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# Check of APpropriaTeness of Antimicrobial therapy In Nursing homes (CAPTAIN):a point prevalence study in Belgium

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**Objectives:** The overall prevalence of antimicrobial therapy (AMT) in nursing homes is well described. However, less is known about the appropriateness of AMT in nursing home residents. Therefore, the Check of APpropriaTeness of antimicrobial therapy in nursing homes (CAPTAIN) study aimed to assess both prevalence and appropriateness of AMT in Belgian nursing homes.

**Methods:** In a prospective, observational, point prevalence study, researchers documented prevalence and identified potentially inappropriate prescriptions (PIPs) by evaluating accordance of AMT with national guidelines. The severity of inappropriateness was assessed by a modified Delphi expert panel.

**Results:** Eleven nursing homes, including 1178 residents, participated in this study. On the survey day, 8.0% of residents took systemic AMT, primarily for urinary tract infections (54.2%), respiratory tract infections (36.5%), and skin and skin-structure infections (6.3%). About half of these prescriptions were used in prophylaxis (52.1%). Registration of indication and stop date was missing in 58.3% and 56.3% of AMTs, respectively. In 89.6% of the systemic AMTs, at least one discordance with national guidelines was identified, resulting in a total of 171 PIPs, with 49 unique PIPs. Of all unique PIPs, 26.5% were assessed with a high severity score (≥4). According to the expert panel, most inappropriate practice was starting AMT for cough without other symptoms. Inappropriate timing of time-dependent AMTs was common, but assessed as 'moderately severe'. One-third of systemic AMT exceeded the recommended duration.

**Conclusions:** AMT in nursing homes is often not prescribed according to national guidelines, highlighting the need for future interventions to promote the rational use of AMT in this setting.

## Introduction

The discovery of antimicrobial therapies (AMTs) was a significant medical advance in the 20th century. However, the rise of MDR microorganisms since the end of the last century is a global health emergency, leading to increased infection risks, treatment challenges, prolonged hospital stays and higher mortality rates, and thus a significant health and economic burden.[1,2] Despite progress in early-stage antibacterial development, challenges in the late-stage pipeline limit new therapeutic options.[3] To address resistance, promoting the appropriate use of existing antimicrobials is crucial.

Nursing home (NH) residents, who are vulnerable to infections, face a high risk of antimicrobial misuse. High staff turnover, limited access to microbiological and rapid diagnostic testing, lack of onsite pharmacists and reliance on nursing staff to communicate resident symptoms in nursing homes contribute to inappropriate antimicrobial prescribing, as per the Organization for Economic Co-operation and Development's analysis.[1]

In Belgium, point prevalence studies (PPSs) indicate an increase in AMT use in NHs from 2010 to 2021; the median prevalence of NH residents treated with at least one systemic AMT increased from 4.3% to 5.1%.[4,5] However, less is known about the appropriateness of AMT in NHs, including the right diagnosis, drug, dose, de-escalation, duration and documentation of AMT (6D strategy). Therefore, we aimed to evaluate (i) current antimicrobial policies, (ii) prevalence and (iii) (in)appropriateness of AMT in NHs.

## Methods

### *Study design and period*

A prospective, observational PPS was set up as part of the 'Hospital Outbreak Support' (HOST) initiative,[6,7] in which hospitals are funded by the Belgian government to share expertise and support their network in the domain of infection prevention and control and antimicrobial stewardship. The study took place on one inclusion day per NH between October and December 2022.

### *Study population*

NHs affiliated to the HOST Plexus network, comprising three non-academic and one academic hospital, were eligible for participation if they had a capacity for at least 50 residents and common rooms. Residential centres for independent living or day care centres were excluded. NHs previously participating in a regional antimicrobial benchmarking programme were also excluded. A total of 96 NHs were invited through an informational letter distributed electronically. All residents present on the PPS day were eligible for inclusion.

### *Data collection*

Prior to the PPS day, the head nurse or coordinating physician of the participating NH completed an online survey via a Google form questioning general characteristics (e.g. number of residents, available staff) and antimicrobial policy (e.g. documentation, available diagnostics). This survey was based on the one used in the Healthcare-associated infections and Antimicrobial use in Long-Term care facilities (HALT) studies.[4]

On the PPS day, researchers screened the medical records of all present residents for the presence of AMT, including antibacterial, antifungal, antiviral and antiparasitic drugs. We screened the medical records for systemic AMT, local AMT and adjunctive therapies used for infections (including adjunctive drugs [ADs] like local oestriol and dietary supplements like cranberry extracts). For residents receiving systemic AMT or ADs, a data form was completed, collecting general health (i.e. age, gender and estimated glomerular filtration rate [eGFR]) and medication information (Table S1, available as Supplementary data at *JAC-AMR* Online).

Incomplete data were discussed with nursing staff. The information source of the indication or rationale for initiation of the AMT and/or AD was noted, i.e. medical record (electronic or paper), NH staff or GP.

### *Data analysis*

The results of the survey were reported descriptively.

The prevalence of AMTs and adjunctive therapies was calculated as the number of residents receiving active therapy for the prevention or treatment of infection on the PPS day over the total number of included NH residents.

In assessing the appropriateness of AMT and ADs, we first considered the need for initiation of therapy based on clinical signs, symptoms or previous infections documented in the medical records or reported by the NH staff, comparing with the Loeb minimum criteria.[8] Second, the appropriateness of drug choice was assessed based on conformity with national guidelines (Belgian guide for anti-infective treatment in outpatient practice provided by the Belgian Antibiotic Coordination Committee, last updated in November 2022, and Formulary Elderly Care provided by the Belgian Centre for Pharmacotherapeutic Information, last updated in February 2021).[9,10]

Third, we assessed the registration of initiation rationale and stop/review date of the AMTs and ADs. For first- or second-line treatments, the appropriateness of the AMTs and ADs used was further evaluated. This included administration route, dose, duration, frequency and timing of administration, based on conformity with national guidelines.[9,10] Drug–drug interactions were checked using Medscape's Drug Interactions Checker and the Delphi database (APB, Belgium).[11,12] Since urinary tract infections (UTIs), respiratory tract infections (RTIs), and skin and skin-structure infections (SSSIs) are the main indications for AMTs in Belgian NHs,[4] the analysis of appropriateness was conducted only for these indications.

Three researchers (I.C., L.V.E., C.Q.) performed the assessment independently. Discrepancies were reviewed by the principal investigator (I.S.) for consensus. Any AMT or AD without indication, or with any non-compliance with national guidelines (based on choice of drug, administration route, dose, duration of treatment, frequency and timing of administration) or with a relevant drug–drug interaction was considered to be a potentially inappropriate prescription (PIP).

In a second phase, the inappropriateness severity of identified PIPs was evaluated using a modified Delphi technique. This technique uses multiple rounds in which the opinions of an expert panel are collected until consensus is reached.[13] To ensure feasibility, the PIPs to be assessed were divided between two similar groups of experts. The panel assessing UTI-related PIPs consisted of a clinical pharmacist, an infectious diseases specialist, a microbiologist, an NH coordinating physician and a geriatrician. The expert panel evaluating PIPs related to RTIs and SSSIs included two clinical pharmacists, an infectious diseases specialist, a microbiologist and an NH coordinating physician. In the first round of the modified Delphi, experts were asked to assign a severity score per PIP on a five-point Likert scale ranging from one (very slightly inappropriate) to five (very much inappropriate). Consensus was reached when the actual SD was less than 50% of the theoretically maximum possible SD. For the PIPs without consensus, a meeting was organized to discuss the experts' opinions, followed by a second round of scoring.

### *Ethics*

Approval by the Ethics Committee Research UZ/KU Leuven (S66823) was obtained in September 2022. Data were pseudonymized, and only the research team had access to the data forms.

## Results

### *General characteristics and antimicrobial policy of NHs*

Out of 96 NHs in the HOST Plexus network, 11 NHs with 1178 residents participated in the CAPTAIN study. Each NH had a coordinating physician overseeing medial activities, with a median of 25 associated GPs (range 13–76), who are responsible for drug prescribing. Most NHs were supplied exclusively by a single community pharmacy (81.8%).

Clinical data of residents were registered in a combination of paper and electronic files in all NHs. In seven NHs (63.6%) residents' renal function was documented. Microbiological results, such as cultured pathogen(s) and susceptibility reports, were mostly documented on paper. For recording AMT treatment details, 63.6% of NHs used a combination of paper and electronic files (Table S2).

Whereas a formulary listing specific AMT options was available in most NHs (63.6%), guidelines for appropriate AMT to treat UTIs, RTIs and SSSIs were present in only three NHs (27.3%). Additionally, three NHs (27.3%) expressed a self-reported need for further training and awareness regarding AMT (Tables S3 and S4).

When NH staff suspected infections, the most common approach (54.6%) to confirm the diagnosis was seeking advice from a physician. In some NHs (27.3%), the first step initiated by the nurses involved sample collection or point-of-care tests (for UTIs). Other NHs used a combination of both options or a watchful waiting approach, e.g. monitoring the resident's temperature, before deciding on further actions.

Microbiological samples were routinely collected from residents with clinical symptoms or suspicion of an infection in six NHs (54.6%). Most NHs (90.9%) collaborated with a single microbiology laboratory. Urine dipstick tests were routinely used in 10 NHs (90.9%).

### AMT prevalence

A total of 142 AMTs were used by 130 of 1178 residents (11.0%). Twelve residents were treated with two AMTs (i.e. two combinations of systemic AMT, six combinations of systemic and local AMT, four combinations of local therapies). The prevalence of residents treated with at least one systemic AMT was 8.0%, whereas 3.6% received at least one topical AMT. Characteristics of residents who received systemic AMT for UTI, RTI or SSSI on the PPS day, are shown in Table 1.

An overview of all AMTs, documented in the medical records on the PPS day, can be found in Table 2. We observed the use of antibacterial and antifungal drugs; however, no resident received antiviral or antiparasitic drugs. The majority of therapies were intended for systemic use (67.6%), and 32.4% were prescribed for topical use. More than half of the systemic AMTs were for prophylaxis ($n=50$; 52.1%); primarily targeting UTIs (84%). All topical AMTs were used to treat active SSSIs.

The majority of systemic AMTs targeted UTIs (54.2%), followed by 36.5% and 6.3% of prescriptions linked to RTIs and SSSIs, respectively. The primary indication was the prevention of recurrent UTIs (46.9%). Almost all systemic AMTs were empirical, with only two (2.1%) AMTs, one with ciprofloxacin and one with trimethoprim/sulfamethoxazole, targeting specific isolated microorganisms from the urine cultures. Among topical therapies, 56.5% were local antifungals, mainly for genital or anal use. Local antibacterials accounted for 43.5% of topical prescriptions, primarily for ophthalmological purposes.

Nitrofurantoin was the most frequently used systemic AMT (26%), followed by fosfomycin (22.9%) and amoxicillin/clavulanate (12.5%).

### Adjunctive therapy prevalence

Dietary supplements, primarily cranberry extracts (86.4%), were used by 3.7% ($n=44$) of residents for the prevention of recurrent UTIs. In addition, three ADs to prevent recurrent UTIs were used, i.e. oral oestriol ($n=1$), local oestriol ($n=1$) and oral *Escherichia coli* extract ($n=1$).

**Table 1.** Characteristics of residents treated with systemic antimicrobial therapy for urinary tract, respiratory tract, or skin and skin-structure infections on the point prevalence survey day

| Characteristics of residents | |
|---|---|
| Age,[a] mean (SD), y | 87.3 (7.1) |
| Male/female, % | 19/81 |
| eGFR,[b] mean (SD), mL/min/1.73 m² | 58.9 (21.1) |
| eGFR ≥ 90, % | 5 |
| eGFR 60–89, % | 47 |
| eGFR 45–59, % | 19 |
| eGFR 30–44, % | 21 |
| eGFR 15–29, % | 5 |
| eGFR <15, % | 3 |

eGFR, estimated glomerular filtration rate.
[a]Age was documented for 87 of 90 residents.
[b]Renal function was documented for 73 of 90 residents.

### Appropriateness of AMTs and adjunctive therapies

*Identified PIPs*

Of the 93 systemic AMTs and 3 ADs for UTIs, RTIs and SSSIs, 52.0% ($n=50$) were first- or second-line treatments with further appropriateness assessment. Overall, 89.6% ($n=86$) were assessed as potentially inappropriate based on the absence of an indication, non-compliance with national guidelines or presence of a drug–drug interaction ($n=54$ for UTIs, $n=26$ for RTIs and $n=6$ for SSSIs). A total of 171 PIPs were identified, summarized in 49 unique PIPs (Table 3). Registration of indication and stop/revision date in the medical record were missing in 56 (58.3%) and 54 (56.3%) therapies, respectively. In prescriptions lacking indication registration, the NH staff provided information about the rationale for initiation. The majority of prescriptions without documented stop/revision date concerned prophylactic therapy ($n=51$; 94.4%).

Due to missing data on signs and symptoms in present or previous UTI episodes, the appropriateness of starting AMT could not be assessed for 26 AMTs and 1 AD. For the remaining UTI therapies (26 AMTs and 2 ADs), initiation was assessed as potentially inappropriate. Specifically, reported signs and symptoms did not align with the Loeb minimum criteria, and residents with prophylactic therapy in prevention of UTIs had fewer than three UTI episodes in 12 months or fewer than two episodes in 6 months. The appropriateness of AMT choice could not be assessed in seven AMTs due to a lack of renal function data. Among the 45 AMTs and 3 ADs for UTIs, only 1 AMT with ciprofloxacin and 1 adjunctive with local oestriol was assessed as appropriate. For 18 prescriptions, timing of administration differed from guideline recommendation; this was always about not taking nitrofurantoin in prophylactic treatment of recurrent UTI in the evening after the last urination. Remarkably, 24 of these AMTs were considered inappropriate regarding therapy duration, often due to the absence of a registered stop date (Table 3).

Initiation of therapy was deemed incorrect in 10 out of 35 AMTs for RTIs. In seven residents, chronic treatment with azithromycin was initiated to prevent COPD exacerbations. Furthermore, amoxicillin/clavulanate was prescribed three times for cough

**Table 2.** Number of antimicrobial therapies by infection focus and indication

| Infection focus, *n* | Indication, *n* | Antimicrobial therapy, *n* |
|---|---|---|
| Systemic use, 96 | | |
| Urinary tract, 52 | Prophylaxis, 42 | Nitrofurantoin, 21 |
| | | Fosfomycin, 21 |
| | Treatment of active infection, 10 | Nitrofurantoin, 4 |
| | | Trimethoprim/sulfamethoxazole, 3 |
| | | Fosfomycin, 1 |
| | | Ciprofloxacin, 1 |
| | | Levofloxacin, 1 |
| Respiratory tract, 35 | Prophylaxis, 7 | Azithromycin, 7 |
| | Treatment of active infection, 28 | Amoxicillin/clavulanate, 12 |
| | | Amoxicillin, 9 |
| | | Moxifloxacin, 3 |
| | | Azithromycin, 2 |
| | | Cefuroxime, 1 |
| | | Ciprofloxacin, 1 |
| Skin, wound, 6 | Treatment of active infection, 6 | Flucloxacillin, 4 |
| | | Levofloxacin, 1 |
| | | Ciprofloxacin, 1 |
| Other, 3 | Prophylaxis of enteral feeding-related *Candida albicans* infection, 1 | Fluconazole, 1 |
| | Treatment of osteomyelitis, 1 | Ceftazidime, 1 |
| | Treatment of periodontitis, 1 | Doxycycline, 1 |
| Topical use, 46 | | |
| Skin, wound, 46 | Treatment of active infection, 46 | Miconazole, 21 |
| | | Ketoconazole, 5 |
| | | Oxytetracycline/polymyxin B, 5 |
| | | Fusidic acid, 5 |
| | | Tobramycin, 4 |
| | | Oxytetracycline, 2 |
| | | Nystatin, 1 |
| | | Ciprofloxacin, 1 |
| | | Mupirocin, 1 |
| | | Ofloxacin, 1 |

without other symptoms. Another common PIP related to RTIs involved the incorrect dosing interval of amoxicillin (with clavulanic acid) administration ($n=9$). Monitoring of drug–drug interactions with an increased risk of corrected QT (QTc) prolongation was not always provided ($n=5$).

The most frequent PIPs related to SSSIs included insufficient follow-up on interactions with co-medication ($n=4$), administering flucloxacillin with a meal ($n=3$), and too short treatment duration with flucloxacillin for cellulitis/erysipelas ($n=2$).

When focusing on the appropriateness of the two targeted AMTs, the therapy with ciprofloxacin was assessed as inappropriate due to incorrect duration (duration of 9 days for UTI in women) and interactions with co-medications (i.e. escitalopram, clozapine and rasagiline). The therapy with trimethoprim/sulfamethoxazole was assessed as inappropriate in terms of incorrect drug choice, based on the recommendation of using trimethoprim as the first-choice therapy.[10]

### *Severity score of PIPs by expert consensus*

Among all unique PIPs, 13 (26.5%) received a mean severity score of 4 or higher (Table 4), whereas six PIPs (12.2%) had a mean severity score of 2 or lower, as detailed in Table 5. The majority of PIPs were rated within the range of >2 to <4 on the severity scale (Table 6).

## Discussion

In this PPS conducted in 11 Belgian NHs, 8.0% of residents received at least one systemic AMT. When considering topical AMT, prevalence increased up to 11.0%. More than half (54.2%) of systemic therapies were prescribed for prophylaxis or treatment of (recurrent) UTI. The majority (89.6%) of systemic AMTs and ADs were assessed as potentially inappropriate, resulting in 171 PIPs comprising 49 unique PIPs. Experts classified 26.5% of these unique PIPs as severe.

Our findings regarding AMT prevalence in NHs differ from previous European studies, such as the HALT study (2016), which reported that 5.6% of Belgian NH residents received at least one systemic AMT.[4] These variations in prevalence could partly be attributed to differences in geographical area, post-pandemic issues or data collection methods. In our current study, researchers performed an in-depth review of each medical record,

**Table 3.** Number of potentially inappropriate prescriptions by infection focus

| PIPs | Urinary tract, *n* | Respiratory tract, *n* | Skin, wound, *n* | Total by type of PIP, *n* (%) |
|---|---|---|---|---|
| No indication | 28 | 10 | 1 | 39 (22.8) |
| Incorrect choice of drug | 46 | 6 | 2 | 54 (31.6) |
| Incorrect daily dose | 4 | 1 | 0 | 5 (2.9) |
| Incorrect dosing interval | 0 | 9 | 0 | 9 (5.3) |
| Incorrect time of administration | 18 | 0 | 3 | 21 (12.3) |
| Incorrect or no de-escalation | 0 | 0 | 0 | 0 |
| Incorrect duration | 24 | 4 | 2 | 30 (17.5) |
| Presence of drug–drug interactions | 3 | 5 | 4 | 12 (7.0) |
| Incorrect allergy label | 0 | 1 | 0 | 1 (0.6) |
| Total by infection focus, *n* (%) | 123 (71.9) | 36 (21.1) | 12 (7.0) | (100) |
| Unique PIPs by infection focus, *n* (%) | 23 (46.9) | 17 (34.7) | 9 (18.4) | (100) |

PIP, potentially inappropriate prescription.

**Table 4.** Number of potentially inappropriate prescriptions with a high severity score (≥4)

| Identified PIP, *n* | Recommended treatment by national guidelines[a] | Mean severity score by experts ($n=5$) after second round |
|---|---|---|
| Initiation of AMT in case of cough without other symptoms, 3 | No AMT | 4.8 |
| Treatment of intertrigo with levofloxacin, 1 | Isoconazole ointment | 4.6 |
| Treatment of tinea pedis with flucloxacillin, 1 | Isoconazole or terbinafine ointment | 4.4 |
| Prophylaxis of recurrent UTI with *E. coli* extract, 1 | Topical oestriol or trimethoprim | 4.4 |
| Treatment of pneumonia with ciprofloxacin without registration of penicillin allergy or initial treatment with amoxicillin (with clavulanic acid), 1 | Amoxicillin (with clavulanic acid) | 4.3 |
| Initiation of AMT in case of recurrent UTI in patients with <3 episodes in 12 months or <2 episodes in 6 months, 25 | No AMT | 4.2 |
| Treatment of pneumonia with cefuroxime in patient with documented penicillin allergy, 1 | Moxifloxacin | 4.0 |
| Duration of moxifloxacin therapy of 10 days in pneumonia treatment, 2 | Duration of 5 to 7 days | 4.0 |
| Simultaneous administration of ciprofloxacin and calcium, 1 | Avoid combination at same time because of complexation | 4.0 |
| Prophylaxis of recurrent UTI with oral oestriol, 1 | Topical oestriol or trimethoprim | 4.0 |
| Prophylaxis of recurrent UTI with nitrofurantoin twice daily, 3 | Once daily | 4.0 |
| Treatment of uncomplicated UTI with levofloxacin empirically, 1 | Trimethoprim | 4.0 |
| Combination of ciprofloxacin, escitalopram and clozapine without ECG monitoring, 1 | ECG monitoring to check QTc interval | 4.0 |

AMT, antimicrobial therapy; PIP, potentially inappropriate prescription; UTI, urinary tract infection.
[a]Belgian guide for anti-infective treatment in outpatient practice provided by Belgian Antibiotic Coordination Committee (BAPCOC). Formulary Elderly Care provided by Belgian Centre for Pharmacotherapeutic Information (BCFI)/BAPCOC.

whereas data on AMT prevalence in the HALT studies were collected by the NH staff.

Consistent with prior national studies in Europe, our study revealed that treatment and prophylaxis of UTIs were most common, followed by treatment of RTIs.[14,15] About half of the systemic AMT prescriptions were designated for prophylactic purposes (52.1%), in contrast to 35.9% in Belgium and 29.4% overall in Europe in the previous HALT study. The majority of prophylactic AMTs concerned UTI prophylaxis, aligning with previous findings.[4] There is evidence supporting continuous low-dose antibiotic prophylaxis for preventing recurrent UTIs, but optimal duration, long-term effects and its use in frail NH residents remain unclear.[16] The prolonged use of antibiotics for prophylaxis raises concerns due to its contribution to antimicrobial resistance.[17]

Topical AMTs were also commonly prescribed in this PPS. Theoretically, topical AMT offers advantages over systemic administrations, such as mitigating systemic toxicity. However, its widespread use in practice also contributes to rising antimicrobial resistance.[18]

**Table 5.** Number of potentially inappropriate prescriptions with a low severity score (≤2)

| Identified PIP, *n* | Recommended treatment by national guidelines[a] | Mean severity score by experts (*n* = 5) after second round |
|---|---|---|
| Treatment of uncomplicated UTI with fosfomycin, 1 | Trimethoprim | 2.0 |
| Interaction between flucloxacillin and paracetamol in high dose, 1 | — | 2.0 |
| Combination of moxifloxacin and flecainide without ECG monitoring, 1 | ECG monitoring to check QTc interval | 2.0 |
| Duration of flucloxacillin therapy of 8 days in cellulitis treatment, 2 | Duration of 10 days | 1.8 |
| Chronic treatment with azithromycin to reduce COPD exacerbations, 7 | GOLD guidelines[b] do recommend it for a maximum of 1 year | 1.8 |
| Interaction between flucloxacillin and paracetamol in low dose, 1 | — | 1.5 |

PIP, potentially inappropriate prescription; QTc, corrected QT interval; UTI, urinary tract infection.
[a]Belgian guide for anti-infective treatment in outpatient practice provided by Belgian Antibiotic Coordination Committee (BAPCOC). Formulary Elderly Care provided by Belgian Centre for Pharmacotherapeutic Information (BCFI)/BAPCOC.
[b]Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.

To justify AMT, accurate diagnosis is crucial. Routine use of urine dipstick tests in nearly all NHs may inadvertently lead to excessive AMT initiation for UTIs, due to the high prevalence of asymptomatic bacteriuria.[19] Despite on-site data collection, documentation of signs and/or symptoms was frequently missing, preventing the assessment of indication appropriateness for 49.1% of UTI prescriptions. Using the Loeb Minimum Criteria for the Initiation of Antibiotics in Residents of Long-Term Care Facilities,[8] we observed no appropriate AMT initiation for suspected UTIs. Furthermore, initiating AMT for recurrent UTIs in residents with insufficient episodes was observed in all prophylactic prescriptions and scored as severe PIPs by experts. The most severe PIP overall concerned initiating AMT for cough without other symptoms.

Next to concerns regarding the number of AMT prescriptions, the choice of antimicrobial drug is also a matter of concern. The researchers identified substantial deviations from national guidelines, e.g. the use of levofloxacin for intertrigo and flucloxacillin for tinea pedis. Also, inadvisable drugs like oral oestriol or *E. coli* extract were prescribed for recurrent UTI prophylaxis.

The further appropriateness assessment of AMTs or ADs was limited to 52.0% of prescriptions, focusing on first- or second-line treatments. Frequently, the timing of time-dependent AMT was observed as inappropriate, though evaluated as moderately severe. Specifically, amoxicillin/clavulanate was often administered during meals (i.e. at 8, 12 and 17 h), potentially for practical considerations or to minimize gastrointestinal side effects. However, optimal bacterial killing for time-dependent antimicrobials is associated with the percentage of time above the MIC, i.e. the longer the time above the MIC, the more effective the treatment, favouring optimal spreading of administrations.[20] Regarding the duration of AMT, half of the AMT prescriptions lacked a documented stop date. One PIP with a severity score of 4 concerned the administration of moxifloxacin for 10 days in pneumonia, despite evidence supporting 3–5 days as effective for community-acquired pneumonia.[21] Overall, one-third of systemic AMTs exceeded the recommended duration according to national guidelines.

Compared with the median proportion of in-hospital PIPs documented in a previous study at the University Hospitals of Leuven, we observed more PIPs in NHs.[22] This disparity can be attributed to several factors. First, documentation of clinical information in NHs is often incomplete, relying on a combination of paper and electronic files, as seen in our survey. Notable gaps included the lack of documentation of past UTIs, clinical signs and symptoms, reason for AMT initiation, start and stop/review dates of AMT, and renal function. These challenges align with those identified in a similar study in 2018, emphasizing among others the importance of adequate documentation of indication and stop/review date of AMT.[23] Another contributing factor is the absence of updates to current national guidelines and their adaptation to the specific characteristics of the NH population. Additionally, there is a need for NHs to enhance their adherence to these guidelines. Moreover, NH staff expressed a self-reported need for training and awareness on AMT in the survey. With the launch of the HOST initiatives in 2020, the Belgian government has already taken the first step to support NHs in antimicrobial stewardship.

For the assessment of (in)appropriateness, two Belgian guidelines (Belgian Centre for Pharmacotherapeutic Information and Formulary Elderly Care) were used as guidance. Non-conformity with these guidelines was considered as a PIP. During the inappropriateness assessment, no discrepancies were observed between these two national guidelines. However, during the consensus meetings with the experts for scoring the severity of inappropriateness, other types of discrepancies did emerge. First there was a discrepancy between additional national guidelines concerning the eGFR cut-off for nitrofurantoin contraindication (i.e. 60 mL/min, 45 mL/min or 30 mL/min). In addition, experts questioned the recommendation of using trimethoprim as the first-choice therapy for uncomplicated UTI in older people due

**Table 6.** Number of potentially inappropriate prescriptions with a moderate severity score (2–4)

| Identified PIP, *n* | Recommended treatment by national guidelines[a] | Mean severity score by experts ($n=5$) after second round |
|---|---|---|
| Duration of azithromycin therapy of 7 days in pneumonia treatment, 2 | Duration of 3 days | 3.8 |
| Dose of azithromycin of 500 mg twice daily in pneumonia treatment, 1 | Once daily | 3.8 |
| Dosing interval of oral amoxicillin/clavulanate, i.e. intake during meals, 9 | Dosing intervals as large as feasible | 3.8 |
| Treatment of pneumonia with moxifloxacin in resident with documented penicillin allergy or previous treatment with penicillin, 1 | Amoxicillin (with clavulanic acid) | 3.8 |
| Treatment of decubitus with ciprofloxacin in resident without signs of infection, 1 | No AMT | 3.8 |
| Prophylaxis of recurrent UTI with nitrofurantoin with unknown duration due to no registered start and stop date, 16 | Duration of 6 months | 3.8 |
| Prophylaxis of recurrent UTI with fosfomycin, 21 | Topical oestriol or trimethoprim | 3.8 |
| Combination of ciprofloxacin and rasagiline, 1 | Dose adjustment of rasagiline or monitoring of toxicity symptoms[b] | 3.8 |
| Combination of ciprofloxacin and clozapine, 1 | Avoid combination due to agranulocytosis[b] | 3.8 |
| Prophylaxis of recurrent UTI with nitrofurantoin twice daily, 1 | Once daily | 3.6 |
| Duration of ciprofloxacin therapy of 9 days in complicated UTI in women, 1 | Duration of 7 days | 3.5 |
| Initiation of AMT in the treatment of uncomplicated UTI without typical and atypical signs or symptoms, 2 | — | 3.5 |
| Treatment of acute COPD exacerbation with amoxicillin, 1 | Amoxicillin/clavulanate | 3.5 |
| Prophylaxis of recurrent UTI with nitrofurantoin longer than 6 months, 4 | Duration of 6 months | 3.4 |
| Combination of azithromycin and amiodarone without ECG monitoring, 1 | ECG monitoring to check QTc interval | 3.4 |
| Combination of moxifloxacin, quetiapine and trazodone without ECG monitoring, 1 | ECG monitoring to check QTc interval | 3.4 |
| Treatment of pneumonia with azithromycin in patient with documented penicillin allergy or previous treatment with penicillin, 2 | Amoxicillin (with clavulanic acid) | 3.3 |
| Combination of ciprofloxacin and anagrelide without ECG monitoring, 1 | ECG monitoring to check QTc interval | 3.2 |
| Registration of a penicillin allergy label in medical record with concomitant therapy of amoxicillin/clavulanate without allergy symptoms, 1 | — | 3.0 |
| Combination of moxifloxacin and risperidone without ECG monitoring, 1 | ECG monitoring to check QTc interval | 3.0 |
| Time of administration of flucloxacillin with meals, 3 | Administration on an empty stomach, 1 h before or 2 h after meal | 3.0 |
| Prophylaxis of recurrent UTI with nitrofurantoin in resident with estimated glomerular filtration rate 30–60 mL/min, 5 | Topical oestriol or trimethoprim | 3.0 |
| Duration of nitrofurantoin therapy of 6 or 7 days in complicated UTI in women, 3 | Duration of 5 days | 3.0 |
| Treatment of uncomplicated UTI with trimethoprim/sulfamethoxazole empirically, 1 | Trimethoprim | 3.0 |
| Prophylaxis of recurrent UTI with nitrofurantoin in resident with estimated glomerular filtration rate 60–90 mL/min, 10 | Topical oestriol or trimethoprim | 2.5 |
| Time of administration of nitrofurantoin in prophylaxis of recurrent UTIs at 8 h, 12 h or 17 h, 18 | In the evening after the last urination | 2.4 |
| Combination of levofloxacin and domperidone without ECG monitoring, 1 | ECG monitoring to check QTc interval | 2.3 |
| Targeted treatment of uncomplicated UTI with trimethoprim/sulfamethoxazole (unknown bacteria with sensitivity for fosfomycin and trimethoprim), 1 | Trimethoprim | 2.3 |
| Treatment of uncomplicated UTI with nitrofurantoin in resident with estimated glomerular filtration rate 60–90 mL/min, 4 | Trimethoprim | 2.3 |
| Initiation of AMT in the treatment of uncomplicated UTI without typical signs or symptoms, but with atypical symptoms, 1 | — | 2.3 |

AMT, antimicrobial therapy; PIP, potentially inappropriate prescription; QTc, corrected QT interval; UTI, urinary tract infection.
[a]Belgian guide for anti-infective treatment in outpatient practice provided by Belgian Antibiotic Coordination Committee (BAPCOC). Formulary Elderly Care provided by Belgian Centre for Pharmacotherapeutic Information (BCFI)/BAPCOC.
[b]Drugs interaction checker by Medscape.

to increasing resistance. Although treatment with fosfomycin is not recommended by the guidelines due to lack of evidence in older populations, risk of accumulation and higher cost, the experts scored this PIP as less severe. Second, there was a discrepancy between the national guidelines and international guideline concerning RTI prophylaxis. Although the national guidelines used in this study discourage the use of azithromycin for preventing COPD exacerbations due to an unfavourable benefit-risk balance, GOLD guidelines[24] recommend azithromycin (250 mg/day or 500 mg three times per week) or erythromycin (250 mg two times per day) for 1 year in exacerbation-prone patients to reduce the risk of exacerbations compared with usual care. The experts did agree with the latter, resulting in a PIP with low severity score. These discrepancies in guidelines make it challenging for prescribers.

Prevalence of adjunctive therapies, including dietary supplements and vaginal oestrogens, is often overlooked in prevalence studies. In our study, 3.7% of residents were prescribed dietary supplements, of which the majority were cranberry products. In the prevention of recurrent UTI, both national guidelines and the NICE guidelines recommend the use of local oestriol (vaginal cream or ring) in postmenopausal women with recurrent UTIs.[25] This therapeutic option seems to be promising and may be beneficial to spare classical AMT. However, the feasibility of using vaginal oestrogens in this population raised concerns among the experts.

The CAPTAIN study has several limitations. First, the inclusion of NHs affiliated with the HOST Plexus network may limit the generalizability of the results. In addition, the response rate of NHs within this network was low (11%), which may result in selection bias (i.e. participating NHs were more aware and interested). However, a balanced sample in underlying organizational structure of the NH—public, private non-profit or private for-profit—and capacity was obtained. Secondly, a potential seasonal effect on AMT prevalence for RTIs should be considered as the study occurred during the fall/winter of 2022. Third, inherent to the nature of the study in an NH setting, high-quality data were sometimes lacking, potentially affecting the accurate assessment of appropriate AMT and identification of PIPs.

There is a large potential for improvement in the NH sector, starting with accurate documentation and initiation of UTI prophylaxis. Development and implementation of NH-specific guidelines is critical, but seems to be challenging. Future studies should therefore focus on the development and evaluation of targeted interventions to improve the rational use of AMT in NHs.

### *Conclusions*

Prescribing AMT in NHs frequently deviates from existing national guidelines. The identified PIPs in the CAPTAIN study offer valuable insights for future interventions to enhance the rational use of AMT in NHs. Updates of the current national guidelines regarding AMT and adjustment of these guidelines to the specific NH population are required.

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## Transparency declarations

All authors: none to declare.

## Supplementary data

Tables S1 to S4 are available as Supplementary data at *JAC-AMR* Online.

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