inclusion of those patients with a first diagnosis of UTI permitted accurate assessment of the number of patients with recurrent UTI over a 12-month follow-up period.

Interestingly, the proportion of patients with recurrent UTI in the Italian cohort was twice that in the Belgian cohort, which may, in part, be associated with the observed differences in prescribing practices within the two countries. For example, the proportion of patients who received no treatment for their first UTI in Italy was markedly higher (26%) compared with that in Belgium (5%), Russia (0.4%) and Brazil (9%). That said, it is important to note that LPDs only generally report on prescribed medicines; therefore, the use of over-the-counter anti-inflammatories and supplements is expected to be under-reported.

Despite the differences highlighted above, fosfomycin trometamol was the most commonly prescribed antibiotic in all four country cohorts. Associated with high rates of antimicrobial susceptibility in uropathogens [2,4] and a low-risk safety profile [18,19], fosfomycin trometamol is recommended as first-line treatment for uncomplicated, community-acquired UTI in both international and European guidelines [20]. In Italy, the use of fosfomycin trometamol in UTI management was described in a previous study using LPDs [10], and is currently recommended in local guidelines [7]. The present study confirms the findings of this previous study, and supports the use of fosfomycin trometamol in Italy and expands the results to three other countries.

In the Belgian cohort, it is important to note that the study data collection period spanned the implementation of the latest (2016) Belgian guidelines, which recommend fosfomycin trometamol for the first time (as a second-line treatment) [8]. Interestingly, this study showed that in real-world practice, fosfomycin trometamol was prescribed more frequently than nitrofurantoin – the recommended first-choice UTI treatment in Belgium [8]. As such, it appears that the prescription practices of GPs in Belgium only partially follow local guidelines, and are instead more aligned with EAU guidance [6]. Low levels of adherence to Belgian UTI management guidelines have been reported previously in a study of 100 cases of UTI treated in an out-of-hours primary care setting; however, it is important to note that the study did not capture the alternative treatments prescribed [9]. The present study supports these earlier findings with data from a considerably larger cohort, and, for the first time, provides a clear indication of the alternative treatments prescribed by GPs in Belgium.

In Russia and Brazil, reported use of fosfomycin trometamol was found to be in line with national recommendations [21–23].

In the Italian cohort, nitrofurantoin was rarely prescribed (<2% of patients treated with antibiotics), despite it being recommended as an alternative to fosfomycin trometamol as a first-line antimicrobial in local guidelines [7]. In comparison, the prescription of fluoroquinolones was found to be high (approximately 40% of patients treated with antibiotics) given that these agents are no longer recommended for the treatment of uncomplicated cystitis [7]. Similarly, fluoroquinolones were found to be widely prescribed in the Belgian, Russian and Brazilian cohorts and for the treatment of pregnant patients. This is of particular note given that,

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since March 2019, the European Medicines Agency has restricted the prescription of fluoroquinolones due to safety concerns, and suspended the marketing authorizations of medicines containing cinoxacin, flumequine, nalidixic acid and pipemidic acid [24]. In particular, fluoroquinolones should no longer be prescribed for the prevention of recurrent UTI and during pregnancy [24].

### 4.3. Strengths and limitations

The REWIND study was conducted on a very large sample of patients. LPDs – which have been used to investigate a wide range of therapeutic areas in previous epidemiological and drug utilization studies – represent a robust source of primary care data which is generalizable to the wider Italian and Belgian populations [12–14]. Similarly, the large number of surveys completed by physicians in Russia and Brazil were designed to collect information that was representative of the broader populations, and therefore also provide a valuable and generalizable description of the clinical management of UTI.

One limitation of this study is that distinction between uncomplicated and complicated UTI diagnoses was not possible in the LPDs; this prevented comparisons between LPD and survey data, and meant that the appropriateness of reporting UTI diagnosis type could not be explored in the Italian and Belgian cohorts. Similarly, information on non-prescribed treatments was scarcely captured in the LPDs. Finally, the surveys in Russia and Brazil relied on the ability of physicians to remember the details of their last five patients, which may have introduced recall bias.

## 5. Conclusions

The REWIND study is the first multi-country study to describe real-world prescribing behaviour and antibiotic use in a large cohort of patients managed for UTI. Despite using different study designs and data sources, fosfomycin trometamol was found to be the most commonly prescribed antibiotic in Italy, Belgium, Russia and Brazil. In Belgium, real-world prescribing patterns appeared to adhere more closely to European guidelines than national guidelines. Although not recommended in international and European guidelines for lower UTI, the use of fluoroquinolones was still widespread.

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**Competing interests:** TC has acted as a speaker for Zambon at international and national conferences. IP has acted as a speaker for a number of pharmaceutical companies including Zambon. RB, EP and SVB have acted as consultants for Zambon. RC is an employee of IQVIA Italy Srl. JCT has acted as a consultant and speaker for Zambon. The authors report no other conflicts of interest.

**Ethical approval:** Not required.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijantimicag.2020.105966.

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