Antibiotic prescription in primary care from the perspective of family physicians: a qualitative study

Salih Hosoglu (shosoglu@uni-koeln.de)
Universitat zu Koln Medizinische Fakultat

Annika Yanina Claßen
Universitat zu Koln Medizinische Fakultat

Research article

Keywords: qualitative evaluation, antibiotics, inappropriate prescription, family physicians, primary care

DOI: https://doi.org/10.21203/rs.3.rs-44066/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

Read Full License
Abstract

Background Antibiotic consumption rates increase worldwide steadily. Turkey is now top on the list of global consumption and a prototype of excessive use of antibiotics. In the last two-decades, family physicians (FPs) have become key figures in the healthcare system. The aim of this study is to understand the reasons for inappropriate prescription and to elicit suggestions for ways of improving antibiotic use in primary care from doctors themselves.

Methods This is a qualitative study using semi-structured interviews with key individuals. Fourteen FPs from different parts of Turkey participated in these interviews. They were questioned on major indications for antibiotic prescription, reasons for inappropriate antibiotic prescription, obstacles to decision making in antibiotic use and their suggestions for improving antibiotic use. The interviews were recorded, transcribed, and analyzed for common themes. Thematic coding was used in the formulation of themes.

Results Interviewees emphasized the coercive factors that lead to inappropriate antibiotic prescription: patient expectations, defensive medical decision making, constraints due to workload and limited access to laboratories. The most powerful suggestions for improving the quality of antibiotic prescription were public campaigns, improvements in the diagnostic infrastructures of primary care centers and enhancing the social status of FPs. The FPs expressed strong concerns related to the complaints that patients make to administrative bodies.

Conclusions Physicians in primary care work under immense pressure stemming mainly from workload, patient expectations and obstacles to diagnostic processes. Improving the social status of physicians, increasing public awareness and the facilitation of diagnostic procedures were the methods suggested for increasing antibiotic prescription accuracy.

Background

Antibiotic consumption rates have increased steadily over the last fifteen years and the most recent reports show this trend is continuing. Between 2000 and 2015, global antibiotic consumption increased by 65%, from 21.1 billion defined daily doses (DDD) to 34.8 billion, while the antibiotic consumption rate increased by 39%, from 11.3 DDDs per 1000 inhabitants per day to 15.7 [1]. In Turkey, total antibiotic consumption was 14.62 DDD per 1000 inhabitants per day in 2001. This value increased to 31.36 in 2006, to 38.8 in 2010 and 42.3 by 2011. In 2019, Turkey was still at the top of the list of global antibiotic consumption [2]. While antibiotic consumption steadily increases, there is a parallel growth in antimicrobial resistance rates [3, 4].

The reasons for increasing antibiotic consumption in Turkey have not yet been fully evaluated. Some researchers point to the populist health policies established over the last two decades. Within this system, FPs have become the main actors in family health centers (FHC). A staggering number of antibiotics are prescribed in FHCs and data shows that the number of visits to physicians have increased year on year
Although the Ministry of Health has implemented some limitations to reduce the inappropriate prescription of antibiotics, there are no reliable reports to suggest a reduction in rates of antibiotic use [9].

A few studies have attempted to analyze physician behavior in terms of antibiotic prescription in primary care, but there have been no qualitative studies related to primary care antibiotic use in Turkey [9–12]. Antibiotic prescription in primary care deserves thorough evaluation so that cultural, economic, social, environmental and organizational dimensions can be understood [13, 14]. This study is, to our knowledge, the first qualitative study of antibiotic prescription in Turkey. Experience of Turkey could be an example for other middle-income countries about antibiotic prescription. The aims of this study are, on one hand, to understand the relevant factors involved in antibiotic prescription in primary care settings and the barriers obstructing appropriate antibiotic use, and on the other, to gain insights from FPs on potential measures that may improve the quality of antibiotic prescription.

**Methods**

In order to evaluate the experiences of primary care physicians around antibiotic prescription, we conducted semi-structured, digitally recorded interviews and transcribed them verbatim. The qualitative method of an open-ended face-to-face interview was chosen to ensure candid and truthful answers from participants.

The interview guide used was developed through a review of the literature and using themes arising from a focus group interview with FPs and specialists from different branches of medicine. The focus group discussion will be published elsewhere. We composed a screening questionnaire to recruit physicians at a national family physicians meeting in Antalya, Turkey, on 4 to 7 December 2014. Potential participants were contacted and informed about the characteristics of the study. Inclusion criteria included self-reporting of full-time medical practice in direct patient contact in a primary care setting for at least three years. Fourteen FPs were selected for the study. Thirteen of them worked in FMCs as family physicians and one worked in a private healthcare center outpatient clinic.

The interviews were all conducted by one researcher. The participants were first introduced to the study, informed of how the data collected was to be used and asked for written consent. They were then questioned about the practice setting in which they worked and the patient populations whom they served. Each interview proceeded through an ordered list of open-ended questions on major indications for antibiotic prescription in their practice, reasons for inappropriate antibiotic prescription and their suggestions for improving antibiotic stewardship (for examples of interview questions, see Appendix I).

The interview recordings were anonymized. Thematic coding was used in the analysis to identify themes using MAXQDA software (Verbi Software, Berlin, Germany). First, key domains and terms were identified. After recurrent reviewing and the progression of important phrases and terms from both data sources, a complete list of domains and themes was laid out. After the development of themes, a final analysis and interpretation was carried out.
Results

We conducted 14 interviews, each taking between 20 and 25 minutes. Eleven of the participants were male. The sample consisted of 14 physicians from different parts of Turkey. Five of them were from the metropolitan north-western cities of Istanbul and Bursa, three of them from eastern Turkey, two from the Black Sea Region in north Turkey three of them from central Anatolia, and one from a Mediterranean city. All of the participants were FPs.

The FPs served an average population of 3,780 and the average number of daily visits/examinations was approximately 58. They reported that approximately 40% of all patients were diagnosed with respiratory tract infections. Antibiotics were mainly prescribed for respiratory tract infections, urinary tract infections, skin and soft tissue infections and fever.

After analyzing the data obtained from the semi-structured interviews and coding it thematically, two main domains were identified. The first domain was “reasons for inappropriate antibiotic prescription in primary care” and the second was “suggestions for the improvement of antibiotic prescription in primary care”. Six main themes were identified within the first domain and five within the second.

Domain 1: Perceived reasons for inappropriate antibiotic prescription in primary care:

Pressure/demand of patient or their relatives (14 participants):

The most important theme that emerged regarding inappropriate antibiotic prescription in primary care, upon which almost all of the participants agreed, was to do with the pressures and demands of patients and their relatives, especially parents. Physicians often felt forced into prescribing antibiotics without compelling symptoms or findings. On this theme, participants stated that:

*Some of them are very demanding, and some do not want to use a lot of antibiotics. They keep on asking, no matter whether antibiotics are necessary or not, but I don’t care how insistent they are. But some really insist on antibiotics. Some demand injectable antibiotics immediately. (FP 12, F)*

Saving time and avoiding complaints from patients/Defensive medicine (14)

Physicians emphasized that they are expected to serve a remarkably large population, which puts them under immense pressure. Most physicians do not have enough time for more in-depth examinations or to wait for laboratory test results. All of them felt an obligation to protect themselves against accusations from patients or their relatives.

*When someone is sick, even with the flu, they want to be given antibiotics so they can keep them in reserve. We can’t say to the patient “enough” or “no.” Because there is social pressure. The neighbors, the relatives tell them “you must use antibiotics. If you don’t use antibiotics, you won’t get better.” So, it doesn’t matter if you give the patient flu medicines. They go even further, for example, and say “my*
husband or my wife, my friend, took these drugs and got better. Would you prescribe me the same drugs?" (FP 8, M)

Diagnostic uncertainty due to insufficiencies in the basic laboratory facilities of family health centers (13)

Insufficiencies in basic laboratory tests (point-of-care tests = POCTs) in primary care centers was seen as significant and one of the main reasons for antibiotic prescription. None of the participants had access to quick diagnosis facilities in their FHCs.

We use a lab sometimes, yes. So, we're looking at CBC and sedimentation. If only we had a quick diagnostic test, it would be great. The lab results do not come on the same day, they come the next day. Patients want to get better as quickly as possible, to heal as soon as possible. (FP 14, M)

Misconceptions of pharmacists (10)

One of the themes that emerged was around the misconceptions of pharmacists. The participants emphasized the major role pharmacists play in antibiotic consumption in the community. Pharmacists have a huge impact on the culture of healthcare in Turkey and they can drive patient choices and demands.

One of my most persistent issues is the direct effect pharmacists have on patients. The pressure from the pharmacists is not on us, but on the patients. It doesn't affect us. It can affect patients from villages with low levels of education. (FP 11, F)

Inadequacies in the education/training of family physicians (7)

Several FPs pointed out that they did not receive enough training after graduation. This situation contributes to the problem in practice, where physicians are unaware of the side effects of inappropriate antibiotic prescription, especially selective pressure and resistance development.

Training of doctors after graduation is required. Postgraduate education is required. Doctors should receive serious training in antibiotic use. (FP 14, M)

Low prestige of family physicians in the community (7)

The theme of FP respectability was expressed by half of the participants. They felt pressure around their public responsibilities from many fronts. On one hand they are expected to accommodate patient expectations, on the other they must keep their autonomy.

It's a family medicine thing. The physician examines the child, who has a cough or something, auscultates his lungs, says nothing, gives a cold medicine, says manage, use them and see me again. That evening they go to a private hospital, receive ceftriaxone, they say pneumonia, sir. Then the father comes, “you said nothing to my child, look what they gave” he says. Then he listens to his lungs again, nothing again. (FP 5, M)
Domain 2: Suggestions for improving antibiotic prescription in primary care

Improving diagnostic infrastructures in primary care centers (13)

All of the physicians were of the same opinion on point-of-care tests (POCTs), saying they would be helpful in avoiding unnecessary antibiotic prescription. They complained about the lack of quick laboratory tests in their daily diagnostic processes. They expressed that at the very least, a complete blood count test result should be available within a few hours for these patients.

*My suggestion is that we get tests, throat swab tests, providing immediate results. I think that makes sense. Even that alone is enough. Or, you know, lab support that works immediately on the hemogram, working in the morning and giving us results in the afternoon. A quick hemogram could be enough. But I think the most important thing is the throat swab test.* (FP 12, F)

Qualifying education of family physicians (13)

There was consensus on the necessity of training in antibiotic use and antimicrobial resistance. The unethical behavior of some damages the position and image of others in the community.

*First of all, it is necessary to increase the awareness of doctors about the prescriptions they write. Doctor training is an absolute must.* (FP 11, F)

Public campaigns and educational materials for patients (13)

The participants attached importance to public campaigns and mass education on antibiotic use. Their expectation is that a public campaign could reduce the pressure they are put under by patients to prescribe antibiotics.

*It’s all about education. The doctors could educate their patients and their relatives using brochures. This would raise awareness just like the vaccination campaign did. People believe everything they hear in the local media etc. and certainly don’t forget what they see. So, I think visual material is important.* (FP 1, M)

Improving the reputation of family physicians in the community (10)

The majority of the participants expressed that they do not feel enough protection from patients and their relatives. Greater prestige in the community would make physicians more resistant to demands from patients for inappropriate antibiotic prescription.

*Patients need to approach the doctor like a doctor, so the state must protect the doctor. Doctors need their social position and perception to be improved.* (FP 3, F)

Restricting the access to antibiotics for patients (8)

More than half of the participants suggested some kind of restriction on and/or extra payment for antibiotics. They pointed to how easy it is to purchase antibiotics from pharmacies without a
Pharmacies must be sanctioned. That is, just as opiates cannot be given without prescription, there should be a penalty when antibiotics are given without a prescription. A 10-year-old can go and give money and get antibiotics. Opiates or drugs are subject to control and cannot be given without a prescription - the same should apply to antibiotics. But there is no control, nothing, it cannot be prevented. *(FP 1, M)*

**Discussion**

This study presents the results of qualitative and semi-structured interviews with primary care clinicians in Turkey, looking at their perceptions with regards to antibiotic prescriptions, barriers to appropriate antibiotic use and their thoughts on strategies to improve the situation. Remarkably, all of the FPs agreed on the role of pressure/demand from patients or their relatives and shared concern about how liability impacts inappropriate antibiotic prescription. The physicians stated that there continues to be a high level of demand for antibiotics, and this remains the largest perceived driver of antibiotic prescription.

This study uncovered that one of the main reasons for avoiding confrontation with patients is related to the economic situation in primary care. This worry was stated clearly by some participants, implied by others. The other important concern related to patient demand was workload and time constraints. FPs serve large populations and have a very limited amount of time for each individual patient, so any kind of additional dispute with patients or accompanying persons is impossible. Physicians are nudged towards prescribing what patients demand in order to avoid such complications.

The fear of liability leads to defensive practice among FPs. Several studies have shown that when physicians perceive a risk of litigation, they may adopt defensive practice as a way to avoid it or to guarantee a form of defense in the case of a malpractice complaint [15–17]. In this study, the participants underlined strategies they adopt to avoid confrontation in their daily practice that can arise due to multiple factors. FPs are involved in a juggling act, trying to utilize their limited time in the best way possible, avoid complaints of malpractice, and deal with all the pressures applied by patients.

Diagnostic uncertainty may be a key driver of antimicrobial prescription for common infections in primary care, especially when associated with the fear of liability and patient demands. Previous studies have suggested considering delaying antibiotic prescription in order to reduce antibiotic use when there is diagnostic uncertainty as well as uncertainty as to bacterial/viral etiology [18–20]. Physicians in primary care settings in Saudi Arabia have stated that they prescribe antibiotics for high fever in the absence of laboratory confirmation [21]. In our study, a majority of the participants emphasized that diagnostic uncertainty, due to a lack of access to diagnostic testing, nudges them into prescribing antibiotics.

FPs also complained that patients are misled by pharmacists. Patients tend to have close relations with pharmacists and follow their suggestions. Medication can be purchased directly from a pharmacy without a prescription, which is subsequently demanded from their FP. Pharmacists are influencers on
antibiotic use in many countries, especially in primary care and physicians sometimes blame them for antibiotic misuse and resistance [21, 22].

Improving antibiotic use was one of the most discussed domains in our study. Almost all of the participants expressed similar suggestions. FPs predict that the establishment of adequate diagnostic infrastructures in FHCs would improve antibiotic use markedly. POCTs can provide strong evidence to combat patient demands for antibiotics in primary care centers. Several studies on the potential benefits of using POCTs in acute respiratory infections in primary care medicine have recently been published. This research points to several barriers to the clinical use of many POCTs and the importance of appropriate training for clinicians and support tools for use in practice [23–25].

One of the remarkable themes was around the content and quality of the undergraduate and postgraduate education of family physicians. Studies have reported contradictory results and pointed out several related factors about the impacts of educational intervention. Most of the studies support the efficacy of long-term antimicrobial stewardship programs [26, 27].

The participants agreed on the efficacy of public campaigns for improving antibiotic prescription and the use of educational material to raise patient awareness. They emphasized that effective public campaigns would be helpful in reducing the demand for antibiotics. Previous studies have supported this suggestion. However, there is no data on the sustainability of reductions in antibiotic prescription after an intervention [28].

Participants also suggested improving the social standing of family physicians in the community. One of the themes that came out of the interviews around improving antimicrobial prescription was the reduction of outpatient access to antibiotics. This could include banning the sale of antibiotics without prescription, but such restrictions are not always effective in daily practices [29].

This study has many strengths. One of them is the design of the questionnaire, which was developed after a series of focus group discussions and a wide-ranging review of the literature (Appendix 1). The participants worked in different parts of the country and this diversity provides a broad representation. The participants are key actors in inappropriate antibiotic use in the healthcare system, as most antibiotics are prescribed within an ambulatory setting. Their perceptions are very important in understanding real problems and solutions. This study could help to understand the countries which have excessive antibiotic prescription rates.

This qualitative study has also some limitations. All but one of the participants were public employees and were careful about criticizing the implementation of official health policy. They preferred to speak indirectly about some problems. Our sample size was also relatively small. However, they also voiced the problems and experiences of their colleagues in the interviews. The family medicine system is relatively new and some of the participants did not have long-term experience within this system. In fact, the intention of this study was to outline the situation healthcare finds itself in, in the early days of a new system.
Conclusion

This qualitative study analyzed the perception of family physicians with regards to antibiotic use in their daily practice. There was consensus that pressure from patients, preventive practice and the absence of point-of-care tests in primary care centers are the most important factors in unnecessary antibiotic prescription. They suggested that providing quick diagnostic tests, better training of physicians, public campaigns for patients and better social standing for physicians would improve antibiotic prescription.

Abbreviations

FPs: Family physicians; DDD: Defined daily doses; FHC: Family health center; M: Male; F: Female; POCT: Point of Care Tests

Declarations

Ethics approval and consent to participate

This study was approved by Dicle University, Faculty of Medicine, Diyarbakir, Turkey, Ethic Committee of Non-interventional Clinical Researches (30 May 2014, Decision No: 222). Written consent has been obtained from each participant.

Consent for publication

Not necessary.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests/Conflicts of interest

There is no conflict of interest in this study.

Funding

There was no financial support for this study.

Acknowledgement

This study was presented as an ePoster at the 26th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in Amsterdam, the Netherlands, 9 to 12 April 2016.

Author contributions
SH conceived and designed the study, performed interviews and analysis, and wrote the manuscript. SH approved the final manuscript.

AL contributed to analyze of data and writing the manuscript.

All authors have read and approved the manuscript.

Author information:

During this study, SH worked at Dicle University Hospital, Diyarbakir, Turkey. Since 2019, SH has worked at the University Hospital Cologne, Department of Internal Medicine, Cologne, Germany.

AL works as a research resident at the University Hospital Cologne, Department of Internal Medicine, Cologne, Germany.

References

1- Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, Goossens H, Laxminarayan R. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci USA, 2018; 115(15):E3463-70.

2- Hosoglu S, Karabay O. Healthcare expenditures and increasing antimicrobial consumption in Turkey. J Chemother, 2012; 24(6):344-7.

3- Antimicrobial Resistance: Global Report on Surveillance, 2014, World Health Organization. https://apps.who.int/iris/bitstream/handle/10665/112642/9789241564748_eng.pdf. Accessed 13 December 2019.

4- Central Asian and European Surveillance of Antimicrobial Resistance: Annual report 2018, World Health Organization. https://apps.who.int/iris/handle/10665/324806. Accessed 12 December 2019.

5- Robertson J, Iwamoto K, Hoxha I, Ghazaryan L, Abilova V, Cvijanovic A, Pyshnik H, Darakhvelidze M, Makalkina L, Jakupi A, Dzhakubekova A, Carp A, Cizmovic L, Rachina S, Radonjic V, Yusufi S, Aksoy M, Ibragimova M, Godman B, Kluge H, Pedersen HB. Antimicrobial Medicines Consumption in Eastern Europe and Central Asia – An Updated Cross-National Study and Assessment of Quantitative Metrics for Policy Action. Front Pharmacol, 2019; 9:1156.

6- Hosoglu S, Karabay O. Healthcare expenditures and increasing antimicrobial consumption in Turkey, J Chemother, 2012; 24(6):344-7.

7- Baris E, Mollahaliloglu S, Aydin S. Healthcare in Turkey: from laggard to leader. BMJ, 2011; 342:c7456.

8- McCourtie SD. Turkey: Greater availability of primary care services results in high patient and physician satisfaction, Primary Health Care Performance Initiative 2015. https://improvingphc.org/turkey-greater-
availability-primary-care-services-results-high-patient-and-physician-satisfaction. Accessed 07 January 2020

9- Number of doctor visits per capita in selected countries as of 2018. Global No.1 Business Data Platform. https://www.statista.com/statistics/236589/number-of-doctor-visits-per-capita-by-country. Accessed 07 January 2020

10- Canli H, Saatci E, Bozdemir N, Akpinar E, Kiroglu M. The antibiotic prescribing behaviour of physicians for acute tonsillopharyngitis in primary care. Ethiop Med J, 2006; 44:139-143.

11- Leblebicioglu H, Canbaz S, Peksen Y, Gunaydin M. Physicians’ antibiotic prescribing habits for upper respiratory tract infections in Turkey. J Chemother, 2002;14(2):181-184.

12- Canbaz S, Peksen Y, Tevfik Sunter A, Leblebicioglu H, Sunbul M. Antibiotic prescribing and urinary tract infection. Int J Antimicrob Agents, 2002; 20(6):407-411.

13- Sahin H, Arsu G, Köseli D, Büke C. [Evaluation of primary health care physicians' knowledge on rational antibiotic use]. Mikrobiyol Bul, 2008; 42:343-348. [English Abstract]

14- Akici A, Kalaça S, Uğurlu MU, Oktay S. Prescribing habits of general practitioners in the treatment of childhood respiratory-tract infections. Eur J Clin Pharmacol, 2004; 60:211-216.

15- Wynants LT, Peters M, Van Audenhove C, Timmerman D, Van Calster B, Jalmbrant M. The impact of complaints procedures on the welfare, health and clinical practise of 7926 doctors in the UK: a cross sectional survey. BMJ Open, 2015; 5: e006687.

16- Kosan Z, Aras A, Cayir Y, Calikoglu EO. Burnout among family physicians in Turkey: A comparison of two different primary care systems. Niger J Clin Pract, 2019; 22:1063-9.

17- Katz ED. Defensive Medicine: A Case and Review of Its Status and Possible Solutions. Clin Pract Cases Emerg Med, 2019;3(4):329-32.

18- Lane I, Bryce A, Ingle SM, Hay AD. Does locally relevant, real-time infection epidemiological data improve clinician management and antimicrobial prescribing in primary care? A systematic review. Fam Pract, 2018; 35(5):542-50.

19- Saliba-Gustafsson EA, Röing M, Borg MA, Rosales-Klintz S, Lundborg CS. General practitioners’ perceptions of delayed antibiotic prescription for respiratory tract infections: A phenomenographic study. PLoS One, 2019; 14(11):e0225506.

20- Whaley LE, Businger AC, Dempsey PP, Linder JA. Visit complexity, diagnostic uncertainty, and antibiotic prescribing for acute cough in primary care: a retrospective study. BMC Fam Pract, 2013; 14:120.
21- Al-Homaidan HT, Barrimah IE. Physicians’ knowledge, expectations, and practice regarding antibiotic use in primary health care. Int J Health Sci (Qassim), 2018;12(3):18-24.

22- Nair M, Tripathi S, Mazumdar S, Mahajan R, Harshana A, Pereira A, Jimenez C, Halder D, Burza S. “Without antibiotics, I cannot treat”: A qualitative study of antibiotic use in Paschim Bardhaman district of West Bengal, India. PLoS One, 2019; 14(6):e0219002.

23- Hardy V, Thompson M, Alto W, Keppel GA, Hornecker J, Linares A, Robitaille B, Baldwin LM. Exploring the barriers and facilitators to use of point of care tests in family medicine clinics in the United States. BMC Fam Pract, 2016;17(1):149.

24- Anthierens S, Tonkin-Crine S, Cals JW, Coenen S, Yardley L, Brookes-Howell L, Fernandez-Vandellos P, Krawczyk J, Godycki-Cwirko M, Llor C, Butler CC, Verheij T, Goossens H, Little P, Francis NA; GRACE/CHAMP INTRO team. Clinicians’ views and experiences of interventions to enhance the quality of antibiotic prescribing for acute respiratory tract infections. J Gen Intern Med, 2015;30:408-416.

25- van Hecke O, Butler C, Mendelson M, Tonkin-Crine S. Introducing new point-of-care tests for common infections in publicly funded clinics in South Africa: a qualitative study with primary care clinicians. BMJ Open, 2019; 9(11):e029260.

26- Wei X, Zhang Z, Walley JD, Hicks JP, Zeng J, Deng S, Zhou Y, Yin J, Newell JN, Sun Q, Zou G, Guo Y, Upshur REG, Lin M. Effect of a training and educational intervention for physicians and caregivers on antibiotic prescribing for upper respiratory tract infections in children at primary care facilities in rural China: a cluster-randomised controlled trial. Lancet Glob Health, 2017; 5(12):e1258-e1267.

27- Peñalva G, Fernández-Urrusuno R, Hernández-Soto R, Pajares I, Carrión L, Vázquez-Cruz I, Botello B, García-Robredo B, Cámara-Mestres M, Domínguez-Camacho JC, Aguilar-Carnerero MM, Lepe JE, de Cueto M, Serrano-Martino MC, Domínguez-Jiménez MC, Domínguez-Castaño A, Cisneros JM, PIRASOA-FIS team. Long-term impact of an educational antimicrobial stewardship programme in primary care on infections caused by extended-spectrum β-lactamase-producing Escherichia coli in the community: an interrupted time-series analysis. Lancet Infect Dis, 2020; 20:199-207.

28- Cross EL, Tolfree R, Kipping R. Systematic review of public-targeted communication interventions to improve antibiotic use. J Antimicrob Chemother, 2017; 72:975-987.

29- Shet A, Sundaresan S, Forsberg BC. Pharmacy-based dispensing of antimicrobial agents without prescription in India: appropriateness and cost burden in the private sector. Antimicrob Resist Infect Control, 2015; 4:55.

**Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.
• Appendix1.docx