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Original Research Paper

## Community pharmacists' role in optimising antibiotic use: The HAPPY PATIENT project to improve dispensing practices in five EU countries

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## ABSTRACT

**Background:** Community pharmacies can play a pivotal role in optimising the use of antibiotics through their dispensing practice.

**Aim:** To evaluate the impact of a multifaceted intervention on community pharmacies' quality of antibiotic dispensing.

**Method:** A prospective before–after study conducted according to the Audit Project Odense methodology in community pharmacies in France, Greece, Lithuania, Poland, and Spain. Pharmacy staff audited dispensing practices through a self-registry form before and after a multifaceted intervention, comprising feedback to participants on dispensing practice, communication training, and providing educational materials for patients. Dispensing of all oral antibiotics for five days in February 2022 and after interventions in February 2023 was registered. Data were analysed by country and overall using ten quality indicators, with Chi-square tests and Students' t-tests applied.

**Results:** A total of 91 pharmacists registered 5.054 dispenses. There was an 18 % ( $p < 0.001$ ) improvement in the mean number of safety checks performed and a 17 % ( $p < 0.001$ ) reduction in the number of dispenses for which no safety checks were performed after the intervention. Pharmacists provided 17 % ( $p < 0.001$ ) more advice to patients and reduced the dispenses for which no advice was provided by 35 % ( $p = 0.006$ ). This came with a 44 % ( $p < 0.001$ ) increase in inappropriate advice that was provided. Large differences between the countries were observed. For performing safety checks, a 13 % ( $p = 0.004$ ) worsening was seen in Greece and a 72 % ( $p < 0.001$ ) improvement in Spain. In France, treatment duration and dose were discussed with patients in 97 % and 98 % of the dispenses at baseline, respectively, without improvements after the intervention. In Spain, this was 66 % and 51 % at baseline, significantly improving to 80 % and 64 % after the intervention.

**Conclusion:** Quality of antibiotic dispensing increased significantly, indicating that intervention is a promising strategy to improve antibiotic use, especially in countries with lower practice standards.

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## 1. Introduction

The World Health Organization deems antimicrobial resistance a serious threat to health and development with misuse and overuse of antibiotics as the main drivers of resistance development.<sup>1,2</sup> Lack of public knowledge and awareness and the use of leftover antibiotics are important factors contributing to misuse of antibiotics in Europe.<sup>3</sup> Most antibiotics are used in the primary care setting, yet most intervention studies are performed in the hospital setting. Therefore, antimicrobial stewardship interventions targeting the primary care setting are needed. Community pharmacists can play a pivotal role in improving the use of antibiotics.<sup>4</sup> To ensure patients are at the centre of pharmacist-led interventions, it is important to consider what patients expect from community pharmacists and which services give the greatest patient satisfaction. Patients appreciate a competent, caring, and knowledgeable pharmacist who provides clinical services such as detecting drug interactions and patient needs for additional education.<sup>5</sup> Patients' preferences align well with the responsibilities of community pharmacists as outlined in the *Guidelines for the Prudent Use of Antimicrobials for Human Consumption*, published by the European Centre for Disease Prevention and Control.<sup>6</sup> So far, only few studies have investigated the implementation of those guidelines in community pharmacy practice, which indicated regional variations in practice and deviations from the EU dispensing guidelines.<sup>7–9</sup> To optimise the use of antibiotics and contribute to reducing antimicrobial resistance, improvements are needed in community pharmacy practice.

Yuan et al.<sup>10</sup> demonstrated the positive impact of community pharmacy services such as patient education, adherence assessment, health/lifestyle advice, and adjusting therapy, on clinical outcomes for various diseases, especially for chronic conditions. A systematic review reported only seventeen studies of community pharmacist-led interventions to optimise antibiotic use.<sup>11</sup> These had limited or ambiguous positive effects.<sup>11</sup> Therefore, new strategies to improve antibiotic dispensing in community pharmacies should be developed. Several interventions have shown some effectiveness in improving healthcare professional practice and patient outcomes, including educational meetings, workshops,<sup>12</sup> and audit-and-feedback interventions.<sup>13</sup> More effective interventions include using mixed interactive and didactic formats for educational interventions.<sup>12</sup> An multifaceted intervention including audit and feedback has been shown to be successful in general practice to improve the use of antibiotics.<sup>14</sup> In a pilot study in community pharmacies in four EU countries, this innovative evidence-based approach was found to be feasible for use in the pharmacy setting.<sup>15</sup> The audit and feedback methodology to improve antibiotic use has been implemented in a multinational study in general practices, out-of-office services, nursing homes and pharmacies.<sup>16</sup> The current describes the results of the pharmacy setting and aimed to evaluate the impact of a multifaceted intervention on the quality of antibiotic dispensing.

## 2. Methods

### 2.1. Study design

This was a prospective, non-randomised, before-after study. The study is part of the international Health Alliance for Prudent Prescribing and Yield of Antibiotics in a Patient-Centred Perspective (HAPPY PATIENT) project. This project was funded by the EU Third Health Programme (ID 900024) and was conducted in four settings: community pharmacies, general practice, out-of-hour services, and nursing homes.<sup>16,17</sup> This study reports the detailed results of the community pharmacy setting. This manuscript was written according to the Standards for Quality Improvement Reporting Excellence (SQUIRE) guidelines.<sup>18</sup>

### 2.2. Study context and participants

The study was conducted in community pharmacies in France, Greece, Lithuania, Poland, and Spain, five EU countries with different levels and patterns of antibiotic use.<sup>19</sup> In each of those countries it was aimed to recruit 25 community pharmacies by local partners. The number of pharmacies recruited was consistent with the number of healthcare professionals in the other settings of the HAPPY PATIENT project and with previous use of the methodology.<sup>17</sup> Purposive sampling was used from local lists of pharmacies. Pharmacists and pharmacy technicians/assistants were eligible for participation and did not need English fluency. There were no inclusion limitations based on pharmacy size or location, staff expertise, experience, or any other factors.

### 2.3. Audit Project Odense methodology

This study was conducted using the Audit Project Odense (APO) methodology. This methodology has been described earlier in the general practice setting to successfully improve primary healthcare quality.<sup>20</sup> The APO method comprises data registration through a self-recording form completed by healthcare professionals and a multifaceted intervention to improve practice.<sup>21</sup> This is the first study to apply the APO methodology in a multinational community pharmacy setting. The development of the self-recording form and its feasibility for practice have been described in a pilot study.<sup>15</sup> For the current study, the self-recording form from the pilot study has been optimised based on pharmacists' suggestions (Appendix 1).

### 2.4. Data collection

Participants were asked to complete a questionnaire to provide demographic information on their pharmacies. Subsequently, the self-registration form and an accompanying instruction document were distributed among the pharmacies. Pharmacy staff were asked to register the process of face-to-face antibiotic dispensing for any patient coming into the pharmacy with a prescription for an oral antibiotic. Antibiotic dispensing for prophylactic or veterinary use was excluded from the study. The participants were asked to register the dispensed type of antibiotic, knowledge of treatment duration and dose, safety checks that were performed, advice given to patients, a professional judgement of the prescription, and whether there was communication (e.g., phone, e-mail) with the prescriber. Dispensed prescriptions were recorded at baseline (February 2022) and after implementing the multifaceted intervention (February 2023) for at least 5 days or until 25 dispensed prescriptions were recorded per pharmacy. The number of recorded dispensed prescriptions was consistent with the number of registrations in the other settings of the HAPPY PATIENT project and with previous use of the methodology.<sup>17</sup> Pharmacy staff were asked to return the registration forms through digital scans or postal couriers.

### 2.5. Multifaceted intervention

The intervention has been described in a protocol<sup>17</sup> and with the results of the overall project.<sup>16</sup> In short, the multifaceted intervention consisted of the following parts: 1) feedback on dispensing practice on the pharmacy and national level and reflection on this through peer-to-peer feedback, 2) communication training, 3) an online platform for testing knowledge and discussing clinical cases and 4) the provision of educational materials on antibiotic use and dispensing for patients. *Feedback and peer-to-peer review.*

Pharmacy staff from each country were invited to attend an online or face-to-face meeting. During this meeting, country average results were presented through collective reports on the dispensing based on the self-registration data. Individual results of the self-registration were sent confidentially to each pharmacy. Pharmacy staff engaged in small group discussions to identify areas for improvement in the dispensing process

and explored ways to enhance it. Discussion among peers is an important part of this intervention; the local coordinators facilitated these discussions using open-ended questions without intending to propose specific actions.

### 2.5.1. Communication training

The communication training was provided either during the same meeting as the discussion among peers or in a separate meeting. During the training, pharmacy staff were educated on basic techniques of patient-professional communication and practised clinical cases with their colleagues through role-playing.

### 2.5.2. Online platform

Participants were given access to an e-learning platform on which they could find materials for the intervention, the results of the first audit, EU guidelines on the prudent use of antimicrobials, and a quiz on dispensing antibiotics. This platform could also be used to discuss clinical cases among staff from different pharmacies.

### 2.5.3. Patient education materials

Patient education materials were developed in a co-design process, using a modified Delphi technique in the five target countries,<sup>22</sup> scientific literature, and the practical experience of the research group. All materials were provided in local languages, following forward and backward translations from English, and were sent by post to each participating pharmacy. The materials were presented during the communication training, and participants practised using them. The materials included a poster on infections caused by viruses or bacteria which pharmacists could display in their pharmacy, a patient information leaflet which the pharmacist could use to tailor information on antibiotic dispensing such as ... and cards with general information about antimicrobial resistance and antibiotic use. The pharmacists were asked to use the educational materials in their pharmacies when dispensing antibiotics.

These materials have been made freely available online.<sup>22</sup>

## 2.6. Outcomes and data analysis

Ten quality indicators were created to measure the quality of antibiotic dispensing before and after the intervention. Quality indicators were based on the self-registration form with which the community pharmacies' staff collected the data on their dispensing of antibiotics (Appendix 1). Quality indicators were developed by an interactive collaboration of the consortium experts. The indicators were categorised into four themes: 1) safety checks (2 indicators) assessing whether safety checks on allergies, contraindications, and interactions were performed; 2) advice provided to patients (3 indicators) assessing the percentage of correct and incorrect advice provided and the percentage of dispensed prescriptions during which no advice was provided; 3) prescription information (2 indicators), assessing the percentage of dispensed prescriptions for which the location of infection or the treatment duration was unknown; and 4) prescription judgment (3 indicators) assessing whether pharmacists and technicians judged prescriptions based on the right prescription information (Appendix 2).

The impact of the intervention was estimated by comparing the quality indicators before and after the intervention. Only data from pharmacies completing both registration rounds were included. All data from the self-registrations of antibiotic dispensings were entered into and analysed using Stata™. Chi-square tests were applied for categorical variables and Students' t-tests for continuous variables to determine the changes in the frequency of the performance according to the quality indicators. Statistical significance was determined at a P-value less than 0.05. To explore the potential impact of the dependence of observations within pharmacies, we also performed multilevel regression analyses that accounted for the clustering of observations at the pharmacy level, which led to the same results (in terms of sign and significance) as those

reported in the manuscript. All data were analysed per country and overall. The intervention effect for the quality indicators was calculated as a percentage of the dispensed prescriptions for which the quality indicator was met in 2023 compared to the percentage in 2022. All data not reported through quality indicators were analysed descriptively.

## 3. Results

### 3.1. Study context

A total of 121 pharmacies recorded for the study and completed the questionnaire on demographic information including information on the number of clients and staff (Table 1). In most pharmacies, safety checks were performed, either manually (55 %) or with software (32 %). In 15 % of the pharmacies, safety checks were not performed. Pharmacy staff of 32 % of the pharmacies had no access to any patient information and staff in 31 % had no contact with prescribers (Table 1).

Overall, 105 (87 %) pharmacies completed the first registration, and

**Table 1**

Demographic information of pharmacies that initially signed up for participation.

|                                                   | France    | Greece    | Lithuania  | Poland     | Spain     |
|---------------------------------------------------|-----------|-----------|------------|------------|-----------|
| <b>Clients per day</b>                            |           |           |            |            |           |
| <50                                               | 0         | 5 (36 %)  | 0          | 8 (31 %)   | 1 (5 %)   |
| 51–200                                            | 17 (71 %) | 2 (14 %)  | 33 (94 %)  | 17 (65 %)  | 16 (73 %) |
| >200                                              | 7 (29 %)  | 7 (50 %)  | 2 (6 %)    | 1 (4 %)    | 5 (23 %)  |
| <b>Pharmacy staff (mean full-time equivalent)</b> |           |           |            |            |           |
| Pharmacists                                       | 2.8       | 1.5       | 2.4        | 2.8        | 2.4       |
| Technician                                        | 3.1       | 2.3       | 0.7        | 2.3        | 2.3       |
| <b>Access to information</b>                      |           |           |            |            |           |
| Medication history                                | 23 (96 %) | 8 (57 %)  | 15 (43 %)  | 14 (54 %)  | 9 (41 %)  |
| Medical history/ (chronic) diseases               | 10 (42 %) | 8 (57 %)  | 2 (6 %)    | 1 (4 %)    | 0         |
| Allergies                                         | 13 (51 %) | 6 (43 %)  | 4 (11 %)   | 1 (4 %)    | 0         |
| Hospital admission                                | 1 (4 %)   | 0         | 0          | 1 (4 %)    | 0         |
| Other                                             | 2 (8 %)   | 0         | 1 (3 %)    | 2 (8 %)    | 0         |
| None                                              | 0         | 0         | 17 (49 %)  | 9 (35 %)   | 13 (59 %) |
| <b>Type of prescriber contact</b>                 |           |           |            |            |           |
| Contact for individual patients                   | 22 (92 %) | 9 (64 %)  | 29 (83 %)  | 11 (42 %)  | 5 (23 %)  |
| Regular organised contact                         | 0         | 0         | 0          | 0          | 0         |
| Both                                              | 2 (8 %)   | 2 (14 %)  | 1 (3 %)    | 1 (4 %)    | 1 (5 %)   |
| No contact                                        | 0         | 3 (21 %)  | 5 (14 %)   | 14 (54 %)  | 16 (73 %) |
| <b>Specific antibiotic training</b>               |           |           |            |            |           |
| Yes, more than once a year                        | 0         | 3 (21 %)  | 3 (9 %)    | 0          | 2 (9 %)   |
| Yes, once a year                                  | 2 (8 %)   | 3 (21 %)  | 8 (23 %)   | 2 (8 %)    | 2 (9 %)   |
| Yes, less than once a year                        | 7 (29 %)  | 4 (29 %)  | 22 (62 %)  | 9 (35 %)   | 8 (36 %)  |
| No                                                | 15 (63 %) | 4 (29 %)  | 2 (6 %)    | 15 (57 %)  | 10 (45 %) |
| <b>Regulation to stay updated in training</b>     |           |           |            |            |           |
| Yes                                               | 4 (17 %)  | 9 (64 %)  | 29 (83 %)  | 2 (8 %)    | 6 (27 %)  |
| No                                                | 20 (83 %) | 5 (36 %)  | 6 (17 %)   | 24 (92 %)  | 16 (73 %) |
| <b>Perform ≥ 1 point-of-care tests</b>            |           |           |            |            |           |
| Yes                                               | 12 (50 %) | 13 (93 %) | 0          | 0          | 11 (50 %) |
| No                                                | 12 (50 %) | 1 (7 %)   | 35 (100 %) | 26 (100 %) | 11 (50 %) |
| <b>Total number of pharmacies</b>                 | 24        | 14        | 35         | 26         | 22        |

2953 dispensed prescriptions were recorded. A total of 91 (75 %) participants also completed the second registration and were included in the final analysis, accounting for a total of 2461 dispensed prescriptions. Participation per country varied from 15 pharmacies in Greece to 25 in Lithuania during the first registration period (Table 2). The percentage of participants attending the intervention meetings differed per country: France had 59 % attendance, Greece had 73 % attendance, Lithuania had 72 % attendance, Poland had 65 % attendance, and Spain had 80 % attendance.

### 3.2. Registration characteristics

About 60 % of the dispensed prescriptions were for female patients in total; the percentage of female patients differed by country, from 64 % in Lithuania to 52 % in Greece. The antibiotics were dispensed by pharmacists in approximately 80 % of the registrations, and 20 % were dispensed by other pharmacy staff. There was variability between the countries, ranging from 67 % by pharmacists in Spain to 93 % in Poland. Amoxicillin, amoxicillin + clavulanic acid, and macrolides or clindamycin were dispensed most often, although there were differences between the countries and between the two registration periods. (Supplementary file 1).

### 3.3. Safety checks

Overall, during the first audit, in 29 % of the dispensed prescriptions, no safety checks were performed. The mean percentage of total possible safety checks performed was 47 %. In Greece, at least one safety check was performed for 90 % of the recorded dispensed prescriptions, in Spain this was done in 60 %. The country performing the lowest percentage of safety checks was Poland (29 %), and the highest was Greece (71 %). Quality indicator 1a showed a significant reduction (17 %,  $p < 0.001$ ) in the number of dispensed prescriptions for which no safety checks were performed and 1b showed a significant increase (18 %,  $p < 0.001$ ) in the percentage of safety checks performed. Variation between countries was seen, from a 34 % ( $p = 0.260$ ) worsening in Greece to a 47 % ( $p < 0.001$ ) improvement in Spain for 1a and 13 % ( $p = 0.004$ ) worsening in Greece and 72 % ( $p < 0.001$ ) improvement in Spain for 1b (Appendix 3). Split per specific safety check, in France and Greece most safety checks were performed at baseline and fewer in the other countries. Most improvements after the intervention were seen in Spain and Lithuania, whereas Greece mainly worsened. To illustrate, at baseline, pharmacists in Spain checked for allergies in 47 % of the dispensed prescriptions; this increased to 67 % after the interventions. In Greece, pharmacists checked for allergies in 82 % of the dispensed prescriptions at baseline, which worsened to 71 % of the dispensed prescriptions after the interventions (Fig. 1, Supplementary file 1).

### 3.4. Advice given to patients

Overall, at baseline, for 4 % of the dispensed prescriptions, pharmacists did not provide any advice to patients. Unnecessary advice was provided in 18 % of the dispensed prescriptions. After the intervention,

quality indicators showed 2a) that the percentage of correct advice provided by pharmacy staff increased by 17 % ( $p < 0.001$ ) and 2b) that the dispensed prescriptions for which no advice was provided was reduced by 35 % ( $p = 0.006$ ). At the same time, quality indicator 2c showed that the risk of providing at least one inappropriate advice increased by 44 % ( $p < 0.001$ ) (Appendix 4). When looking at the advice individually, treatment duration and treatment dose were most discussed at baseline. In France, duration and dose were discussed in 97 % and 98 % of the dispensed prescriptions, respectively. In Spain, this was 66 % and 51 % (Fig. 2, Supplementary file 1).

### 3.5. Prescription information

At baseline for the five countries, pharmacists did not have any information regarding the diagnosis and duration of treatment in 23 % and 3 % of the dispensed prescriptions, respectively. Quality indicators showed 3a) a 5 % improvement ( $p = 0.367$ ) for knowing about the location of infection and 3b) a 21 % improvement ( $p = 0.186$ ) for knowing the treatment duration (Appendix 5). These effects were not statistically significant. For the individual countries, significant improvements were seen in Spain and Lithuania regarding the knowledge of the location of the infection (Appendix 5).

### 3.6. Pharmacist judgement and contact with prescribers

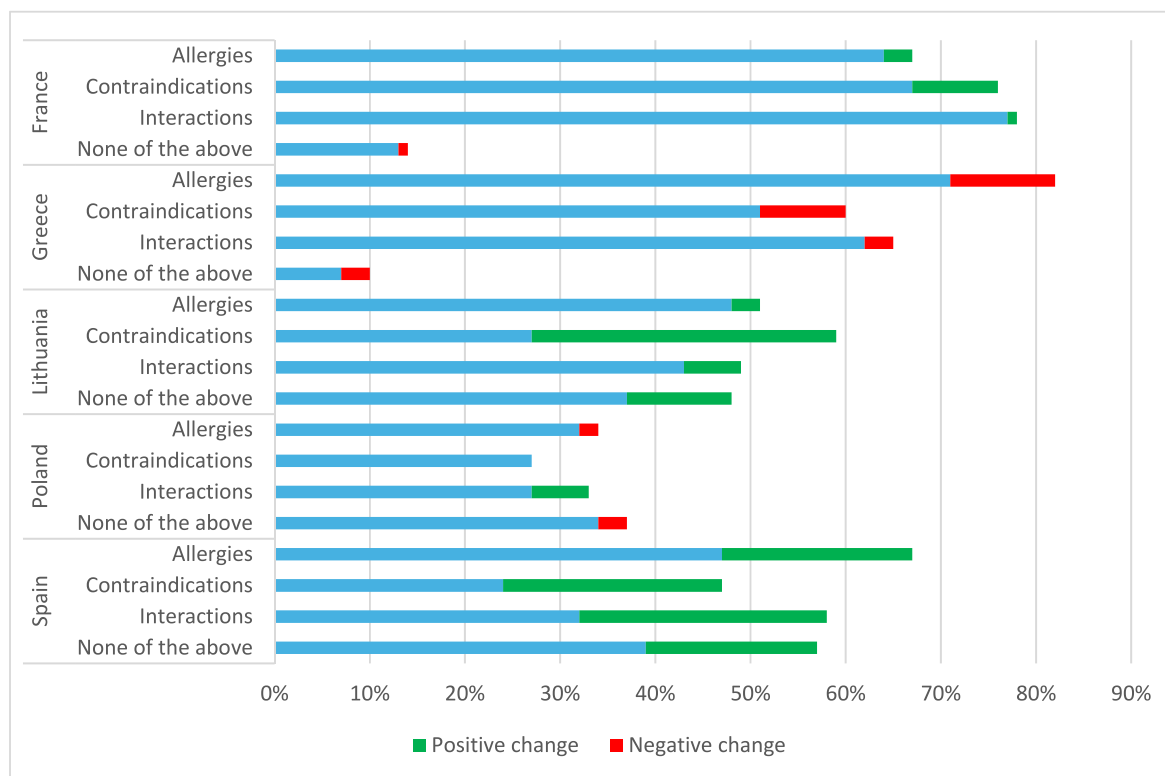
Based on the prescription information, pharmacy staff were asked to judge the appropriateness of antibiotic prescriptions. Their clinical judgement aligned with the prescribers' in about 70 % of the antibiotic prescriptions dispensed in their pharmacies, and in about 25 %, they did not have sufficient information to make this judgment (Fig. 3). There was a 2 % increase ( $p = 0.863$ ) in inappropriate judgement by the pharmacy staff overall. Individually, France was the only country with significant worsening (133 %,  $p < 0.001$ ) and Lithuania with significant improvement (60 %,  $p = 0.001$ ). When splitting up the judgement based on the education of the dispenser, the judgement provided by pharmacists improved by 2 % ( $p = 0.857$ ) overall. Non-pharmacists (i.e., assistants) showed worsening in all countries and overall (34 %,  $p = 0.283$ ) (Appendix 6). Contact with prescribers due to prescriptions for which pharmacists do not agree or do not have sufficient information to form a professional judgment is uncommon in all countries. In 2022 and 2023, prescribers were contacted for 3 % of the dispensed prescriptions of antibiotics (Supplementary file 1).

## 4. Discussion

The APO methodology has, for the first time, been successfully applied to the community pharmacy setting in five EU countries. Adapting the methodology to this context has provided insights into how European pharmacists dispense antibiotics and how they can enhance their practices. This study shows that in many pharmacies, antibiotics are not dispensed following the Guidelines for the Prudent Use of Antimicrobials for Human Consumption.<sup>6</sup> Pharmacies offer a limited number of safety checks when dispensing antibiotics, and patients

**Table 2**  
Number of participating pharmacies and registrations per country and in total for the two registration periods.

| Country   | Number of pharmacies | Number of antibiotic prescriptions recorded | Number of pharmacies | Number of antibiotic prescriptions recorded | Pharmacy dropout (%) |
|-----------|----------------------|---------------------------------------------|----------------------|---------------------------------------------|----------------------|
|           | 2022                 |                                             | 2023                 |                                             |                      |
| France    | 22 (21 %)            | 603 (23 %)                                  | 21 (23 %)            | 626 (25 %)                                  | 4.5                  |
| Greece    | 15 (14 %)            | 308 (12 %)                                  | 14 (15 %)            | 270 (11 %)                                  | 6.7                  |
| Lithuania | 25 (24 %)            | 628 (24 %)                                  | 20 (22 %)            | 542 (22 %)                                  | 20                   |
| Poland    | 23 (22 %)            | 584 (23 %)                                  | 20 (22 %)            | 573 (23 %)                                  | 13                   |
| Spain     | 20 (19 %)            | 470 (18 %)                                  | 16 (18 %)            | 450 (18 %)                                  | 20                   |
| Total     | 105                  | 2593                                        | 91                   | 2461                                        | 12.5                 |



**Fig. 1.** Percentage of dispensed prescriptions for which specific safety checks were performed by country, at baseline and after the intervention. Positive change is demonstrated by green bars, where the results at baseline are shown by the blue bar, and the results after the intervention are the total of the blue and green bars combined. Negative change is demonstrated by red bars, where the baseline results are shown by the blue and red bars combined, and the results after the intervention are shown by the blue bar. A single blue bar indicates no change. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

receive minimal advice. Additionally, for approximately a quarter of antibiotic prescriptions, pharmacists were unaware of the location of infection, preventing them from making informed judgments on the appropriateness of prescriptions. The multifaceted intervention implemented in the HAPPY PATIENT project has shown promising results and has succeeded in steering pharmacy practice towards a better future. Nevertheless, the intervention was not equally effective in all countries or all aspects of pharmacy practice.

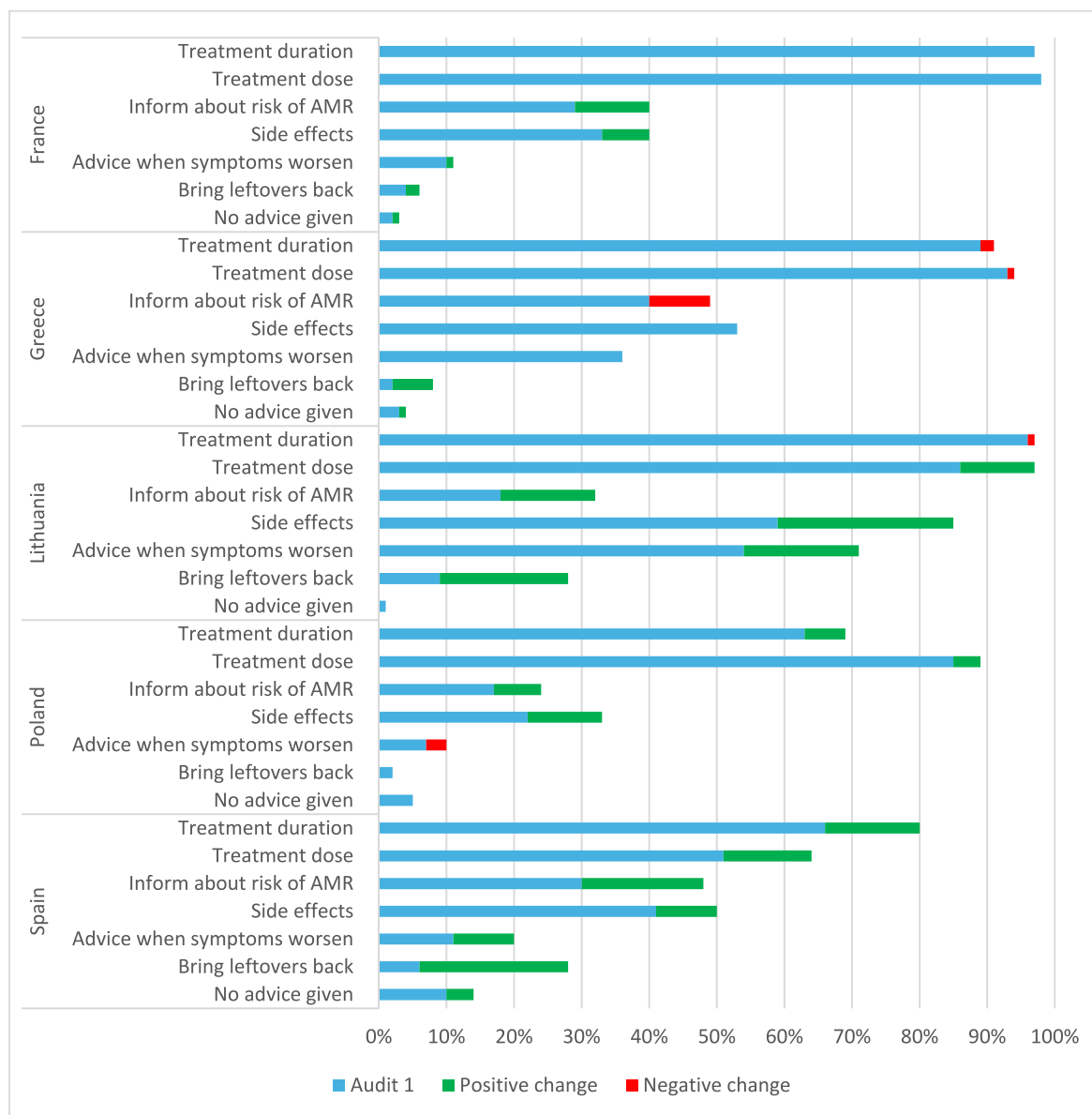
The improvement in practice seen in this study is in accordance with previous studies where the APO methodology was used in primary care to optimise antibiotic prescribing.<sup>23</sup> The intervention seems to have had the most significant impact in countries with a lower baseline of dispensing quality. For example, in Spain 72 % improvement in the mean number of safety checks provided, but at baseline, the average percentage of safety checks performed was only 35 %, compared to 70 % in France, where only a 6 % improvement was seen. This aligns with literature that suggests targeting healthcare professionals who are not performing well initially and providing them with a clear goal and action plan could enhance the effectiveness of audit and feedback interventions.<sup>13</sup> In contrast, pharmacies in Poland also exhibited a lower baseline of dispensing practice but did not improve to the same extent. Other factors may play a role here; the interventions in Lithuania and Spain were conducted, at least partially, face-to-face. Conversely, most or all interventions in the other countries were conducted online due to the COVID-19 pandemic or geographical distance, potentially affecting the effectiveness of the interventions. Also, differences in healthcare systems and social norms may contribute to the variations that were observed across the different countries. This notion is supported by the observation that improvements in dispensing practices were largest for pharmacists who actively participated in the interventions, e.g., 24 % improvement for providing all safety checks compared to 18 % when all

pharmacists who participated in both audits were included (supplementary file 2).

#### 4.1. Strengths and limitations

A major strength of this study is that it has implemented a proven effective methodology<sup>20,24</sup> of measuring the quality of healthcare practice for the first time in the community pharmacy setting. The feasibility of the approach was tested in a pilot study and the results of the pilot study have been used to optimise the self-recording form for the current study.<sup>15</sup> This study was conducted in five countries with different levels of antibiotic consumption and differences in community pharmacy practice. This implies that the methodology can be implemented in pharmacies in different countries. The study was part of the HAPPY PATIENT project which evaluated the same multifaceted intervention also in general practice, nursing homes and out-of-hour settings.<sup>16</sup> Although only the results of the community pharmacy setting are presented here, working in this multidisciplinary team was essential for the success of the work.

This study has several limitations related to the methodology. As an implementation study, no control group was involved. Changes between the first and second registration periods may have been induced by factors other than the implemented intervention. An example of this was seen in Lithuania, where, due to a shortage of amoxicillin, more broad-spectrum antibiotics were dispensed, which may also have influenced the dispensing process. Shortages of various drugs in European community pharmacies may have played a role, as resolving them is time-consuming. The self-registration of the dispensing process may introduce reporting bias, which may influence the accuracy of the recorded data among participants. Additionally, a multifaceted intervention has been implemented at once, therefore making it impossible to analyse

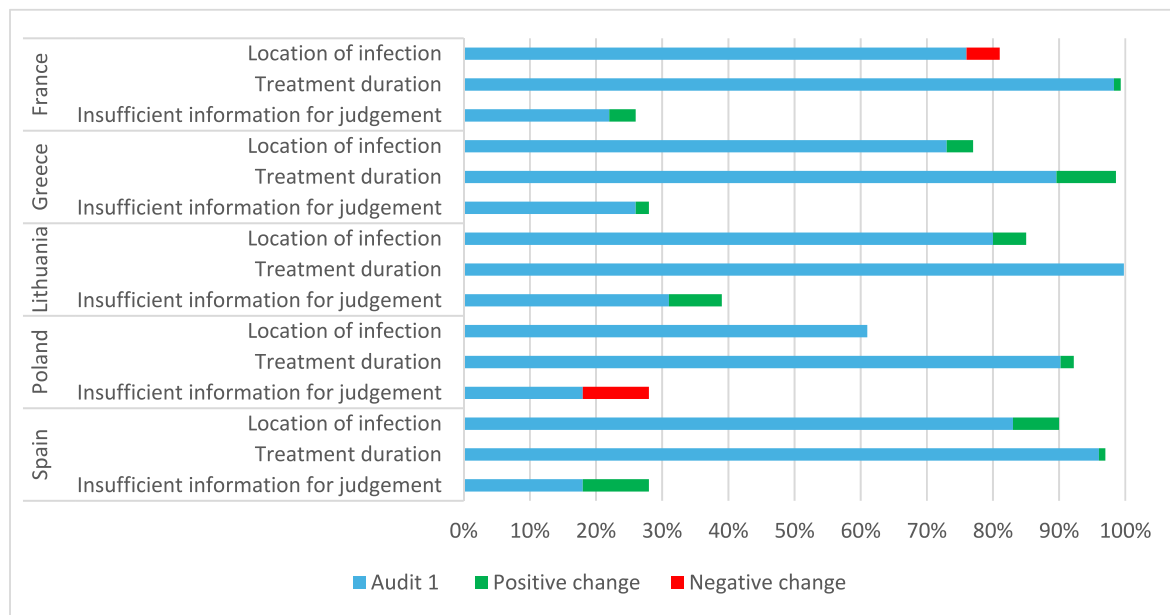


**Fig. 2.** Percentage of dispensed prescriptions for which specific advice was provided to patients by country, at baseline and after the intervention. Positive change is demonstrated by green bars, where the results at baseline are shown by the blue bar, and the results after the intervention are the total of the blue and green bars combined. Negative change is demonstrated by red bars, where the baseline results are shown by the blue and red bars combined, and the results after the intervention are shown by the blue bar. A single blue bar indicates no change. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

which component of the intervention had the largest effect. Another constraint of the study was that pharmacists chose to participate voluntarily, possibly inducing selection bias. It is probable that those participating had a particular interest in antibiotics or were very motivated to enhance their dispensing practices. This suggests that the participant sample may be more aligned with best practice rather than reflecting average practice. Finally, conducting this study during the COVID-19 pandemic gave some difficulties. Pharmacists received additional work, e.g., providing COVID-19 vaccination in France, making recruiting participants difficult. Moreover, originally, it was planned only to provide the education only in-person, but this was changed to either online or in-person based on possibilities per country. The variation in the content and intensity of the multifaceted intervention between countries may have contributed to differences in results between the countries.

#### 4.2. Future implications

This study shows the potential of community pharmacy as an important part of primary healthcare to ensure the safe use of antibiotics, as a source of advice to patients and prescribers, and as a partner in optimising antimicrobial use. This role is especially important since community pharmacists are the most accessible healthcare professionals for patients.<sup>25,26</sup> To fulfil this potential in line with the EU guidelines and the 'first do no harm' principle in healthcare, pharmacists must ensure that any antibiotic treatment does not cause harm to patients through allergies, contraindications, interactions, or inappropriate use. A recently published pharmacy expert consensus study<sup>27</sup> further outlines the role of the community pharmacist when dispensing antibiotics in greater detail. This more detailed description of antibiotic dispensing practice should be considered for further projects that aim to improve community pharmacy practice. Such projects in primary care should



**Fig. 3.** Percentage of dispensed prescriptions for which specific prescription information was available by country, at baseline and after the intervention. Positive change is demonstrated by green bars, where the results at baseline are shown by the blue bar, and the results after the intervention are the total of the blue and green bars combined. Negative change is demonstrated by red bars, where the baseline results are shown by the blue and red bars combined, and the results after the intervention are shown by the blue bar. A single blue bar indicates no change. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

actively engage pharmacists. In the five target countries, there was limited interaction between pharmacists and prescribers. To foster collaboration between pharmacists and general practitioners in the future, involving professionals from the same regional context and facilitating discussions on enhancing communication would be beneficial. This is particularly significant because pharmacists can advise prescribers on antibiotics, aligning with the EU Guidelines for the prudent use of antimicrobials in human health.

While some aspects of the dispensing process improved after the intervention, not all showed progress. Although pharmacists provided more advice, they also offered more inappropriate advice to patients. In future studies, caution should be exercised when encouraging additional pharmacist advice, considering the differences between antibiotic classes.

Pharmacists from all participating countries expressed enthusiasm about their involvement. They firmly believe that pharmacists have a crucial role in optimising antibiotic use and feel that their contribution has been insufficiently recognised in earlier research—a sentiment that resonates with the views previously reported by French pharmacists.<sup>28</sup> Pharmacists should be considered important collaborators for further research on improving antibiotic usage. Strategies need to be developed involving relevant stakeholders such as policymakers and pharmacy associations (e.g., the International Pharmaceutical Federation, Pharmaceutical Group of the EU) for upscaling and wider implementation of the intervention. Tools and materials which have been developed in this project are available.<sup>15,22</sup>

## 5. Conclusion

In the HAPPY PATIENT project, the successful implementation of the APO methodology has been documented within the community pharmacy setting of five European Union countries. The contextual adaptation of this methodology has yielded valuable insights into the antibiotic dispensing practices of European pharmacists, shedding light on potential areas for improvement. At baseline, there were strong deviations from EU pharmacy practice guidelines. The multifaceted intervention that was implemented improved several aspects of the dispensing

process, although differences between the countries occurred.

## CRediT authorship contribution statement

**Maarten Lambert:** Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ria Benko:** Writing – review & editing, Methodology, Investigation, Formal analysis, Conceptualization. **Jesper Lykkegaard:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Jens Søndergaard:** Writing – review & editing, Resources. **Jonas Olsen:** Writing – review & editing. **Ana Garcia-Sangenis:** Writing – review & editing, Data curation. **Marilena Anastasaki:** Writing – review & editing, Data curation. **Christos Lionis:** Writing – review & editing, Data curation. **Malene Plejdrup Hansen:** Writing – review & editing, Methodology, Conceptualization. **Pia Touboul Lundgren:** Writing – review & editing, Data curation. **Pascale Bruno:** Writing – review & editing, Data curation. **Fabiana Raynal:** Writing – review & editing, Data curation. **Laura Vallejo-Torres:** Writing – review & editing, Formal analysis. **Lars Bjerrum:** Writing – review & editing. **Lina Jaruseviciene:** Writing – review & editing, Data curation. **Ruta Radzeviciene:** Writing – review & editing, Data curation. **Anna Kowalczyk:** Writing – review & editing, Data curation. **Carl Llor:** Writing – review & editing, Data curation, Conceptualization. **Katja Taxis:** Writing – review & editing, Supervision, Methodology, Investigation, Formal analysis, Conceptualization.

## Transparency declarations

None to declare.

## Data availability statement

The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy reasons.



**Appendix 2. Description of the ten quality indicators used for data analysis**

| Quality indicator description |                                                                                                                                                                                                |
|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1a                            | The percentage of dispensed prescriptions for which no safety checks were performed                                                                                                            |
| 1b                            | The mean percentage of safety checks performed                                                                                                                                                 |
| 2a                            | The mean percentage of correct advice provided                                                                                                                                                 |
| 2b                            | The percentage of dispensed prescriptions for which at least one unnecessary advice was provided                                                                                               |
| 2c                            | The percentage of dispensed prescriptions for which no advice was provided                                                                                                                     |
| 3a                            | Percentage of dispensed prescriptions of prescriptions of which the location of infection was unknown                                                                                          |
| 3b                            | Percentage of dispensed prescriptions of prescriptions of which the treatment duration was unknown                                                                                             |
| 4a                            | Percentage of prescriptions for which pharmacists clinically agreed with a prescription when the location of infection or the duration of the treatment was unknown to the dispenser           |
| 4b                            | Percentage of prescriptions for which pharmacist assistants clinically agreed with a prescription when the location of infection or the duration of the treatment was unknown to the dispenser |
| 4c                            | The combined percentage of 4a and 4b                                                                                                                                                           |

**Appendix 3. Statistical data of the quality indicators for safety checks for the separate countries and in total, comparing 2022 and 2023. Data from participants who completed the first and the second registration period. \* p-value statistically significant (<0.05)**

| Country   | 1a) No safety checks performed |      |      |      |                     | Chi-square p-Value | 1b) Safety checks performed |        |      |        |                     | T Student p-Value |
|-----------|--------------------------------|------|------|------|---------------------|--------------------|-----------------------------|--------|------|--------|---------------------|-------------------|
|           | 2022                           |      | 2023 |      | Intervention effect |                    | 2022                        |        | 2023 |        | Intervention effect |                   |
|           | n                              | %    | n    | %    |                     |                    | n                           | Mean % | n    | Mean % |                     |                   |
| France    | 585                            | 13.7 | 624  | 14.6 | 7 %                 | 0.651              | 585                         | 69.6   | 624  | 73.6   | 6 %                 | 0.060             |
| Greece    | 290                            | 10.3 | 254  | 13.8 | 34 %                | 0.218              | 290                         | 70.6   | 254  | 61.7   | −13 %               | 0.004*            |
| Lithuania | 613                            | 37.7 | 536  | 25.9 | −31 %               | 0.000*             | 613                         | 40.2   | 536  | 53.7   | 34 %                | 0.000*            |
| Poland    | 581                            | 37.2 | 573  | 40.3 | 8 %                 | 0.274              | 581                         | 29.2   | 573  | 30.5   | 4 %                 | 0.469             |
| Spain     | 453                            | 40.2 | 424  | 21.5 | −47 %               | 0.000*             | 453                         | 35.0   | 424  | 60.1   | 72 %                | 0.000*            |
| Total     | 2522                           | 29.3 | 2411 | 24.3 | −17 %               | 0.000*             | 2522                        | 47.0   | 2411 | 55.3   | 18 %                | 0.000*            |

**Appendix 4. Statistical data of the quality indicators for advice provided during dispensing for the separate countries and in total, comparing 2022 and 2023. Data from participants who completed the first and the second registration period. \* p-value statistically significant (<0.05)**

| Country   | 2a) Correct advice  |        |      |        |                     |                    | 2b) At least one bad or unnecessary advice |      |      |      |                     |                    |
|-----------|---------------------|--------|------|--------|---------------------|--------------------|--------------------------------------------|------|------|------|---------------------|--------------------|
|           | 2022                |        | 2023 |        | Intervention effect | T Student p-Value  | 2022                                       |      | 2023 |      | Intervention effect | Chi-square p-Value |
|           | n                   | Mean % | n    | Mean % |                     |                    | %                                          | n    | %    | n    |                     |                    |
| France    | 568                 | 45.6   | 584  | 48.8   | 7 %                 | 0.000*             | 568                                        | 1.6  | 584  | 2.6  | 63 %                | 0.242              |
| Greece    | 284                 | 53.7   | 256  | 52.1   | −3 %                | 0.372              | 284                                        | 59.5 | 256  | 33.6 | −44 %               | 0.000*             |
| Lithuania | 614                 | 53.7   | 530  | 67.6   | 26 %                | 0.000*             | 614                                        | 25.1 | 530  | 46.6 | 86 %                | 0.000*             |
| Poland    | 562                 | 32.5   | 560  | 38.0   | 17 %                | 0.000*             | 562                                        | 10.0 | 560  | 21.4 | 114 %               | 0.000*             |
| Spain     | 445                 | 34.3   | 424  | 49.2   | 43 %                | 0.000*             | 445                                        | 14.6 | 424  | 35.8 | 145 %               | 0.000*             |
| Total     | 2473                | 43.5   | 2354 | 50.9   | 17 %                | 0.000*             | 2473                                       | 18.3 | 2354 | 26.4 | 44 %                | 0.000*             |
| Country   | 2c) No advice given |        |      |        |                     |                    |                                            |      |      |      |                     |                    |
|           | 2022                |        | 2023 |        | Intervention effect | Chi-square p-Value |                                            |      |      |      |                     |                    |
|           | n                   | %      | n    | %      |                     |                    | %                                          |      |      |      |                     |                    |
| France    | 585                 | 1.5    | 624  | 1.0    | −33 %               | 0.365              |                                            |      |      |      |                     |                    |
| Greece    | 299                 | 3.3    | 259  | 2.3    | −30 %               | 0.468              |                                            |      |      |      |                     |                    |
| Lithuania | 627                 | 1.1    | 540  | 0.7    | −36 %               | 0.508              |                                            |      |      |      |                     |                    |
| Poland    | 584                 | 4.8    | 572  | 5.4    | 13 %                | 0.629              |                                            |      |      |      |                     |                    |
| Spain     | 459                 | 10.2   | 422  | 3.6    | −65 %               | 0.000*             |                                            |      |      |      |                     |                    |
| Total     | 2554                | 4.0    | 2417 | 2.6    | −35 %               | 0.006*             |                                            |      |      |      |                     |                    |

**Appendix 5. Statistical data of the quality indicators for having information available on the location of infection and treatment duration of the dispensed antibiotic, for the separate countries and in total, comparing 2022 and 2023. Data from participants who completed the first and the second registration period. \* p-value statistically significant (<0.05)**

| Country | 3a) Location of infection unknown |      |                     |  | Chi-square p-Value | 3b) Treatment duration unknown |      |                     |  | Chi-square p-Value |
|---------|-----------------------------------|------|---------------------|--|--------------------|--------------------------------|------|---------------------|--|--------------------|
|         | 2022                              | 2023 | Intervention effect |  |                    | 2022                           | 2023 | Intervention effect |  |                    |

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(continued)

| Country   | 3a) Location of infection unknown |      |      |      |                     |        | Chi-square p-Value | 3b) Treatment duration unknown |      |                     |       |       |  | Chi-square p-Value |
|-----------|-----------------------------------|------|------|------|---------------------|--------|--------------------|--------------------------------|------|---------------------|-------|-------|--|--------------------|
|           | 2022                              |      | 2023 |      | Intervention effect | 2022   |                    | 2023                           |      | Intervention effect |       |       |  |                    |
|           | n                                 | %    | n    | %    |                     | n      |                    | %                              | n    |                     | %     |       |  |                    |
|           | n                                 | %    | n    | %    | %                   |        | n                  | %                              | n    | %                   | %     |       |  |                    |
| France    | 583                               | 18.7 | 624  | 23.7 | 27 %                | 0.033* | 579                | 0.5                            | 623  | 0.6                 | 20 %  | 0.778 |  |                    |
| Greece    | 286                               | 23.8 | 255  | 21.2 | −11 %               | 0.470  | 269                | 0                              | 255  | 0                   | −     | −     |  |                    |
| Lithuania | 621                               | 19.6 | 533  | 13.7 | −30 %               | 0.007* | 627                | 0                              | 539  | 0                   | −     | −     |  |                    |
| Poland    | 583                               | 38.8 | 573  | 38.7 | 0 %                 | 0.994  | 584                | 9.8                            | 573  | 7.8                 | −20 % | 0.253 |  |                    |
| Spain     | 440                               | 11.6 | 427  | 7.0  | −40 %               | 0.021* | 459                | 2.4                            | 433  | 1.2                 | −50 % | 0.163 |  |                    |
| Total     | 2513                              | 22.9 | 2412 | 21.8 | −5 %                | 0.367  | 2518               | 2.8                            | 2423 | 2.2                 | −21 % | 0.186 |  |                    |

**Appendix 6. Statistical data of the quality indicators for judgement of the prescription by pharmacists and non-pharmacists for the separate countries and in total, comparing 2022 and 2023. Data from participants who completed the first and the second registration period. \* p-value statistically significant (<0.05)**

| Country   | 4a) Inappropriate judgment by pharmacist |      |      |      |                     |                    | 4b) Inappropriate judgment by non-pharmacist |      |      |      |                     |                    |
|-----------|------------------------------------------|------|------|------|---------------------|--------------------|----------------------------------------------|------|------|------|---------------------|--------------------|
|           | 2022                                     |      | 2023 |      | Intervention effect | Chi-square p-Value | 2022                                         |      | 2023 |      | Intervention effect | Chi-square p-Value |
|           | n                                        | %    | n    | %    |                     |                    | %                                            | n    | %    | n    |                     |                    |
| France    | 334                                      | 5.7  | 397  | 17.4 | 205 %               | 0.000*             | 99                                           | 11.1 | 113  | 11.5 | 4 %                 | 0.928              |
| Greece    | 130                                      | 13.1 | 143  | 17.5 | 34 %                | 0.314              | 41                                           | 12.2 | 36   | 13.9 | 14 %                | 0.825              |
| Lithuania | 377                                      | 11.7 | 372  | 4.6  | −61 %               | 0.000*             | 46                                           | 0    | 30   | 0    | −                   | −                  |
| Poland    | 381                                      | 23.1 | 337  | 20.5 | −11 %               | 0.396              | 4                                            | 0    | 17   | 35.3 | 35 %                | 0.160              |
| Spain     | 260                                      | 7.7  | 259  | 3.1  | −60 %               | 0.020*             | 65                                           | 7.7  | 96   | 8.3  | 8 %                 | 0.884              |
| Total     | 1482                                     | 12.7 | 1508 | 12.5 | −2 %                | 0.857              | 255                                          | 8.2  | 292  | 11.0 | 34 %                | 0.283              |

| Country   | 4c) Inappropriate judgment by total pharmacy staff |      |      |      |                     |                    |
|-----------|----------------------------------------------------|------|------|------|---------------------|--------------------|
|           | 2022                                               |      | 2023 |      | Intervention effect | Chi-square p-Value |
|           | n                                                  | %    | n    | %    |                     |                    |
| France    | 433                                                | 6.9  | 510  | 16.1 | 133 %               | 0.000              |
| Greece    | 171                                                | 12.9 | 179  | 16.8 | 30 %                | 0.306              |
| Lithuania | 423                                                | 10.4 | 402  | 4.2  | −60 %               | 0.001              |
| Poland    | 385                                                | 22.9 | 354  | 21.2 | −7 %                | 0.584              |
| Spain     | 325                                                | 7.7  | 355  | 4.5  | −42 %               | 0.081              |
| Total     | 1737                                               | 12   | 1800 | 12.2 | 2 %                 | 0.863              |

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