SCIENTIFIC REPORT

HAPPY PATIENT

Health Alliance for Prudent Prescription and Yield of Antibiotics in a Patient-centred Perspective

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

AN INTRODUCTION

In Europe alone, u**p to 35,000 people lose their lives annually due to the direct consequences of antimicrobial resistance**, according to the European Centre for Disease Prevention and Control (an Agency of the European Union).

The primary cause of antimicrobial resistance is the **excessive and unnecessary use of antibiotics**, partly caused by inappropriate prescription and dispensing of these drugs.

AMR is a priority for the European Commision, publishing in 2017 the guidelines on prudent use of antimicrobials in human medicine, intended to inform and assist activities to promote the prudent use of antimicrobials in humans targeting all actors that play a role in antimicrobial use https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52017XC0701%2801%29.

With this context, a consortium formed by partners from various universities, research centers, and, ultimately, qualified professionals in the field of health and science from around Europe is the driving force behind the ambitious project HAPPY PATIENT (The Health Alliance for Prudent Prescription and Yield of Antibiotics from a Patient-Centred Perspective).

HAPPY PATIENT has implemented, over three years of intense work, a simple methodology in **four healthcare settings** (general practice, out-of-hours services, nursing homes, and pharmacies) **across five European Union countries** (Spain, France, Lithuania, Poland, and Greece) to reduce the inappropriate use of antibiotics and contribute to the fight against antimicrobial resistance, a public global health problem.

Up to 407 professionals from the four aforementioned healthcare settings have participated in this project implementing **HAPPY PATIENT** in their practices. They have done so through the **Audit Project Odense method**. This involves self-registering encounters with patients related to antibiotic prescribing and dispensing before and after an intervention (February-April 2022 and 2023). Before the second registration, healthcare professionals (HCPs) underwent a **multifaceted intervention**, which included reviewing and discussing feedback on the results of the first registration, enhancing **communication skills, and providing communication tools**.

After these three years of work, the entire team of HAPPY PATIENT is pleased to present the final results of the project in this report. In this document, we describe the outcomes related to the 4 settings, as well as the **economic impact that HAPPY PATIENT** could have if implemented in all European Union countries.

METHOD: AN INTERVENTION MARKED BY SIMPLICITY

About the study design*

A prospective, non-randomized, before-and-after study was conducted across France, Greece, Lithuania, Poland, and Spain, each with diverse cultural backgrounds and healthcare organizational structures.

The study has a patient centred approach, as we engaged HCPs acting as first points of contact to the health care system and being responsible for the management of community-acquired infections: general practice general practice, out-of-hours services, nursing homes, and community pharmacies.

The data collection occurred in two phases: the first from February to April 2022, and the second post-intervention from February to April 2023. A pilot test in November 2021 confirmed the relevance and comprehensibility of the registration chart for healthcare professionals.

Registrations

Data were collected using the Audit Project Odense (APO) methodology, employing a prospective self-registry approach with a simple reporting template. Specific templates were created for each of the four settings.

Participants were instructed to register all contacts with community-acquired infections in the case of general practice and out of hours services and all antibiotics prescribed or dispensed, respectively, in nursing homes and pharmacies.

For general practice, out-of-hours services and nursing homes, HCP recorded age, symptoms, duration, tests performed, suspected diagnosis and treatement, as well as other setting-specific information. In pharmacies, information recorded was focused on analyzing the core elements of the dispensing process, including safety checks and advice given to patients. In nursing homes all residents treated with antibiotics were included in the registration sheets

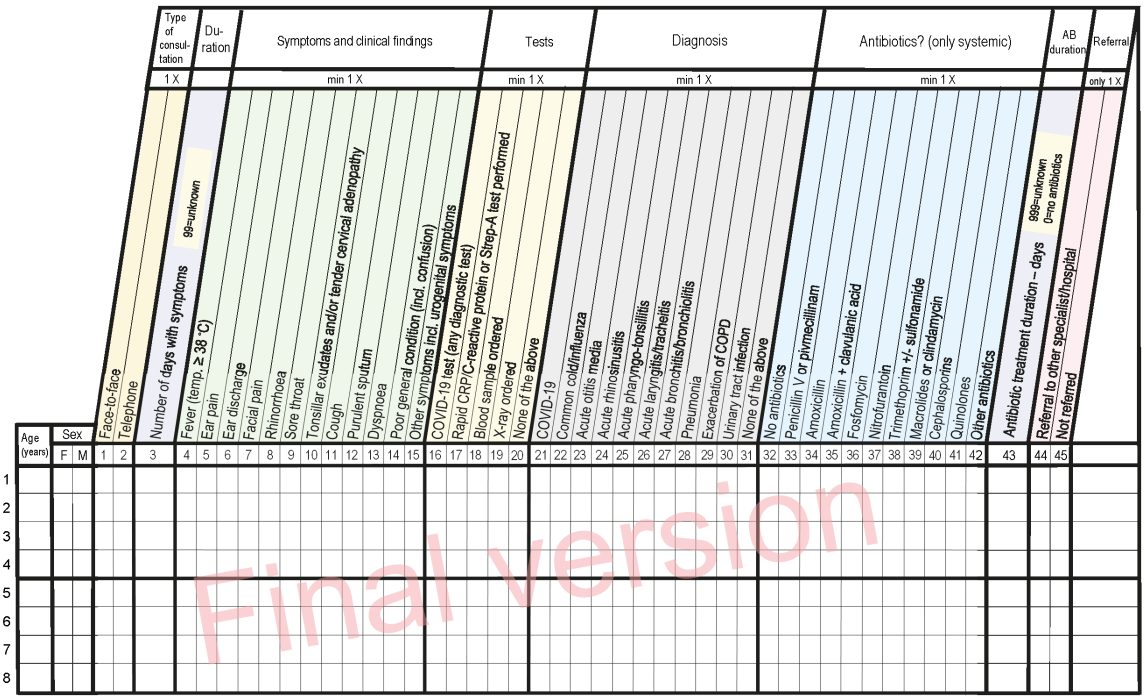
* https://rdcu.be/drUF0

Bjerrum A, García-Sangenís A, Modena D, Córdoba G, Bjerrum L, Chalkidou A, Lykkegaard J, Hansen MP, Søndergaard J, Nexøe J, Rebnord I, Sebjørnsen I, Jensen JN, Hansen MB, Taxis K, Lambert M, Benko R, González López-Valcárcel B, Raynal F, Barragán N, Touboul P, Bruno P, Radzeviciene R, Jaruseviciene L, Bandzaite A, Godycki-Cwirko M, Kowalczyk A, Lionis C, Karkana MN, Anastasaki M, Coleman J, Glasová H, van Agtmael M, Tattevin P, Borràs A, Llor C. Health alliance for prudent prescribing and yield of antibiotics in a patient-centred perspective (HAPPY PATIENT): a before-and-after intervention and implementation study protocol. BMC Prim Care. 2022 May 2;23(1):102. doi: 10.1186/s12875-022-01710-1. PMID: 35501712; PMCID: PMC9063370.

ID:
9-9-999

HAPPY PATIENT-1:

Suspected acute respiratory- or urinary tract infections in general practice



GP-UK

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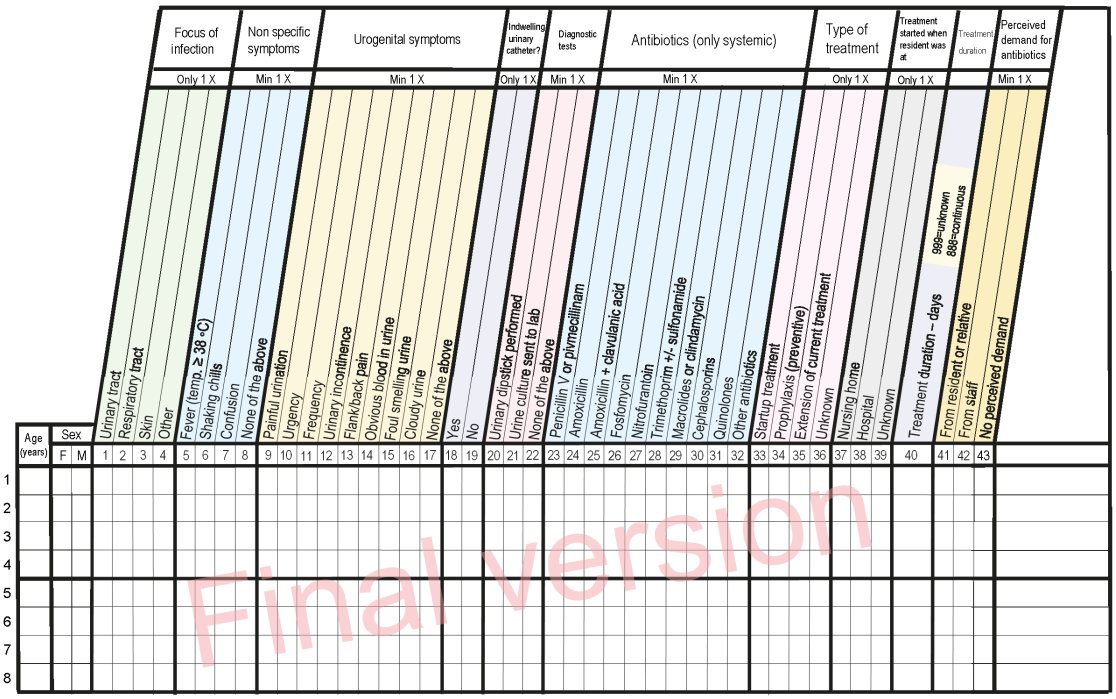
9-9-999

HAPPY PATIENT-1:

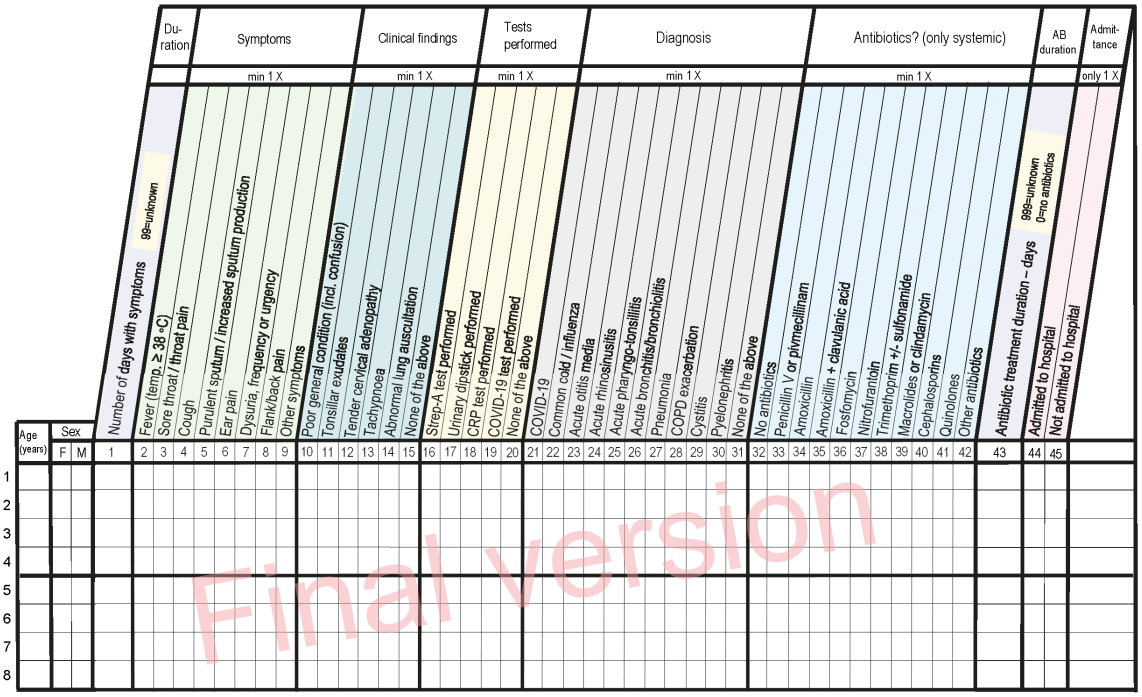
Infections in nursing homes (resident receiving antibiotics)



NH-UK

ID:
9-9-999

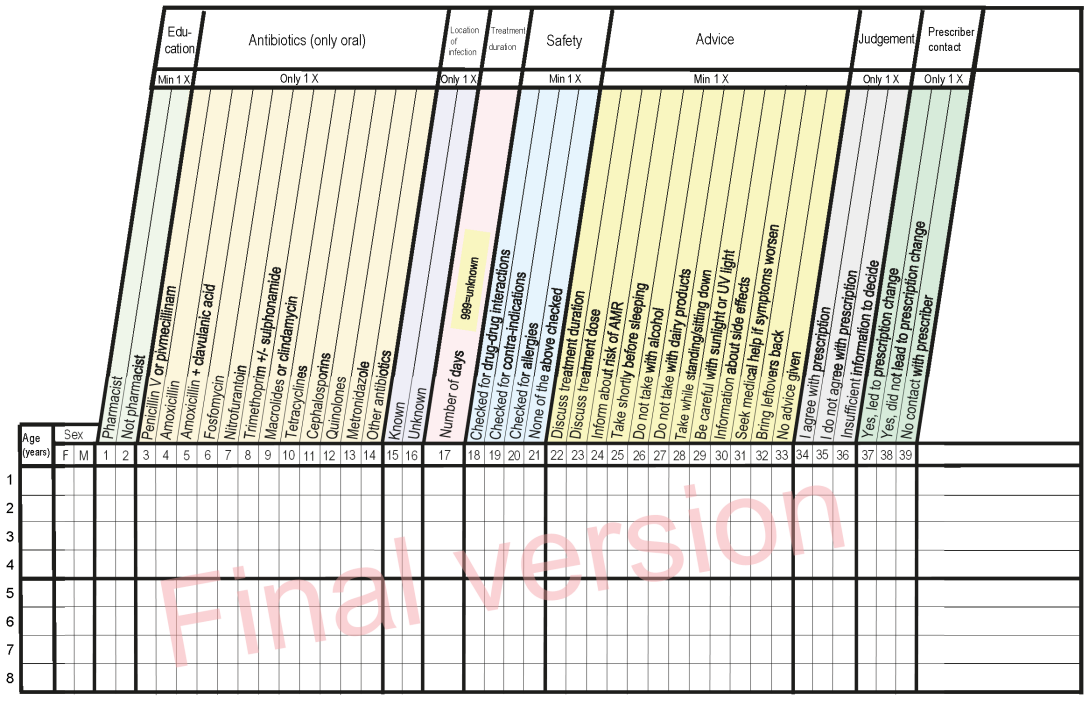
HAPPY PATIENT-1:
Suspected acute respiratory- or urinary tract infections in OOH-services



OOH-UK

ID:
9-9-999

HAPPY PATIENT-1: Acute infections in community pharmacies
Patient with any oral antibiotic prescription issued by any doctor picked-up inside the pharmacy



PH-UK

About the intervention

Changing practice behavior is challenging, and it requires the implementation of a systematic approach. Our multifaceted intervention was based on the Normalization Process theory, including: a) peer feedback with reflection and discussion, b) improvement of communication skills to enhance communication between healthcare professionals and patients, c) patient information brochures and posters, and d) country-specific information on antibiotic use.

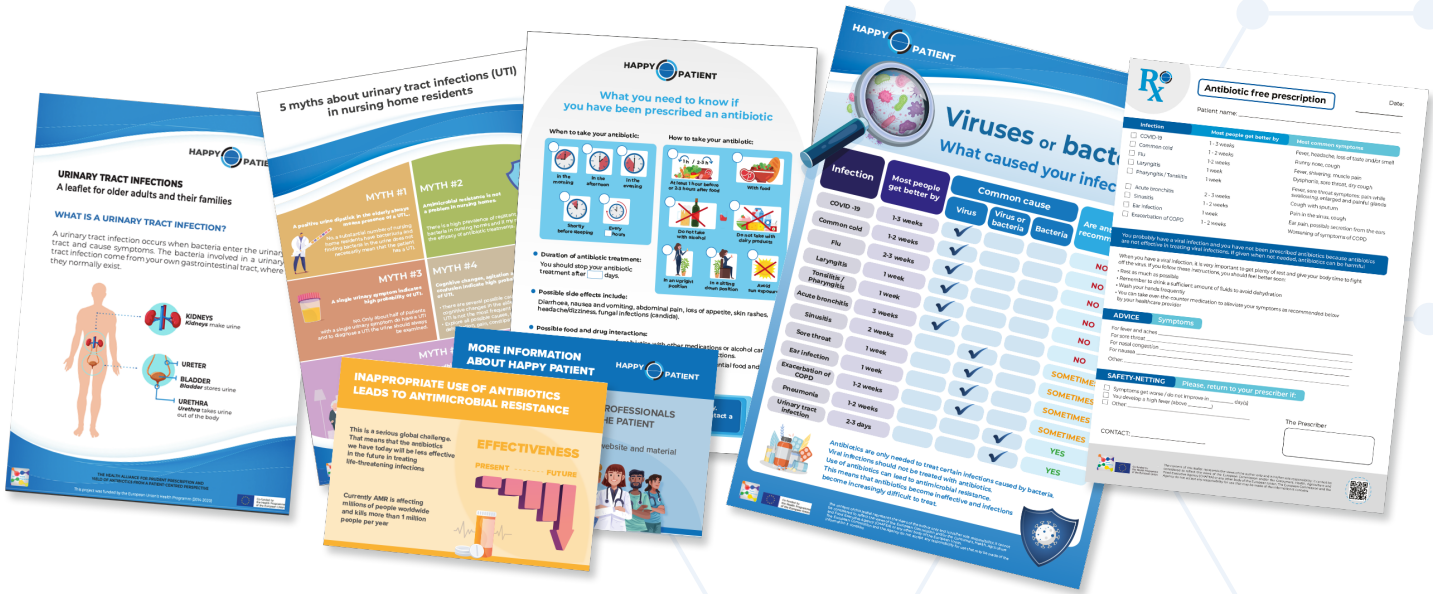
A Delphi consensus study guided the content of our intervention material, with a panel of experts from the 4 settings and 5 countries involved in HAPPY PATIENT.

We also developed 6 patient educational tools to support the communication between HCP and patient about use of antibiotics:

- Antibiotic free prescription pad
- Viruses or bacteria - what caused your infection?
- Urinary tract infections informative leaflet for nursing homes.
- Bursting myths about use of antibiotics in UTIs.
- Antibiotic dispensing checklist for pharmacists.
- Informative cards about antimicrobial resistance and use of antibiotics for patients.

These tools and the rest of the intervention material can be found in our website:

https://happypatient.eu/outcomes/happy-patient-communication-tools/

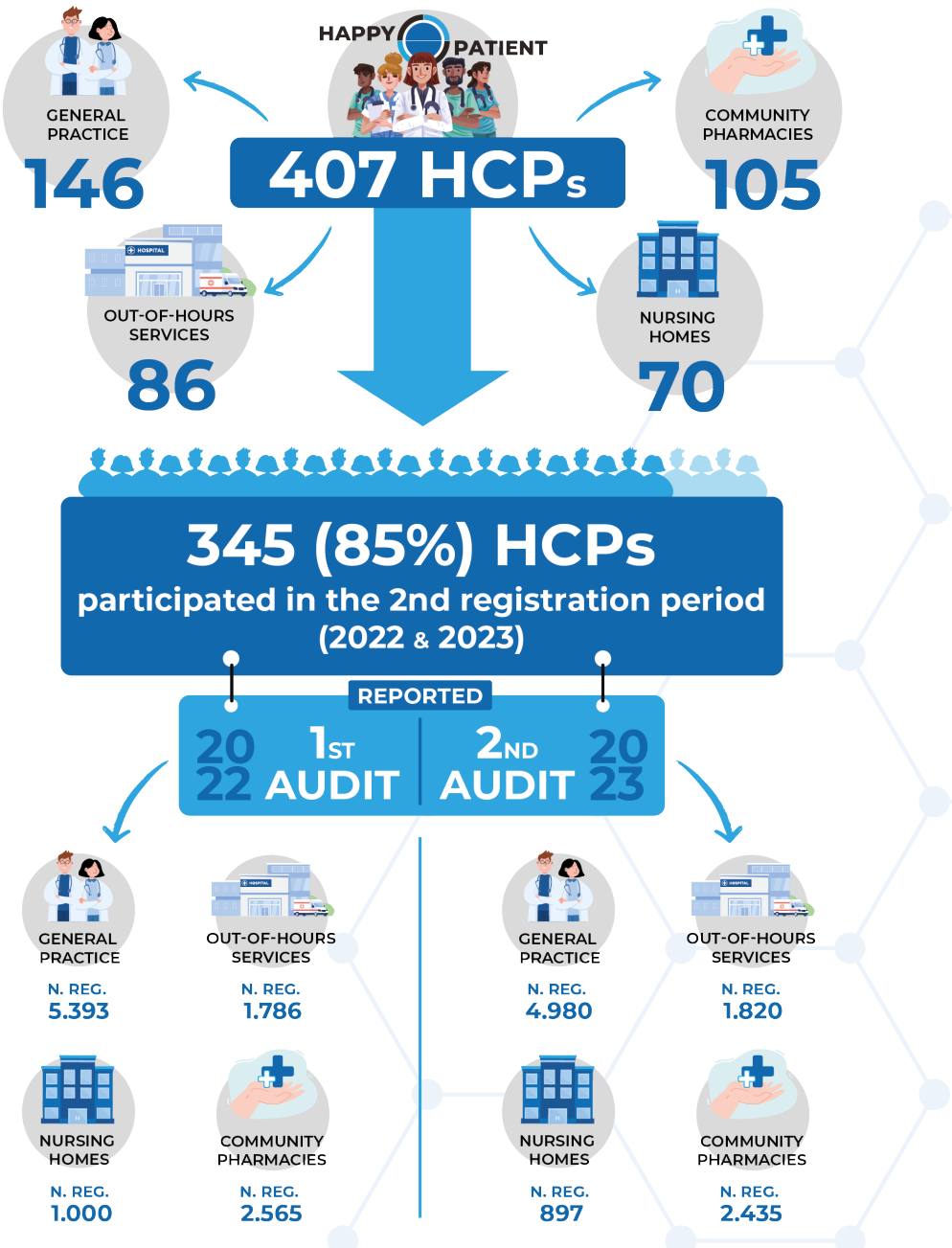


About the participants

Over 400 healthcare providers (HCPs) were involved in the project

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), out of which **a total of 345 (84.8%) undertook the intervention and participated in the second registration period**. The main results presented in this dossier are based on data from HCPs participating in both registration periods (2022 and 2023). They **reported a total of 10,744 common infections** during the initial registration and 10,132 cases during the second registration.

General practice was the setting with most registrations, followed by community pharmacies, out of hours services and nursing homes.



N. REG = number of registrations

RESULTS: AN AMAZING IMPACT AT AN EUROPEAN LEVEL

Here, we outline the outcomes of each setting: pharmacies, general practice, out-of-hours services, and nursing homes, across the five target countries where the HAPPY PATIENT project has been executed.

Spain, France, Lithuania, Poland and Greece have been targeted for the **HAPPY PATIENT** project.

They have diverse healtyh systems, incomes and level of antimicrobial medicines consumption.


GENERAL PRACTICE

OUT-OF-HOURS SERVICES


NURSING HOMES


COMMUNITY PHARMACIES

PHARMACIES

A great improvement achieved

One of the most significant results are the great improvement achieved in pharmacies, how **pharmacists and pharmacy technicians have improved the way of dispensing an antibiotic**, as well as providing information on safety and offering advice on the drug: it is a very interesting finding that opens the door to conducting other studies with the same methodology in pharmacies.

The overall **increase in appropriate antibiotic dispensing** following the multifactede intervention in the five target countries is 18% regarding safety checks (contraindications, allergies and interactions) and 17% when it comes to the general advice given.

In total, from the five countries evaluated, 2,522 antibiotic dispensing cases were analysed in the first phase of the audit (2022), where safety checks were provided in 47% of the cases and patient advice in 43.5%. After implementing the HAPPY PATIENT intervention, 2,473 cases were recorded and analysed, observing an increase on both safety checks performed and advice given to the patient (55.3% and 50.9%, respectively).
The intervention effect improved by 18% regarding safety checks and by 17% regarding advice to patients, improving antibiotic dispensing practices.

Breaking down the results by country, in France, in the first registration period 69.6% performed safety checks, which then increased (6%) to 73.6% in 2023; in Greece, in the 70.6% of the cases safety checks were performed during the first registration and 61.7% during the second. In Lithuania, safety checks increased from 40.2% to 53.7%, being the intervention effect of 34%. In Poland, the highest improvement belong to the % of advice given to patients, from 32.5% in the first registration to 38% in the second.

Community pharmacies

91
Professionals

5.000
Registrations

2022	2023
2.565	2.435

2022: Before intervention	2023: After intervention
Percentage of safety checks performed 47%	Percentage of safety checks performed 55,3%
Percentage of advice to patients 43,5%	Percentage of advice to patients 50,9%

Percentage of safety checks performed, including interaction, contraindications and allergies, before and after the intervention and intervention effect when dispensing an antibiotic prescription in community pharmacies:

PHARMACIES						
Country	Before		After		Intervention effect (%)	P
	n	%	n	%		
France	585	69.6	624	73.6	6.0	0.060
Greece	290	70.6	254	61.7	-13.0*	0.004*
Lithuania	613	40.2	536	53.7	34.0*	0.000*
Poland	581	29.2	573	30.5	4.0	0.469
Spain	453	35.0	424	60.1	72.0*	0.000*
Total	**2,522**	**47.0**	**2,411**	**55.3**	**18.0***	**0.000***

*P < 0.05
n= number

GENERAL PRACTICE

Good results achieved in General Practice

Globally in general practice a substantial variability across countries was noted and data was strongly influenced by the first line narrow antibiotic shortages in Europe.

The overall **data on unnecessary antibiotic prescribing in General Practice have improved after the intervention**, with a global reduction of -9.7%; it went from 72.2% inappropriate prescriptions to 65.2% in the second registration period, conducted in 2023. On the other hand, non first line antibiotic choice, where the selection of first line antibiotics according to national guidelines was assessed, increased by 29.2%, from 39.7% to 51.3%.

This figure is technically conditioned by the results of Lithuania and Poland. In the former, although a significant decrease of -19.9% in unnecessary prescriptions was evident after the intervention, the erroneous choices of antibiotics experienced a notable increase of 117.5%. Regarding Poland, potentially unnecessary prescribing showed a decrease of -5.0%, and erroneous choices of antibiotics increased significantly by 27.6%.

Regarding potentially unnecessary prescriptions of antibiotics, Lithuania had a positive intervention effect of 20%, followed by France, 16%.

GENERAL PRACTICE

133
Professionals

10.373
Registrations

2022	2023
5.393	4.980

Unnecessary antibiotic prescription

2022: Before intervention		2023: After intervention
72.21%	-9.7%	65.2%

Wrong antibiotic prescription

2022: Before intervention		2023: After intervention
39.7%	28.5%	51.3%

Percentage of unnecessary antibiotic prescribing and non-first line antibiotic choices before and after the intervention and intervention effect:

GENERAL PRACTICE												
Country	Unnecessary antibiotic prescribing						Non-first line antibiotic choices					
	Before		After		Intervention effect (%)	P	Before		After		Intervention effect (%)	P
	n	%	n	%			n	%	n	%		
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

n=number

OUT-OF-HOURS SERVICES

Encouraging results in out-of-hours services, especially in Spain

In total, taking into account data of all target countries, the choice of first line antibiotics did not improve during the second registration period, clearly affected by the shortage of first line antibiotics that ocurred in some of the countries participating in HAPPY PATIENT.

Potentially inappropriate antimicrobial prescribing decreased by 0.8% after the interventions.

A particularly significant data is the results from Spain as the decrease in the potentially inappropriate antibiotic prescription was 16.5% after the intervention, and the choice of non first line antibiotic was reduced by 17.4%.

To understand the variation of the results per country, it is essential to consider that out-of-hours services have a very different organisation between the 5 participating countries.

The intervention had the most positive effect in Spain regarding the reduction of potentially unnecessary prescriptions of antibiotics, by 16.5%, and in France and Spain regarding the non first line antibiotic choice (66% and 17%).

OUT-OF-HOURS SERVICES

63
Professionals

3.606
Registrations

2022	2023
1.786	1.820

Potentially unnecessary antibiotic prescribing

2022: Before intervention	2023: After intervention
52.5%	52.1%

Non-first line antibiotic choices

2022: Before intervention	2023: After intervention
51.7%	54.1%

Percentage of unnecessary antibiotic prescribing and non-first line antibiotic choices before and after the intervention and intervention effect:

OUT-OF-HOURS SERVICES												
Country	Unnecessary antibiotic prescribing						Non-first line antibiotic choices					
	Before		After		Intervention effect (%)	P	Before		After		Intervention effect (%)	P
	n	%	n	%			n	%	n	%		
France	17	23.5	33	42.4	80.4	0.187	13	30.8	19	10.5	-65.9	0.001
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

n=number

NURSING HOMES

Improvement of interventions in the long term care facilities is necessary

In nursing homes, the results after the intervention did not improve. Specifically, non first line antibiotics rose by 25.1% although it improved in France (33%) and Greece (17%).

Reasons for that might be that the context of nursing homes is complex and heterogeneous, and it could be interesting to consider in future projects more involvement of the nursing home staff in the design of the intervention and the inclusion of all professionals of the nursing home including prescribers into the project.

The worsening of the non-first line antibiotic choices in the second registration in nursing homes, also noticed in general practice and out-of-hours services is mainly due to the shortage of first-line narrow antibiotics affecting Europe from September 2022, particularly greater in the eastern countries, that was present during the whole second registration period elapsing from February to April 2023.

In this context, the majority of organizations working on **HAPPY PATIENT** consortium also participate in **IMAGINE: a project focused specifically on nursing homes with a more complex approach that includes the involvement of HCP in the design of the intervention and the improvement in Infection Prevention and Control measures**, addressing mainly urinary tract infections.

NURSING HOMES

58
Professionals

1.897
Registrations

2022	2023
1.000	897

Potentially unnecessary antibiotic prescribing

2022: Before intervention	2023: After intervention
56.1%	58.6%

Non-first line antibiotic choices

2022: Before intervention	2023: After intervention
45.5%	56.9%

Percentage of unnecessary antibiotic prescribing and non-first line antibiotic choices before and after the intervention and intervention effect:

NURSING HOME												
Country	Unnecessary antibiotic prescribing						Non-first line antibiotic choices					
	Before		After		Intervention effect (%)	P	Before		After		Intervention effect (%)	P
	n	%	n	%			n	%	n	%		
France	42	57.1	33	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	86.6	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

n=number

ECONOMIC IMPACT OF THE PROJECT

HAPPY PATIENT could achieve significant savings in the healthcare budgets of the European Union

HAPPY PATIENT project has a cost-effectivenes analysis regarding the recorded improvements and concludes, through two different scenarios, the following:

- **Realistic scenario:** We would have an **ATB prescription redimensionar** of **23 million**, which would represent a **cost saving of 114 million euros annually**.
- **Optimistic scenario:** we would have an **ATB prescription reduction** of **47 million**, which would represent a **cost saving of 385 million euros annually**.

These estimates were calculated through the application of **a coefficient that considers**:

1. Population per country
2. Antibiotic prescription ratio
3. Percentage of unnecessary prescriptions
4. Different scenarios of unnecessary prescription reduction, as well as the cost of antibiotic prescription.

It is noteworthy that sensitivity analyses were conducted using extreme values for various estimates, including unit costs and the prevalence of adverse events.

Additionally, detailed measurements of costs associated with antibiotic consumption, adverse events, and antimicrobial resistance were considered for each target country. These data included information such as the unit cost of each antibiotic, common daily dosage, the percentage of adverse events requiring medical attention or hospitalization, and costs associated with antimicrobial resistance. This comprehensive approach ensures the robustness and reliability of our economic projections

CONCLUSIONS

HAPPY PATIENT

one of the most ambitious projects that have been carried out in Europe, provides promising results to combat the global health issue posed by antimicrobial resistance.

Despite the high use of antibiotics and the growing development of antimicrobial resistance, **only a few initiatives have been carried out** to reduce the inappropriate use of antibiotics **in more than one setting**.

The **HAPPY PATIENT** project constituted a pragmatic study where registration of patients was performed in four different natural practice settings in five different countries, demonstrating a **significant reduction of unnecessary antibiotics in general practice and a better dispensing process in community pharmacies**, while showing no or limited effect in the other two clinical settings.

The high variability of the five participating countries, with different backgrounds, healthcare systems and antibiotic prescribing rates suggests that generalizing the results to a wide range of settings and healthcare organisations should be done with caution.

Four outpatient settings and five countries have been able to **collaborate to reduce the potentially unnecessary use of antibiotics** at a time when the fight towards antibiotic resistance has become one of the most urgent issues in public health.

This project, financed with European funds, represents a big step forward to address the serious health problem that antimicrobial resistance already represents, and which will be extremely worrying for future generations.

From the **HAPPY PATIENT** consortium, we advocate the implementation of more projects of these characteristics and of this depth, which, through knowledge and collaboration between different countries and scientific organizations, promote a better future that guarantees safety of patients and quality of life of the population.

THE HAPPY PATIENT CONSORTIUM: A MULTIDISCLIPLINARY AND EXPERIENCED TEAM FROM AROUND EUROPE

The HAPPY PATIENT consortium has had a wide diversity of geographical and professional coverage throughout the European Union during its duration from 2021 to 2023.
Thus, the partners of this team are the following:

Academia research and clinical practice

Professional umbrella organisations

- Institut Català de la Salut (ICS)
- Institut Universitari d'Investigació en Atenció Primària (IDIAP Jordi Gol)
- Kobenhavns Universitet (UCPH)
- Syddansk Universitet (RUPO)
- Norce Norwegian Research Center (NORCE)
- Region Hovedstaden (CAPREG)
- Rijksuniversiteit Groningen (RUG)
- University of Las Palmas de Gran Canaria (ULPGC)
- Fundación Parque Científico Tecnológico
- Center Hospitalier Universitaire de Nice (CHUNICE)
- Mano Seimos Gydytojas (FDC), Universytet Medyczny W Lodzi. (MUL)
- Panepistimio Kristis (UOC)
- Sociedad Española de Medicina de Familia y Comunitaria (semFYC)
- Europaische Vereinigung fur Klinische Pharmakologie und Therapie EV (EACPT)
- Center Hospitalier Universitaire de Rennes (CHURE)
- Universitat Internacional de Catalunya (UIC)

HAPPY PATIENT

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