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Research Methods

Impact of a multifaceted intervention programme on antibiotic prescribing and dispensing in four patient-centred settings in five European countries. The HAPPY PATIENT project

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Key messages

- Multifaceted antimicrobial stewardship interventions show varying effectiveness, with a modest reduction in antibiotic inappropriateness.
- Impact of multifaceted interventions varies across settings, with notable improvement in antibiotic dispensing in community pharmacies.
- External factors influence clinician behaviour, highlighting the complexity of antibiotic prescribing.

Abstract

Background: The primary cause of antimicrobial resistance is excessive and non-indicated antibiotic use.

Aim: To evaluate the impact of a multifaceted intervention aimed at various healthcare professionals (HCPs) on antibiotic prescribing and dispensing for common infections.

Design and setting: Before-and-after study set in general practice, out-of-hours services, nursing homes, and community pharmacies in France, Greece, Lithuania, Poland, and Spain.

Methods: Following the Audit Project Odense method, HCPs from these four settings self-registered encounters with patients related to antibiotic prescribing and dispensing before and after an intervention (February–April 2022 and February–April 2023). Prior to the second registration, the HCPs undertook a multifaceted intervention, which included reviewing and discussing feedback on the first registration's results, enhancing communication skills, and providing communication tools. Indicators to identify potentially unnecessary prescriptions and non-first-line antibiotic choices were developed, and the results of the two registrations were compared.

Results: A total of 345 HCPs registered 10 744 infections in the first registration period and 10 207 infections in the second period. In general practice, participants showed a significant 9.8% reduction in unnecessary antibiotic prescriptions in the second period, whereas limited or no effect was observed in out-of-hours services and nursing homes (0.8% reduction and 4.5% increase, respectively). Pharmacies demonstrated an 18% increase in safety checks, and correct advice in pharmacies rose by 17%.

Conclusion: External factors like COVID-19, antibiotic shortages, and a streptococcal epidemic impacted the intervention's benefits. Despite this, the intervention successfully improved antibiotic use in both settings.

Keywords: antimicrobial stewardship; medical audit; anti-bacterial agents; primary healthcare; nursing homes; pharmacies; after-hours care

Introduction

Common infections caused by multi-drug-resistant bacteria are challenging, leading to higher mortality rates, prolonged hospitalizations, and increased healthcare costs [1]. Excessive antibiotic use drives the spread of antimicrobial resistance (AMR), with southern and eastern European countries experiencing high resistance rates due to inappropriate use [2]. In 2022, the European Commission identified AMR as a top three priority health threat [3]. An estimated 30%–50% of antibiotics prescribed in outpatient settings are unnecessary [4]. To combat AMR, the European Union published guidelines in 2017 on the prudent use of antibiotics in human medicine, supporting national guidelines [5]. These recommendations, aligned with the One Health approach, are designed for various stakeholders involved in antibiotic use, including governments, healthcare entities, practitioners, pharmacists, patients, and international collaborators [6].

The key strategy in combating AMR is minimizing unnecessary antibiotic prescriptions, particularly for respiratory and urinary tract infections in general practice [7]. To enhance stewardship, the focus should primarily be on community-acquired infections. Despite various initiatives targeting antibiotic misuse, few have proven effective. Generally, multifaceted interventions show greater efficacy than singular ones, yet most studies occur in isolated settings [8]. The HAPPY PATIENT project (Health Alliance for Prudent Prescription and Yield of Antibiotics in a Patient-Centred Perspective), https://happypatient.eu/, was a European Commission-funded project aimed at increasing the impact of European Union recommendations on the prudent use and dispensing of antimicrobials in human health. It focused on the critical interaction between patients and healthcare professionals (HCPs) and has been the first to evaluate the impact of a multifaceted intervention on appropriate antibiotic prescribing across diverse patient-centred settings, including general practice, out-of-hours services, nursing homes, and community pharmacies. This study aimed to assess the impact of a multifaceted intervention program on appropriate antibiotic treatment for common infections, targeting different types of HCPs who constitute the first point of contact with patients (doctors, nurses, and pharmacists).

Methods

A prospective, non-randomized, before–after study was carried out in five European countries: France, Greece, Lithuania, Poland, and Spain, with varying antibiotic prescribing rates. Despite a slight decrease over the last 4 years, Greece, France, Poland, and Spain still rank among the top eight European countries with the highest rates of antibiotic prescribing, according to the latest report from the European Centre for Disease Prevention and Control [9]. However, Lithuania has experienced a significant increase in antibiotic consumption in recent years but remains below the European average [9]. Detailed information about the study method and the intervention can be found in the study protocol [10]. In a nutshell, per country, a minimum number of 25 HCPs were expected to be purposively recruited in each of four different settings: (a) general practice, including general practitioners and nurses; (b) out-of-hours services, including doctors; (c) nursing homes, involving mainly nurses; and (d) community pharmacies, with pharmacists and pharmacy technicians. The HCPs were invited to participate in self-registration of their clinical practice, conducted before and after they had received a multifaceted intervention on prudent antibiotic prescribing and dispensing. In November 2021, a pilot test for

registration was conducted to confirm that the content of the registration chart was pertinent to their professional practice and readily comprehensible. The first registration took place from February to April 2022, and a second registration was made after the intervention, from February to April 2023.

The data were registered according to the methodology of the Audit Project Odense (APO), which follows a prospective self-registry methodology in which a simple reporting template is used [11]. A specific template was designed for each of the four settings, with each row representing one patient (Supplementary Figure S1). In general practice and out-of-hours services, all participant HCPs were instructed to fill in a template for each consecutive patient with common infections during the registration period (from February to April 2022 and 2023). In nursing homes, on the contrary, HCPs registered residents with suspected infections who were treated with antibiotics. Regarding pharmacists, participants considered all patients who were going to the pharmacies to pick up prescriptions for systemic antibiotics. For general practice, out-of-hours services and nursing homes, the HCPs registered the age and gender of the patient, the number of days of symptoms, symptoms present, examinations performed, diagnosis, treatment, assessment, and other information specific for each setting. The template used for pharmacies was different and was specific for analysing the core elements of the dispensing process including several indicators based on the safety and the appropriate advice given to the patients [12]. In the period from October 2022 to January 2023, the four groups of HCPs were invited to face-to-face or online meetings to receive a 5-hour multifaceted intervention (Table 1).

For general practice, out-of-hours services and nursing homes, two indicators were calculated to measure the impact of the intervention: (i) potentially unnecessary antibiotic prescribing, defined as the prescription of antibiotics when they were not required based on the information provided by the registration template, and (ii) choice of non-first-line antibiotic, which occurred when an antibiotic was necessary, but a different, non-first-line antibiotic was prescribed for the condition in that specific country according to national guidelines. These quality indicators were established through interactive collaboration with experts within the consortium. Several quality indicators were defined for community pharmacies, including the percentage of good and wrong safety advice given for each prescription, out of a list of antibiotic-specific possible good and wrong advice on interactions, contraindications, and allergies when dispensing an antibiotic prescription. This list was developed by the project team. The impact of the intervention was estimated by comparing these indicators overall between the first and the second registration periods. Chi-squared tests were applied to determine the changes in the frequency of potentially unnecessary prescriptions and choice of non-first-line antibiotic before and after the interventions. Student *t*-tests were used to compare quantitative variables. Analyses were conducted separately for each country and using the pooled data (all patients and countries combined). For the latter, as a robustness check, we also performed regression analyses that accounted for the clustering of observations at the country level, which led to the same results as those reported in the manuscript. Statistical significance was determined at a *P*-value less than 0.05, and the data analysis was performed using Stata v16.

Results

Professionals and patients

A total of 407 HCPs participated in the first registration period (146 in general practice, 86 in out-of-hours services, 70 in nursing homes, and 105 in community pharmacies), of whom a total of 345 (84.8%) undertook the intervention and participated in the second registration period (Supplementary Table S1). Supplementary Table S2 shows the description of the interventions in different countries and the percentage of HCPs who completed the two registrations and attended the 5-hour intervention. All the HCPs who received the intervention completed the two registrations. The main results presented here are based on data from HCPs participating in both registration periods (2022 and 2023). They reported a total of 10 744 community-acquired infections during the initial registration and 10 132 cases during the second registration. Table 2 provides a comprehensive overview, categorized

Table 1. Overview of the multifaceted intervention for healthcare professionals participating in the project.

Intervention	Mean duration	Description
Problem of AMR	1 hour	Presentation. What is HAPPY PATIENT? Importance of the problem of AMR. Strategies aimed at tackling AMR.
Individual feedback on the first results	2 hours	The results of the first registration were given at an individual and group level, allowing the identification of potential quality problems, reflection, and peer-to-peer feedback. This session set goals and strategies to achieve the quality improvement goals.
Communication skill enhancement	2 hours	Workshop including role playing in different scenarios on consultations with patients with common infections at clinical settings and pharmacies. The communication tools were included in this session.
Presentation of communication tools	–	Prepared by the HAPPY PATIENT team based on the previous Delphi study aimed at identifying and prioritizing knowledge gaps and misconceptions about antibiotic use, with educational material on antibiotic use, including brochures, handouts to patients about prudent antibiotic use, and an explanation of the concept of the antibiotic footprint.
e-learning platform (voluntary)	3 hours	Short e-learning course addressing part of the intervention meeting of HAPPY PATIENT, including generalities of AMR and European guidelines, enhancement of communication skills and a quiz to review the most frequent situations in each setting when managing an infection, focusing on the appropriate use of antibiotics for common infections, with an explanation on their natural course and updated clinical guidelines with recommendations for diagnosis and management.

ARM = Antimicrobial resistance.

by country and various settings. General practice was the setting with the most registrations, with 5393 contacts collected in the first year and 4980 after the intervention. A total of 1765 contacts in 2022 and 364 in 2023 were phone consultations, accounting for 32.7% and 7.3% of all the consultations, respectively.

Diagnoses

In general practices, the most frequently reported diagnosis in the initial registration was COVID-19 infection, followed by common cold/influenza infection, with 1584 and 1549 cases, respectively, making up 58.1% of all infections. There was an increase in the number of common cold/influenza cases in the second year, totalling 2154 infections. The combination of these two types of infections accounted for 48.5% of all infections in 2023 (Table 3). In 2023, the remaining diagnoses were more commonly reported, except for urinary tract infections, which were more prevalent in the initial registration. This pattern of infections was also observed in out-of-hours services, with more COVID-19 cases in 2022 than in 2023 and an increase in common cold/influenza cases in 2023 (Table 3).

Intervention effect analysis

Overall, in the general practice setting, the prescription of potentially unnecessary antibiotics was 72.2% in the first registration and 65.2% after the intervention, with a significant reduction of 9.7% ($P < 0.001$). A substantial variability across countries was noted, ranging from a reduction of 19.9% observed in Lithuania and an increase of 1.3% in Greece. However, the overall choice of non-first-line antibiotics significantly increased in the second registration period by 29.2% ($P < 0.001$), with a 117.5% increase observed in Lithuania and a 27.6% increase in Poland (Table 4). Doctors

Table 2. Number of participants and registrations in the two registrations.

Country	General practice			Out-of-hours services			Nursing homes			Community pharmacies			Total		
	n HCP	*n* reg. 2022	*n* reg. 2023	*n* HCP	*n* reg. 2022	*n* reg. 2023	*n* HCP	*n* reg. 2022	*n* reg. 2023	*n* HCP	*n* reg. 2022	*n* reg. 2023	*n* HCP	*n* reg. 2022	*n* reg. 2023
France	17	659	642	3	49	69	9	118	107	21	586	624	50	1,412	1,442
Greece	23	553	619	8	193	234	5	73	58	14	300	259	50	1,119	1,170
Lithuania	28	1,861	1,295	25	630	690	17	161	86	20	628	540	90	3,280	2,611
Poland	23	1,100	1,213	12	446	424	13	330	372	20	584	573	68	2,460	2,582
Spain	42	1,220	1,211	15	468	403	14	318	274	16	467	439	87	2,473	2,327
Total	133	5,393	4,980	63	1,786	1,820	58	1,000	897	91	2,565	2,435	345	10,744	10,132

HCP = healthcare professionals; *n* = number, reg. = registration.

Table 3. Diagnoses registered by doctors in general practice and out-of-hours services in the two registration periods.*

Diagnosis	General practice				Out-of-hours services			
	2022		2023		2022		2023	
	Total number, *n*	% of all diagnoses	Total number, *n*	% of all diagnoses	Total number, *n*	% of all diagnoses	Total number, *n*	% of all diagnoses
COVID-19	1,584	29.4	262	5.3	317	17.8	111	6.1
Common cold/influenza	1,549	28.7	2,154	43.2	347	19.4	522	28.7
Acute otitis media	209	3.9	244	4.9	69	3.9	89	4.9
Acute rhinosinusitis	196	3.6	255	5.1	59	3.3	57	3.1
Acute pharyngotonsillitis	491	9.1	724	14.5	226	12.6	302	16.6
Acute laryngitis/tracheitis	151	2.8	207	4.2	–	–	–	–
Acute bronchitis	425	7.9	500	10.0	149	8.3	175	9.6
Pneumonia	127	2.3	159	3.2	185	10.4	163	9.0
COPD exacerbations	94	1.7	94	1.9	39	2.2	34	1.9
Urinary tract infection	533	10.0	295	5.9	357	20.0	312	17.1

*"Other infections" not included in this table. The out-of-hours service template did not include "Acute laryngitis/tracheitis" and differentiated cystitis from pyelonephritis; both infections have been merged under "Urinary tract infection" for improved comparison between the two settings. COPD = chronic obstructive pulmonary disease.

participating in out-of-hours services prescribed potentially unnecessary antibiotics in 52.5% and 52.1% of the cases in the two registration periods, respectively, with a mean non-significant reduction of 0.8% as well as high variability across countries. Table 3 shows that the results for nursing homes differed with a slight but non-significant increase in the number of antibiotics used unnecessarily being observed in the second registration compared to the first registration period (58.6% vs. 56.1%). When considering all the participating HCPs (i.e. including HCPs who did not participate in the second registration) the use of potentially unnecessary antibiotics decreased after the intervention in three clinical settings, namely by 7.6% in general practice, 5.1% in out-of-hours services and 7.1% in nursing homes (Supplementary Table S3).

Improving advice to patients on the use of antibiotics in community pharmacies was one of the goals of the intervention, which led to a 17% increase in the provision of correct advice to patients ($P < 0.001$). Pharmacists were also trained to perform a safety check, comprising the assurance of prescription safety based on interactions with, contraindications for and allergies to the antibiotics dispensed. The percentage of safety checks that were performed significantly increased from 47% before the intervention to 55.3% 1 year later, with an 18% increase ($P < 0.001$) (Table 5). Further improvements

Table 4. Percentage of potentially unnecessary and non-first-line antibiotic prescribing before and after the intervention and intervention effect in general practice, out-of-hours services and nursing homes.

Country	Potentially unnecessary antibiotic prescribing						Non-first-line antibiotic prescribing					
	Before		After		Intervention effect (%)	*P*	Before		After		Intervention effect (%)	*P*
	n	%	*n*	%			*n*	%	*n*	%		
General practice												
France	117	65.8	152	55.3	−16.0	0.080	88	28.4	98	26.5	−6.7	0.774
Greece	189	70.4	254	71.3	1.3	0.839	116	69.8	127	72.4	3.7	0.653
Lithuania	204	75.0	268	60.1	−19.9	0.001	106	29.2	156	63.5	117.5	0.000
Poland	361	75.9	344	72.1	−5.0	0.249	173	57.2	126	73.0	27.6	0.005
Spain	203	68.5	277	61.4	−10.4	0.109	333	26.4	222	29.3	11.0	0.461
Total	1,074	72.2	1,295	65.2	−9.7	0.000	816	39.7	729	51.3	29.2	0.000
Out-of-hours services												
France	17	23.5	33	42.4	80.4	0.187	13	30.8	19	10.5	−65.9	0.150
Greece	118	71.2	160	64.4	−9.6	0.232	34	64.7	57	66.7	3.1	0.849
Lithuania	322	54.4	358	58.1	6.8	0.325	147	55.8	150	64.0	14.7	0.148
Poland	236	51.3	155	47.7	−7.0	0.495	115	53.0	81	64.2	21.1	0.120
Spain	187	41.7	181	34.8	−16.5	0.173	109	43.1	118	35.6	−17.4	0.246
Total	880	52.5	887	52.1	−0.8	0.862	418	51.7	425	54.1	4.6	0.477
Nursing homes												
France	42	57.1	36	91.7	60.6	0.001	18	50.0	3	33.3	−33.4	0.593
Greece	3	33.3	9	33.3	0.0	1.000	2	100.0	6	83.3	−16.7	0.537
Lithuania	22	54.6	18	50.0	−8.4	0.775	10	40.0	9	44.4	11.0	0.845
Poland	74	16.2	103	19.4	19.8	0.585	62	66.1	83	67.5	2.1	0.865
Spain	139	77.7	114	86.8	11.7	0.061	31	0	15	0	–	–
Total	280	56.1	280	58.6	4.5%	0.550	123	45.5	116	56.9	25.1	0.079

Table 5. Percentage of safety checks performed, and correct advice provided to patients before and after the intervention and intervention effect when dispensing an antibiotic prescription in community pharmacies.

Country	Safety checks performed						Advice to patients					
	Before		After		Intervention effect (%)	*P*	Before		After		Intervention effect (%)	*P*
	n	%	*n*	%			*n*	%	*n*	%		
France	585	69.6	624	73.6	6.0	0.060	568	45.6	584	48.8	7.0	0.000
Greece	290	70.6	254	61.7	−13.0	0.004	284	53.7	256	52.1	−3.0	0.372
Lithuania	613	40.2	536	53.7	34.0	0.000	614	53.7	530	67.6	26.0	0.000
Poland	581	29.2	573	30.5	4.0	0.469	562	32.5	560	38.0	17.0	0.000
Spain	453	35.0	424	60.1	72.0	0.000	445	34.3	424	49.2	43.0	0.000
Total	2,522	47.0	2,411	55.3	18.0	0.000	2,473	43.5	2,354	50.9	17.0	0.000

were seen in the information pharmacists had about antibiotic prescriptions, pharmacists knew the treatment duration of the prescription 21% more often. There was no significant change in information on the indication for which the antibiotic was prescribed.

Discussion

Summary

The HAPPY PATIENT study aimed to assess the impact of a multifaceted intervention programme focused on the appropriate antibiotic treatment of common infections, targeting various types of HCPs—doctors, nurses, pharmacists, and pharmacy technicians—who are the initial points of contact for individuals seeking health care. We found a modest reduction in unnecessary antibiotic prescriptions for community-acquired infections following the multifaceted intervention. However, the effects varied across settings, with more marked improvements seen in general practice. Additionally, there was a notable enhancement in the dispensing process in community pharmacies.

Strengths and limitations

The study has several limitations, classified into two types. Some limitations stem from the methodology used, while others are attributable to the time frame during which the study was conducted. The before-and-after design lacking a control group has inherent limitations as changes in antibiotic prescribing may stem from factors other than the intervention performed by the investigators. The most important limitation is that templates can only accommodate a limited number of variables. This is the main reason why some other potentially important variables were not considered. For example, non-biomedical factors that might represent powerful predictors of antibiotic prescription, such as socio-economic and/or cultural factors or perceiving patient's pressure for antibiotic prescribing, were not considered in general practice and out-of-hours services, but the pressure to prescribe antibiotics was considered in nursing homes, constituting a common phenomenon in this setting [13]. HCPs participated on a voluntary basis and as shown in some studies volunteer HCPs might have a greater interest in quality improvement programmes and research than the general population of HCPs [14]. Another limitation of the study is the fact that clinical outcomes were not considered, making it unclear whether complication rates or clinical failures differed among the groups. However, the registration in both general practice and out-of-hours services did track patient transfer to the hospital. Another limitation is the potential influence of the self-registration itself on prescribing habits. Nevertheless, the APO methodology has shown high reliability in various European projects and correlates well with actual prescribing [11, 15]. From a theoretical perspective, the treatment decision ideally follows the diagnosis decision-making. Diagnostic procedures and treatment decisions are closely intertwined. Doctors may determine antibiotic prescription concurrently with or even prior to definitively diagnosing the patient's condition. Subsequently, HCPs might adapt the diagnosis to align with the treatment decision, potentially introducing a diagnostic misclassification bias [16]. However, this potential bias would have affected the validity of the diagnosis both before and after the intervention and only has a small likelihood of influencing the effect of the intervention.

The sizes of groups differed across settings and countries, with a higher number of participants in general practice and a lower number in nursing homes. This variation can be attributed primarily to the study coordinators being general practitioners responsible for recruiting professionals. Not all the HCPs received the entire intervention, but this is inherent to any study. Nonetheless, the strengths of this study include a substantial number of HCPs and a low participant dropout rate, aligning with other quality improvement studies. The APO cycles were conducted within real-life practice settings with factors that could potentially influence patients' behaviours, and thus, influence the intervention. HCPs involved in both registrations did not allocate additional time for consultations or dispensations, maintaining their regular practice routines and ensuring the findings' relevance in countries with different backgrounds. Noticeably, this study is unique in comprising a total of four patient-centred sectors, including pharmacists, who play a crucial role in directly reinforcing messages about appropriate antibiotic use when dispensing antibiotics to patients or carers and are amongst the groups most trusted to convey such messages [17]. The study spanned not only five European countries with varying levels of antibiotic consumption but also countries with diverse cultural backgrounds and healthcare systems, which enhances the generalizability of the findings.

Several external factors might have limited the benefits of this multifaceted intervention. The first registration occurred in 2022, during which many COVID-19 cases were recorded, and a significant number of general practice consultations, especially in Lithuania, were conducted by phone. This situation improved in 2023. Despite higher motivation among HCPs, pandemic fatigue may have played a role [18]. The initial registration showed more viral infections, including common cold, influenza, COVID-19, and acute bronchitis. Additionally, some European countries saw a rise in invasive group A streptococcus cases among children under 10 after September 2022, affecting the second registration period [19]. These factors complicate year-to-year comparisons and might have minimized the intervention's impact. The relatively modest reduction in unnecessary antibiotic use and the worsened choice of antibiotics in all clinical settings, mainly due to shortages of first-line antibiotics, were particularly evident in eastern Europe, notably Lithuania and Poland [20].

Implications for practice

The results of this study show that a planned intervention in community pharmacies can have a significant impact on increasing safety checks and general advice for patients attending community pharmacies with antibiotic prescriptions. There was also a modest reduction in potentially unnecessary antibiotic use, although the decrease varied depending on the country and clinical setting. A statistically significant improvement was observed in general practice, while the impact was little or absent in out-of-hours services and nursing homes, respectively. In 2023, a slightly higher percentage of unnecessary antibiotic prescriptions was noted in nursing homes compared to the initial registration. Despite most professionals in nursing homes being nurses, the responsibility for prescribing antibiotics lies with doctors. The anticipated outcome was a greater empowerment of nurses leading to a reduced use of antibiotics. However, the results obtained

in the second registration were worse. These findings highlight the need for alternative and tailored approaches in antimicrobial stewardship programmes in long-term care facilities. These findings highlight the need for alternative and tailored approaches in antimicrobial stewardship programs in long-term care facilities, with a greater focus on nurses. This includes implementing hygiene measures and empowering nurses to improve the diagnosis of suspected infections, such as urinary tract infections, while debunking prevalent myths and providing clear-cut information for better management of these common infections.

Various strategies to reduce unnecessary antibiotic use include antimicrobial stewardship programs, which reduce outpatient antibiotic use by an average of 4% [21]. Implementation in primary care varies, and its impact wanes with time. Peer comparison audits and feedback, addressing psychological and social factors, have proven effective, with reductions of 0%–15% [22–24]. However, identifying the most impactful elements of prescribing patterns remains unclear. Previous studies using the APO methodology to reduce inappropriate antibiotic use show context-dependent results. In one general practice study, clinicians reduced antibiotic prescriptions by 9%–42%, with greater reductions when point-of-care tests were used [25]. Another trial in four South American countries found intervention groups reduced antibiotic prescriptions from 37.4% to 28.1% for acute otitis media or acute bronchitis, while the control group saw a marginal decrease from 29.0% to 27.2% [26]. These studies, conducted before COVID-19, had similar diagnostic distributions across registration periods.

Growing evidence shows that reasons for potentially unnecessary and non-first-choice antibiotics are at least partly psychologically and socially rooted, meaning that antibiotic prescribing is as much a behaviour as a scientific decision [27]. We cannot rule out that these external factors could have affected the main outcomes of our study. Changing practice behaviour is challenging and requires the implementation of a systematic approach following components of the normalization process theory, in which individual and group reflection on the actions that need to be implemented to reduce inappropriate prescribing of antibiotics will ensure the achievement of high-impact and sustainable results [28]. However, multifaceted interventions are more successful and which interventions should accompany this reflection remain to be determined for each setting.

Conclusions

Despite widespread antibiotic use and the escalating threat of AMR, few initiatives have tackled inappropriate antibiotic use across multiple settings. The HAPPY PATIENT project constituted a pragmatic study, conducted in diverse practice settings across five countries, demonstrating a slight decrease in potentially unnecessary antibiotics in general practice and improved dispensing processes in community pharmacies. However, it showed limited or no impact on the other two clinical settings—nursing homes and out-of-hours services. The high complexity of this project, encompassing four different settings with diverse backgrounds and healthcare systems, along with some unpredictable external factors, might explain the limited reduction in inappropriate prescribing achieved.

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Supplementary material

Supplementary material is available at *Family Practice* online.

Author contributions

C.Ll. conceived the study. A.G.-S. and C.Ll. drafted the manuscript. B.G.L.-V., F.R., and L.V.-T. are responsible for the statistical analyses. A.G.-S., J.L., M.P.H., L.B., A.C., J.N.J., I.R., B.H.L., K.T., M.L., R.R., L.J., P.T.L., P.B., V.L., A.K., M.G.-C., C.Li., M.-N.K., M.A., M.B.H., J.K.O., J.S., D.M., S.M., and L.A. reviewed the manuscript and provided critical revisions. All authors read, commented, and approved the final manuscript.

Conflict of interest

J.S. reports fees from Abbott Rapid Diagnostics A/S, Roche Diagnostics A/S, Roche a/s, NovoNordisk a/s, and is member of the board of Steno Diabetes Center, Odense. All other authors declare no competing interests.

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Data availability

Zenodo.

Ethical approval

Ethical boards from Greece and Spain reviewed the study and approved it (codes 215/07.12.2020 and 21/120-P, respectively). In Lithuania, Poland, and France, there was no need for the Ethical Committee to review this type of projects. This was confirmed by the national coordinators together with their Ethical Committee Boards. Local coordinators reached out to healthcare professionals, providing an overview of the study and the information sheet to the professionals, allowing them sufficient time to review the material and seek clarification for any queries they had. If the participant agreed to participate in the study, they would then proceed to sign the consent form before actively taking part. Patient registrations were completely anonymous; thus, no respective signed informed consent was required.

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