






Effect of a multifaceted intervention on potentially unnecessary antibiotic prescriptions in general practice, out-of-hours services, and nursing homes in Spain

Efecto de una intervención polifacética en la prescripción antibiótica potencialmente innecesaria en medicina general, servicios de urgencias y residencias geriátricas en España

Ana García-Sangenís^{1,2} , Fabiana Raynal-Florianó³ , Beatriz González López-Valcárcel³ ,
Laura Vallejo-Torres³ , Carl Llor^{1,2*} 
HAPPY PATIENT Study Group

¹Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol, Barcelona, Spain

²CIBER Enfermedades Infecciosas, Instituto de la Salud Carlos III, Madrid, Spain

³Department of Quantitative Methods for Economics and Management, University of Las Palmas de Gran Canaria Las Palmas de Gran Canaria, Spain

Received: February 19, 2025

Accepted: March 19, 2025

Published: March 27, 2025

*Correspondence: Carl Llor. carles.ller@gmail.com

Abstract

Objective: To evaluate the impact of a multifaceted antimicrobial stewardship intervention on potentially unnecessary antibiotic prescribing.

Material and methods: Before and after quality control study carried out in three different settings—general practice, out-of-hours services, and nursing homes—in Spain. Healthcare professionals (both doctors and nurses) self-registered common infections using a specific template for each setting before (2022) and after (2023) receiving a 5-hour intervention on prudent antibiotic use.

Results: Eighty-nine professionals participated in the first registration (48 in general practice, 23 in out-of-hours services, and 15 in nursing homes), with 71 (79.8%) completing the intervention and second registration. Potentially unnecessary antibiotic prescriptions were 68.5%, 41.7%, and 77.7% in the first registration, respectively, and 61.4%, 34.8%, and 86.8% after the intervention, showing reductions of 10.4% in general practice and 16.5% in out-of-hours services, and an 11.7% increase in nursing homes, albeit without statistically significant differences.

Conclusions: The study found that this intervention slightly improved antibiotic use, with minimal impact, but worsened in nursing homes.

Keywords: Antimicrobial stewardship. Anti-bacterial agents. Primary healthcare. Medical audit.

Resumen

Objetivo: Evaluar el impacto de una intervención multifacética en la prescripción antibiótica potencialmente innecesaria.

Material y métodos: Estudio de calidad antes-después realizado en tres ámbitos distintos—medicina general, servicios de urgencias de atención primaria y residencias geriátricas—en España. Los profesionales sanitarios (tanto médicos como personal de enfermería) registraron infecciones comunes utilizando una plantilla específica para cada entorno antes (2022) y después (2023) de recibir una intervención de 5 horas sobre prescripción prudente de antibióticos.

Resultados: 89 profesionales participaron en el primer registro (48 en medicina general, 23 en urgencias y 15 en residencias), de los cuales 71 (79,8%) completaron la intervención y el segundo registro. La prescripción antibiótica potencialmente innecesaria fue 68,5%, 41,7% y 77,7% respectivamente en el primer registro, y 61,4%, 34,8% y 86,8% después de la intervención, mostrando reducciones del 10,4% en medicina general y 16,5% en urgencias y aumento del 11,7% en residencias, sin diferencias estadísticamente significativas.

Conclusiones: La intervención mejoró ligeramente la prescripción antibiótica después de la intervención, con mínimo impacto. En residencias geriátricas, su calidad empeoró.

Palabras clave: Programa de optimización de antimicrobianos. Antibióticos. Atención primaria. Audit Médico.

Introduction

The main strategy to combat antimicrobial resistance is to reduce unnecessary antibiotic use, especially for respiratory and urinary tract infections. Addressing overuse in these contexts is crucial, as it contributes to the development of resistant bacteria that are harder to treat. Focusing on community-acquired infections is vital for enhancing antimicrobial stewardship, which aims to optimise antibiotic use to improve patient outcomes while minimizing harm, such as the emergence of resistance [1]. While many initiatives have targeted antibiotic misuse, few have proven effective. A major challenge is that while numerous interventions have been introduced, many have failed to produce lasting changes in prescribing behaviours or have had limited reach and impact. Furthermore, these initiatives often focus on isolated settings, such as hospitals or specific healthcare systems, rather than addressing the broader, interconnected nature of antimicrobial resistance across different settings [2]. The HAPPY PATIENT project (<https://happypatient.eu/>) is the first to evaluate the impact of such an intervention across diverse patient-centred settings, aimed at improving appropriate antibiotic prescribing for common infections.

Material and methods

Study design and settings

A prospective, non-randomised, before–after study was conducted across five European countries (France, Greece, Lithuania, Poland, and Spain) in four patient-centred settings (general practice, out-of-hours services, nursing homes, and community pharmacies) [3]. This report presents the results from the three medical settings in Spain. Healthcare professionals (HCPs), including both doctors and nurses, were recruited to self-register their clinical practice before and after receiving a multifaceted intervention

on prudent antibiotic prescribing. The first registration occurred from February to April 2022, and the second from February to April 2023. The study was approved by the Ethical Committee of Clinical Research (code 21/120-P).

Data collection

Data were collected using the Audit Project Odense (APO) methodology, a self-registry system with a simple reporting template (**Suppl. Figures 1-3**) [4]. Specific templates were created for each setting. In general practice and out-of-hours services, HCPs filled out a template for each consecutive patient with an infection during the registration periods. For nursing homes, data on all antibiotic-treated cases were collected. HCPs recorded patient details, symptom duration, symptoms, examinations performed, diagnoses, treatments, and other setting-specific information.

A quality indicator of potentially unnecessary antibiotic prescribing was developed, defined as the prescription of antibiotics when not required based on the registration data. This quality indicator was developed in collaboration with experts in the consortium (**Suppl. Figures 4-6**) [5].

Intervention

In November 2022, the HCPs participated in face-to-face or online meetings, in which they received a 5-hour multifaceted intervention on prudent antibiotic use. The intervention included a one-hour presentation on the purpose of the project, and the threat of antimicrobial resistance, followed by individual feedback on the first registration results and a two-hour discussion group to identify potential quality issues, and receive peer feedback. A two-hour communication skills workshop, using role-playing scenarios for consultations on common infections, was conducted,

also covering communication tools, such as brochures and handouts, to address knowledge gaps and misconceptions about antibiotic use. Additionally, a voluntary three-hour e-learning course was offered, covering key aspects of the project, including a quiz on infection management, appropriate antibiotic use, the natural course of infections, and updated clinical guidelines for diagnosis and treatment.

Ethics

The study has been assessed and approved by the Ethics and Research Committee of the centre (code 21/120-P).

Statistical analysis

The minimum number of professionals per audit cycle was estimated assuming each participant registered approximately 25 cases. A sample size of 25 per setting was calculated, considering a 15% decrease in antibiotic prescribing after the intervention (from 40% before to 25% after), a 5% significance level (two-sided), 80% power, and a within-practice correlation coefficient of 0.1. The impact of the intervention was assessed by comparing unnecessary prescribing rates between the two registration periods. Chi-squared tests were used to evaluate changes in the frequency of potentially unnecessary prescriptions, with statistical significance set at a P-value of less than 0.05. Data analysis was performed using Stata v16.

Results

Participants

A total of 89 HCPs participated in the first registration period (48 in general practice, 23 in out-of-hours services, and 15 in nursing homes), of whom a total of 71 (79.8%) undertook the intervention and participated in the second registration period. 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). General practice was the setting with the maximum number of registrations, with a total of 1,220 community-acquired infections during the initial registration and 1,211 cases during the second audit. **Table 1** shows the number of registrations in two periods, the different infections recorded, and the number of antibiotics administered.

Change in the potentially unnecessary antibiotic use in the different settings

As shown in **Figure 1**, in the general practice setting, the prescription of potentially unnecessary antibiotics was 68.5% in the first registration and 61.4% after the intervention, with a non-significant reduction of 10.4%

($p=0.11$). Doctors participating in out-of-hours services prescribed potentially unnecessary antibiotics in 41.7% and 34.8% of cases during the two registration periods, respectively, showing a non-significant reduction of 16.5% ($p=0.17$). The results for nursing homes differed, with a slight but non-significant increase in the number of unnecessarily prescribed antibiotics in the second registration compared to the first (77.7% vs. 86.8%; 11.7% increase after the intervention, $p=0.06$).

Discussion

The main results of this study clearly indicate that this 5-hour multifaceted intervention led to a slight, albeit not statistically significant, improvement in antibiotic prescriptions, but failed in nursing homes, where potentially unnecessary antibiotic prescriptions worsened after the intervention.

The study has several limitations. The before-and-after design without a control group is a clear limitation. In uncontrolled before-and-after studies, the assumption of causal inference regarding changes observed before and after the intervention is less robust than it would be if a control group were included for comparison [6]. A control group helps provide evidence that changes occurring over time were not due to natural temporal trends or unmeasured events that coincided with the intervention studied. However, the audit registration was performed in two consecutive years during the same months, and no other interventions were provided during this period. While the risk of unidentified confounders remains, it is unlikely that this significantly affected the results of our study. Socio-economic, cultural, or patient pressure factors were not considered in general practice or out-of-hours services, although patient pressure was addressed in nursing homes [7]. HCPs participated voluntarily, which may have introduced selection bias, as volunteers may be more engaged in quality improvement. Clinical outcomes were not assessed, making it unclear if complication rates differed between groups, although patient referrals to hospitals were recorded. The self-registration process may have influenced prescribing behaviour, but the APO methodology has shown high reliability [4]. Another limitation is potential diagnostic misclassification bias, as treatment decisions may influence diagnoses. Additionally, pandemic fatigue could have affected the motivation of HCPs during the initial registration in 2022, which observed higher rates of viral infections. Despite these limitations, the strengths of this study include a large number of HCPs, low dropout rates, and real-life practice settings, making the findings relevant for understanding antibiotic prescribing in everyday healthcare environments.

Table 1. Demographic data and types of infections reported in the three settings during the two registration periods.

| Settings and infections | 2022 | 2023 |
|--------------------------------------|-------------|-------------|
| | n (%) | n (%) |
| General practice | | |
| Number of infections registered | 1,220 | 1,211 |
| Age, mean (SD) | 46.7 (21.2) | 46.2 (22.3) |
| Female gender | 755 (61.9) | 785 (64.8) |
| Types of infections | 1,220 | 1,211 |
| COVID-19 | 160 (13.1) | 25 (2.1) |
| Common cold or flu infection | 343 (28.1) | 492 (40.6) |
| Acute otitis media | 38 (3.1) | 42 (3.5) |
| Acute rhinosinusitis | 35 (2.9) | 73 (6.0) |
| Acute pharyngotonsillitis | 141 (11.6) | 164 (13.5) |
| Acute laryngitis/tracheitis | 12 (1.0) | 24 (2.0) |
| Acute bronchitis | 98 (8.0) | 154 (12.7) |
| Pneumonia | 16 (1.3) | 31 (2.6) |
| COPD exacerbations | 36 (3.0) | 40 (3.3) |
| Urinary tract infections | 270 (22.1) | 118 (9.7) |
| Unknown | 73 (6.0) | 50 (4.1) |
| Infections treated with antibiotics | 472 (38.7) | 392 (32.4) |
| Out-of-hours services | | |
| Number of infections registered | 468 | 403 |
| Age, mean (SD) | 41.2 (20.4) | 40.6 (19.2) |
| Female gender | 243 (52.0) | 208 (51.6) |
| Types of infections | | |
| COVID-19 | 62 (13.2) | 5 (1.2) |
| Common cold or flu infection | 105 (22.4) | 118 (29.3) |
| Acute otitis media | 8 (1.7) | 10 (2.5) |
| Acute rhinosinusitis | 22 (4.7) | 8 (2.0) |
| Acute pharyngotonsillitis | 83 (17.7) | 86 (21.3) |
| Acute bronchitis | 24 (5.1) | 42 (10.4) |
| Pneumonia | 13 (2.8) | 18 (8.7) |
| COPD exacerbations | 10 (2.1) | 10 (2.5) |
| Cystitis | 86 (18.4) | 66 (16.4) |
| Pyelonephritis | 19 (4.1) | 11 (2.7) |
| Unknown | 44 (9.4) | 27 (6.7) |
| Infections treated with antibiotics | 187 (40.0) | 181 (44.9) |
| Nursing homes | | |
| Number of infections registered | 318 | 274 |
| Age, mean (SD) | 85.5 (9.0) | 87.0 (8.5) |
| Female gender | 228 (76.3) | 208 (75.9) |
| Type of infections | | |
| Urinary tract infections | 176 (55.3) | 145 (22.9) |
| Respiratory tract infections | 78 (24.5) | 182 (33.6) |
| Skin and soft tissue infections | 32 (10.1) | 23 (8.4) |
| Other infections | 27 (8.5) | 13 (4.7) |
| Infections treated with antibiotics* | 318 (100.0) | 274 (100.0) |

Data are reported as n (%) unless otherwise stated.

*Nurses were requested to register all the infections treated with antibiotics.

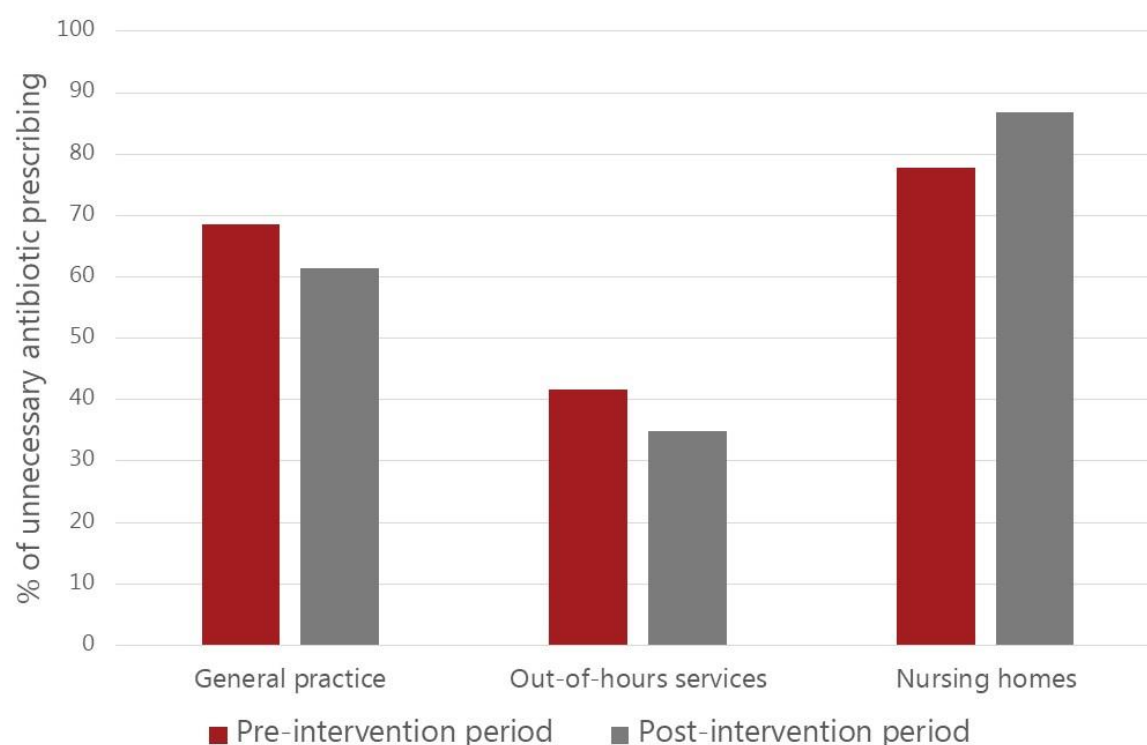


Figure 1. Impact of the multifaceted intervention on unnecessary antibiotic use in three settings.

Several approaches to minimize unnecessary antibiotic use include antimicrobial stewardship programmes, which typically slightly decrease outpatient antibiotic prescription. Peer comparison audits and feedback, which take into account not only clinical but also psychological and social factors, and the use of decision aids have been shown to be effective, leading to reductions of up to 20% [8-11]. However, it remains unclear which factors have the most significant influence on prescribing behaviour. Furthermore, the implementation of these programmes in primary care settings is inconsistent, and their effectiveness tends to diminish over time. The findings of this study regarding general practice and out-of-hours service settings align with existing evidence, although no statistically significant differences were observed. This highlights the need for exploring alternative, creative, and innovative strategies to more effectively tackle the issue of unnecessary antibiotic prescribing.

The results observed in nursing homes, however, are of concern and suggest that the intervention did not yield the expected outcomes. There are several factors that may help explain why the intervention was deemed unsatisfactory in this setting. While nurses make up the majority of HCPs in nursing homes, the responsibility for prescribing antibiotics ultimately lies with doctors. The goal of the intervention was to empower nurses more effectively, encouraging them to play a more active role in truly diagnosing urinary

tract infections and antibiotic stewardship and, as a result, reduce unnecessary antibiotic use. However, the data from the second round of assessment showed even poorer outcomes. This unexpected decline in results raises important questions about the dynamics of antibiotic prescribing in nursing homes. One potential explanation could be that nurses, despite their key role in patient care, may not have sufficient authority or influence over prescribing decisions, which remain under the control of physicians. Furthermore, the complexity of long-term care environments—where patients often have multiple comorbidities, and the risk of infection and the turnover of professionals are high—could make it more challenging to implement effective antimicrobial stewardship practices [12]. It is clear that a one-size-fits-all strategy may not be effective in this context. A more nuanced approach, perhaps one that includes closer collaboration between nurses and doctors, as well as tailored training and support for both groups—covering infection prevention and control elements and increasing the implementation of hygiene measures aimed at reducing infections—may also be necessary to address the unique challenges of reducing unnecessary antibiotic use in nursing homes [13].

Acknowledgements

We would like to acknowledge the contribution of the other members of the HAPPY PATIENT project: Ana Moragas, Ramon Monfà, Stella Mary, Rosa Morros,

Lars Bjerrum, Athina Chalkidou, Jesper Lykkegaard, Malene Plejdrup Hansen, Jonas Kanstrup Olsen, Jens Søndergaard, Anders Munck, Susanne Døssing-Berntsen, Nina Camilla Døssing-Poulsen, Jette Nygaard Jensen, Matilde Bøgelund Hansen, Ingrid Rebnord, Bent-Håkan Lindberg, Katja Taxis, Maarten Lambert, Ruta Radzeviciene, Lina Jaruseviciene, Pia Touboul-Lundgren, Pascale Bruno, Anna Kowalczyk, Maciej Godycki-Cwirko, Christos Lionis, Maria-Nefeli Karkana, Marilena Anastasaki, Pere Vilanova, Nieves Barragán, Marta Ricart, Sergi Briones, María Rodríguez, Lucía Arias, Sara Davies, Pierre Marquet, Pierre Tattevin, Alicia Borràs, Ria Benkő, and Marine Cailleaux.

Funding

This project is co-funded by the European Union's Third Health Programme (2014-2020), grant number 900024. The content of this manuscript represents the views of the author only and is their sole responsibility; it cannot be considered to reflect the views of the European Commission and/or the Health and Digital Executive Agency (HaDEA), replacing the former CHAFAEA since April 1, 2021, or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

Conflict of interest

The authors declare that they have no conflict of interest.

Author contributions

Conceptualization, A.G-S. and C.L.; methodology, A.G-S., B.G.L-V. and C.L.; software, A.G-S.; validation, B.G.L-V. and L.V-T.; formal analysis, F.R-F., B.G.L-V. and L.V-T.; investigation, C.L.; resources, A.G-S. and C.L.; data curation, B.G.L-V.; writing—original draft preparation, C.L.; writing—review and editing, C.L.; visualization, A.G-S.; supervision, B.G.L-V.; project administration, A.G-S.; funding acquisition, C.L. All authors have read and agreed to the published version of the manuscript.

Supplementary data

Supplementary Figures 1–6 are available as [supplementary data](#) on REQ online.

References

1. Majumder MAA, Rahman S, Cohall D, Bharatha A, Singh K, Haque M, et al. Antimicrobial stewardship: Fighting antimicrobial resistance and protecting global public health. *Infect Drug Resist.* 2020;13:4713–4718. <https://doi.org/10.2147/IDR.S290835>.
2. Dyar OJ, Beović B, Vlahović-Palčevski V, Verheij T, Pulcini C; on behalf of ESGAP (the ESCMID [European Society of Clinical Microbiology and Infectious Diseases] Study Group for Antibiotic Policies). How can we improve antibiotic prescribing in primary care? *Expert Rev Anti Infect Ther.* 2016;14(4):403–413. <https://doi.org/10.1586/14787210.2016.1151353>.
3. Bjerrum A, García-Sangenís A, Modena D, Córdoba G, Bjerrum L, Chalkidou A, et al. 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;23(1):102. <https://doi.org/10.1186/s12875-022-01710-1>.
4. Hansen MP, Lykkegaard J, Søndergaard J, Munck A, Llor C. How to improve practice by means of the Audit Project Odense method. *Br J Gen Pract.* 2022;72:235–236. <https://doi.org/10.3399/bjgp22X719417>.
5. García-Sangenís A, Lykkegaard J, Hansen MP, González López-Valcárcel B, Raynal F, Vallejo-Torres L, et al. Impact of a multifaceted intervention programme on antibiotic prescribing and dispensing in four patient-centred settings in five European countries. The HAPPY PATIENT project. *Fam Pract.* 2025;42(2):cmæ064. <https://doi.org/10.1093/fampra/cmæ064>.
6. Harris AD, Bradham DD, Baumgarten M, Zuckerman IH, Fink JC, Perencevich EN. The use and interpretation of quasi-experimental studies in infectious diseases. *Clin Infect Dis.* 2004;38(11):1586–1591. <https://doi.org/10.1086/420936>.
7. Baker R, Robertson N, Farooqi A. Audit in general practice: factors influencing participation. *BMJ.* 1995;311(6996):31–34. <https://doi.org/10.1136/bmj.311.6996.31>.
8. King LM, Fleming-Dutra KE, Hicks LA. Advances in optimizing the prescription of antibiotics in outpatient settings. *BMJ.* 2018;363:k3047. <https://doi.org/10.1136/bmj.k3047>.
9. Xu AXT, Brown K, Schwartz KL, Aghlmandi S, Alderson S, Brehaut J, et al. Audit and feedback interventions for antibiotic prescribing in primary care: A systematic review and meta-analysis. *Clin Infect Dis.* 2024;ciae604. <https://doi.org/10.1093/cid/ciae604>.
10. Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, et al. Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev* 2012;6:CD000259. <https://doi.org/10.1002/14651858.CD000259.pub3>.
11. Steurer J, Held U, Spaar A, Bausch B, Zoller M, Hunziker R, et al. A decision aid to rule out pneumonia and reduce unnecessary prescriptions of antibiotics in primary care patients with cough and fever. *BMC Med.* 2011;9:56. <https://doi.org/10.1186/1741-7015-9-56>.
12. Bocquier A, Erkilic B, Babinet M, Pulcini C, Agrinier N; ORANEAT Study Group. Resident-, prescriber-, and facility-level factors associated with antibiotic use in long-term care facilities: a systematic review of quantitative studies. *Antimicrob Resist Infect Control.* 2024;13(1):29. <https://doi.org/10.1186/s13756-024-01385-6>.
13. Gonthier D, Ricci L, Buzzi M, Birgand G, Kivits J, Agrinier N. Exploration of interprofessional collaboration for the diagnosis of infections and antibiotic prescription in nursing homes using multiple case study observational research. *JAC Antimicrob Resist.* 2025;7(1):dlæ205. <https://doi.org/10.1093/jacamr/dlae205>.