ABSTRACT

Background: In 1999, the Pharmacists Association of Gipuzkoa, a Spanish province with a population of 700,000, initiated a campaign to reduce the common practice in community pharmacies of dispensing antibiotics without prescription.

Objective: The study was designed to assess the ongoing effectiveness of this program in reducing nonprescription dispensing of antibiotics.

Methods: In March 2009, 2 young women posed as simulated patients and visited each of the 280 operating community pharmacies in Gipuzkoa. In 139 of these pharmacies, randomly selected, the simulated patients feigned the symptoms of an uncomplicated urinary tract infection and requested an unspecified antibiotic. In the remaining 141, the actress requested a specific antibiotic, only describing her symptoms upon request by the dispensing staff. The rate of nonprescription dispensing had previously been estimated at 70.5% in 2000 and 42.2% in 2004. Univariate and multivariate analyses were performed, based on a number of variables related to the pharmacy and staff.

Results: In the current study, antibiotics were dispensed without prescription by 49 of 280 pharmacies (17.5%). The product- and symptom-based scenarios had similar rates of 16.3% and 18.7%, respectively. The only variables which appeared to affect the nonprescription dispensing rate were the gender of the dispenser, being males more likely to dispense (OR=3.135, 95%CI [1.286, 7.646]), and the number of previous antibiotic-awareness campaigns in which the pharmacy had participated (OR=1.057, 95% CI [1.008, 1.107]). The community population, its number of pharmacies, the years in business of each pharmacy, or its revenue, did not appear to influence the nonprescription dispensing rate.

Conclusion: A long-term multifactorial program set up by the pharmacists association of Gipuzkoa, Spain, appears to have been effective in reducing the rate at which antibiotics are dispensed without a prescription in community pharmacies.

Keywords: Anti-Bacterial Agents; Self Medication; Drug Utilization; Pharmacies; Professional Practice; Patient Simulation; Spain

IMPACTO DE UN PROGRAMA PARA REDUCIR LA DISPENSACIÓN DE ANTIBIÓTICOS SIN RECETA EN ESPAÑA

RESUMEN

Antecedentes: En 1999, el Colegio de Farmacéuticos de Gipuzkoa, una provincia española con una población de 700 000 habitantes, inició una campaña para reducir la práctica común de dispensar antibióticos sin receta.

Objetivo: Este estudio fue diseñado para evaluar la efectividad de este programa en la reducción de la dispensación de antibióticos.

Métodos: En marzo 2009, 2 mujeres jóvenes actuaron como pacientes simuladas y visitaron todas las 280 farmacias comunitarias en ejercicio en Gipuzkoa. En 139 farmacias aleatoriamente seleccionadas, las pacientes simuladas fingieron síntomas de una infección urinaria no complicada y solicitaron un antibiótico sin especificar. En las restantes 141, las actrices solicitaron un antibiótico específico, describiendo sus síntomas solo si se lo solicitaba el personal dispensador. La tasa de dispensación sin receta había sido establecida previamente en el 70.5% en 2000 y 42.2% en 2004. Se realizaron análisis univariados y multivariados basados en algunas variables relacionadas con el personal de la farmacia.

Resultados: En el presente estudio 49 de las 280 farmacias (17.5%) dispensaron antibióticos sin receta. Los escenarios de producto y de síntomas tuvieron tasas similares de 16.3% y 18.7%, respectivamente. Las únicas variables que parecían influir en la tasa de dispensación sin receta fueron el género del dispensador, siendo los hombres más proclives a dispensar (OR=3.135, IC95% [1.286, 7.646]), y el número de campañas de concienciación en las que había participado la farmacia previamente (OR=1.057, CI95% [1.008, 1.107]). La población de la localidad, su número de farmacias, la antigüedad de la farmacia o su cifra de negocios no parecieron influir en la tasa de dispensación sin receta.
Conclusión: El programa multifactorial a largo plazo del Colegio de Farmacéuticos de Gipuzkoa, España, parece que fue efectivo en la reducción de la tasa de antibióticos dispensados sin receta en farmacias comunitarias.

Palabras clave: Antibacterianos; Automedicación; Utilización de Medicamentos; Farmacias; Ejercicio profesional; Simulación de Paciente; España

INTRODUCTION

Although antibiotics represent one of the major improvements in public health, their excessive use, particularly as a result of self-medication, has led to an increasing problem in antibiotic resistance. Although, self-medication with antibiotics is most common in developing countries, developed countries in Europe are not immune. For example, a study that included 19 different European countries and regions reported rates of antibiotic self-medication ranging between 0.1 and 21%. The attitude toward self-medication appears to differ between northern and southern European countries, with countries in the southern regions having much higher rates. Self-medication with antibiotics is a major concern in Spain, whose rate of both antibiotic consumption and resistance is one of the highest in Europe. In a survey carried out in 1995 and 1996, 32.1% of antibiotics dispensed in community pharmacies were without a prescription order. Another study reported that the European Surveillance of Antimicrobial Consumption (ESAC) underestimated the extent of antibiotic consumption in Spain by between 31.6 and 34.3%, because it failed to include private physicians’ prescriptions and nonprescription sales. The magnitude of the problem was illustrated by a recent study that found that an individual posing as a patient was able to obtain antibiotics without a prescription in 54.8% of requests.

Different strategies have been employed in Spain to reduce the sale of antibiotics without prescription. In 2006, the Ministry of Health launched a mass-media advertising campaign using the message “Responsible use of antibiotics. Using them properly today, they will protect us tomorrow.” Between 2004 and 2006, a health department in the Valencia region established a multidisciplinary program targeting physicians, community pharmacies, and patients. In the same year, major physicians’ and pharmacists’ associations in Spain released a joint declaration containing directives for physicians, pharmacists, and the national healthcare administration.

Gipuzkoa is a Spanish province with a population of 700,000. In 1999, the Gipuzkoa Pharmacists’ Association, in association with the local health administration, launched a program to reduce nonprescription dispensing of antibiotics in the region’s community pharmacies. This program had three components. First, staff in community pharmacies was trained in the appropriate use of antibiotics and in the dangers of antibiotic resistance. Second, posters and leaflets were circulated to community pharmacies, primary care centers, and dental clinics, describing five basic principles on the rational use of antibiotics. In a third arm of the program, pharmacies were required to submit a report each time a patient requested an antibiotic without a prescription. In the first set of these records analyzed, pharmacists reported that 68.9% of the antibiotics they sold were dispensed without a prescription. Four further assessments were carried out between 1999 and 2004, revealing antibiotic dispensing without prescription percentages of 70.5, 67.5, 46.0, and 42.2%, respectively. The last of these assessments found that requests for nonprescription antibiotics in Gipuzkoa community pharmacies had declined in parallel, with corresponding rates of 10.6, to 8.5, 5.3, and 3.6% out of the total of antibiotics sold in the province.

Because these figures were based on community pharmacists’ self-reported data, they were possibly affected by social desirability bias and the Hawthorne effect.

Therefore, the current study aimed to assess the practice of dispensing antibiotics without prescription in Gipuzkoa community pharmacies, using simulated patients.

METHODS

Study design

In this descriptive, cross-sectional study, two young women were trained to act as simulated patients requesting antibiotics in two different scenarios. Training consisted of one three-hour session per scenario, in which the actresses were taught how they should perform, how they should answer various questions, and what information they were and were not allowed to give the pharmacy staff.

At each of the 281 pharmacies studied, one of two different request scenarios was randomly chosen to be enacted. In the symptom-based scenario, the simulated patient asked for an unspecified antibiotic after reporting symptoms of a urinary-tract infection. In the product-based scenario, the simulated patient specifically requested Augmentine® 500 mg (a combination of amoxicillin and clavulanic acid), describing symptoms of a urinary-tract infection only if questioned. In both scenarios, actresses were asked to make every attempt to purchase the drug.

Data collection

The simulated patients visited all Gipuzkoa community pharmacies in March of 2009. At the end of each purchasing attempt, the actress completed a questionnaire with information such as who initially served her, who completed the dispensing, the details of any staff identification badges, and whether a private consultation area existed and was used.

For each pharmacy visited, the database of the Pharmacists’ Association was used to retrieve information that included the population of the
municipality and the number of pharmacies it contained, the gender of the owner and their academic degrees, and the number of the staff members in the pharmacy.

To maintain confidentiality, the data were collected into two separate Excel datasheets, one for the Association data and another for the patient simulation information. Each spreadsheet contained an identification number of the pharmacy but no other identifying data. After all the data were collected, the two datasheets were merged in a way that prevented identification of the participating pharmacies.

The study was approved by the Executive board of the Gipuzkoa Pharmacists Association. Ethical approval is not required for this kind of study in Spain.

Statistical analysis

The main variable for the study was categorical: whether or not an antibiotic was dispensed. Univariate analysis was carried out using the chi-square test for categorical variables and the Mann-Whitney test for discrete and continuous variables. A multivariate analysis with a binary logistic regression was also performed.

RESULTS

Of a total of 281 pharmacies, 141 were randomly allocated to the product-based request group and 140 to the symptom-based request group. The number in the symptom-based request group was reduced to 139 after one of its pharmacies was closed for maintenance. The groups did not differ significantly in any of the studied covariates (Table 1).

Simulated patients successfully obtained an antibiotic in a total of 17.5% of pharmacies (49/280). In the product-based scenario, simulated patients obtained antibiotics in 18.7% of pharmacies (23/141), while the antibiotic was obtained in 16.3% of pharmacies (n=36) where more than 3 pharmacies existed (Pearson’s chi-square, p=0.638). An antibiotic was provided by 27.3% of pharmacies (n=9) in municipalities with fewer than 5,000 inhabitants, 16.1% of pharmacies (n=5) where the population was between 5,000 and 9,999, 19.7% (n=15) where the local population was 10,000 to 24,999, 12.5% (n=4) where the population was between 25,000 and 49,999, 8.3% (n=2) where the population exceeded 50,000, and 16.7% (n=14) in the capital city (Pearson’s chi-square, p=0.483).

Whether an antibiotic was provided similarly did not depend on the owner’s gender, with 18.2% of requests (n=12) successful in male-owned pharmacies, 16.4% (n=31) when the owner was female, and 24.0% (n=6) when the pharmacy was owned by a partnership (Pearson’s chi-square, p=0.634). The number of the years the pharmacy had been owned by the current owner also did not influence the chance of a successful request, as pharmacies providing the antibiotic had been owned for an average of 20.0 years (SD=12.0) while those that refused had been owned for an average of 18.3 years (SD=11.6) (Mann-Whitney, p=0.388). Pharmacies who provided an antibiotic were owned by pharmacists who had finished their degree an average of 25.7 years previously (SD=10.5), while owners of non-providing pharmacies had completed their degree an average of 24.0 years previously to the study (SD=9.8) (Mann-Whitney, p=0.619).

| Table 1. Characteristics of the pharmacies investigated |
|-------------------------------------------------------|
| Product-based | Symptom-based | p-value |
|----------------|---------------|---------|
| Gender         |               |         |
| Male           | 36 (25.5%)    | 30 (21.6%) | 0.703*  |
| Female         | 92 (65.2%)    | 97 (69.8%) |
| Societies      | 13 (9.2%)     | 12 (8.6%)  |
| Number of pharmacies in the Municipality |         |         |
| Unique         | 13 (9.2%)     | 12 (8.6%)  |
| Two            | 12 (8.5%)     | 12 (8.6%)  |
| Three          | 2 (1.4%)      | 4 (2.9%)   |
| More than three| 114 (80.9%)   | 111 (79.5%)|
| Population in the municipality |         |         |
| < 5,000        | 17 (12.1%)    | 16 (11.5%)  |
| 5,000 to 9,999 | 14 (9.9%)     | 17 (12.2%)  |
| 10,000 to 24,999| 37 (26.2%)   | 39 (28.1%) |
| 25,000 to 49,999| 18 (12.8%)   | 14 (10.1%) |
| > 50,000       | 9 (6.4%)      | 15 (10.8%) |
| Capital city   | 5 (3.6%)      | 38 (27.3%) |
| Years owning   | 17.3 (SD=11.4)| 19.9 (SD=11.8)| 0.067** |
| Years since degree | 24.0 (SD=9.6) | 25.6 (SD=10.2) | 0.247** |
| Technicians in staff | 1.1 (SD=0.9)  | 1.1 (SD=0.9) | 0.980** |
| Participation in campaigns | 9.4 (SD=8.2) | 9.0 (SD=8.3) | 0.797** |

* Pearson’s chi-square; ** Mann-Whitney

www.pharmacypractice.org (ISSN: 1886-3655)
The size of the pharmacy, as measured by the number of pharmacists and technicians on staff, also appeared not to influence whether antibiotics were provided without prescription. Pharmacies that did provide the antibiotic had an average of 1.0 technician (SD=0.8), while non-dispensers had an average of 1.1 (SD=0.9) (Mann-Whitney, \( p=0.560 \)). Whether there was a private consultation area also appeared to have no influence, with the antibiotic being provided in 20% of pharmacies with such an area (\( n=2 \)) and 16.2% lacking one (\( n=42 \)) (Fisher’s Exact Test, \( p=0.751 \)).

In the pharmacies visited, 33.2% of the dispensing staff (\( n=93 \)) wore an identification badge. Of these, 30.7% were pharmacists (\( n=86 \)) and 2.5% were technicians (\( n=7 \)). Whether or not identification badges were worn did not appear to influence whether antibiotics were provided, with 19.4% of badge-identified staff (\( n=18 \)) and 16.6% of unidentified staff (\( n=31 \)) providing the antibiotic (Fisher’s exact test, \( p=0.565 \)).

Two variables did influence the provision of antibiotics. First, 31.9% of men (\( n=15 \)) provided antibiotics without prescription, while only 14.6% of women did so (\( n=34 \)) (Fisher’s exact test, \( p=0.010 \)). The second important variable was the number of previous campaigns to promote the rational use of antibiotics in which the potential dispensers had participated. Antibiotic providers had participated in an average of 7.0 campaigns (SD=7.9), compared to an average of 9.7 campaigns (SD=8.3) for those who refused to provide without prescription (Mann-Whitney test, \( p=0.041 \)).

In a logistic regression analysis including all the studied variables, only the latter two showed a significant degree of association with whether or not antibiotics were provided without prescription order. The corresponding regression model allowed the correct classification of 84.4% of cases, with a high negative predictive value (100%) but a low positive predictive value (4.5%) (Hosmer and Lemeshow, \( p=0.372 \)). The regression coefficient for each act of participation in a campaign was 1.057 (95%CI [1.008, 1.107], \( p=0.021 \)), while the regression coefficient for male versus female dispensers was 3.135 (95%CI [1.286, 7.646], \( p=0.012 \)).

**DISCUSSION**

Simulated patients have been used for assessing a number of different aspects of community pharmacists’ performance, including the sale of antibiotics without prescription. This research methodology is necessary wherever professionals may be tempted to hide their actual behavior and performance because of a potential desirability bias. The use of a simulated patient in this study allowed us to test the actual performance of a pharmacist confronted with the choice of dispensing antibiotics without a prescription, rather than assessing knowledge, attitudes, or behavior that would normally be obtained by surveys and questionnaires.

We chose to use symptoms of an uncomplicated urinary tract infection in both test scenarios because this is a prevalent condition among young females like the two actresses were. In addition, studies have indicated that there is a low compliance to treatment guidelines for this group of patients in Spain and elsewhere. Furthermore, Spanish laws explicitly prohibit the dispensing of any antibiotics without prescription, regardless of the patient’s medical condition or symptoms.

We found that male staff appeared to be more predisposed to dispense antibiotics to a young female complaining of urinary tract symptoms than did female staff. More research should be done to find out if this gender association prevails with other medical conditions or patient characteristics. Although with weak impact, we also identified an association with a pharmacy’s previous participation in antibiotic rational use campaigns. This finding reinforces the utility of these awareness campaigns. As in previous studies, we could find no association between antibiotic dispensing practices and the age and other characteristics of the pharmacy itself.

Large-scale campaigns to reduce the use of antibiotics are common in the U.S. and the European Union, where they have met with varying success rates. However, there has been little published research regarding campaigns directed specifically toward reducing the contribution of pharmacists to self-medication by dispensing without prescription orders. The current analysis, using simulated patients, has allowed us to assess directly the consequences of an existing ten-year program directed toward reducing the provision of nonprescription antibiotics in community pharmacies. Previous evaluations estimated that antibiotics were provided without prescription in response to 87.9% of requests in 2000 and to 42.2% in 2004. Our current results indicate that after a ten-year campaign of public and pharmacist education in Spain, only 17.5% of requests for antibiotics without prescription in Gipuzkoa community pharmacies were successful.

**CONCLUSIONS**

A ten-year campaign by the Gipuzkoa Pharmacists Association has been successful in significantly reducing the rate at which antibiotics are dispensed without prescription in community pharmacies. Although more remains to be done, this result underscores the ability of Pharmacists’ institutions in changing the dispensing practices of their members with respect to antibiotics and potentially other medications.

**ACKNOWLEDGEMENTS**

We are grateful for the participation of Miren Garate and Oier Jimenez, administrative staff members of the Gipuzkoa Pharmacist Association who assisted in keeping all data confidential.

**CONFLICT OF INTEREST**

Nothing to declare.
Funding: This work was partially supported by Pfizer and by the Gipuzkoa Pharmacist Association. Pfizer has played no decision-making role in any aspect of the design, execution, analysis, or reporting of the research.

References

1. Goossens H, Ferech M, Vander Stichele R, Elseviers M; ESAC Project Group. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet. 2005;365(9459):579-587.

2. Bronzwaer SL, Cars O, Buchholz U, Mölstad S, Goetsch T, Veldhuijzen IK, Kool JL, Sprenger MJ, Degener JE; European Antimicrobial Resistance Surveillance System. A European study on the relationship between antimicrobial use and antimicrobial resistance. Emerg Infect Dis. 2002;8(3):278-282.

3. Ebert SC. Factors contributing to excessive antimicrobial prescribing. Pharmacotherapy. 2007;27(10Pt2):1265-130S.

4. Shankar PR, Partha P, Shenoy N. Self-medication and non-doctor prescription practices in Pokhara valley, Western Nepal: a questionnaire-based study. BMC Fam Pract. 2002;3:17.

5. Raz R, Edelstein H, Grigoryan L, Hajaier-Ruskamp FM. Self-medication with antibiotics by a population in northern Israel. Ier Med Assoc J. 2005;7(11):722-726.

6. Fuentes Albarran K, Villa Zapata L. Analysis and quantification of self-medication patterns of customers in community pharmacies in southern Chile. Pharm World Sci. 2008;30(6):663-668. doi: 10.1007/s11096-008-9241-4

7. Apisarnthanarak A, Tunporchm J, Taniwli M, Mundy LM. Nonjudicious dispensing of antibiotics by drug stores in Pratunamthi, Thailand. Infect Control Hosp Epidemiol. 2008;29(5):572-575. doi: 10.1086/587496

8. Barah F, Morris J, Goncalves V. Irrational use and poor public beliefs regarding antibiotics in developing countries: a pessimistic example of Syria. Int J Clin Pract. 2009;63(8):1263-1264. doi: 10.1111/j.1742-1241.2009.02093.x

9. Matuz M, Benko R, Doro P, Hajdu E, Soos G. Non-prescription antibiotic use in Hungary. Pharm World Sci. 2007;29(6):695-698.

10. Awad AI, Eltayeb IB. Self-medication practices with antibiotics and antimarials among Sudanese undergraduate university students. Ann Pharmacother. 2007;41(7):1249-1255.

11. Väänänen MH, Pietilä H, Airaksinen M. Self-medication with antibiotics—does it really happen in Europe? Health Policy. 2006;77(2):166-171.

12. Grigoryan L, Hajaier-Ruskamp FM, Burgerhof JG, Mechtler R, Deschepper R, Tambic-Andrasavic A, Andrajati R, Monnet DL, Munsey R, Di Matteo A, Edelstein H, Valiente Riende A, Arkeni A, Sciulena E, Grzesiowski P, Bara AC, Tész T, Cizman M, Campos J, Lundborg CS, Birkin J. Self-medication with antimicrobial drugs in Europe. Emerg Infect Dis. 2006;12(3):452-459.

13. Deschepper R, Grigoryan L, Lundborg CS, Hofstede G, Cohen J, Kelen GV, Deijls L, Hajaier-Ruskamp FM. Are cultural dimensions relevant for explaining cross-national differences in antibiotic use in Europe? BMC Health Serv Res. 2008;8:123. doi: 10.1186/1472-6963-8-123

14. Grigoryan L, Burgerhof JG, Degener JE, Deschepper R, Lundborg CS, Monnet DL, Sciulena EA, Birkin J, Hajaier-Ruskamp FM. IAR consortium. Attitudes, beliefs and knowledge concerning antibiotic use and self-medication: a comparative European study. Pharmacoepidemiol Drug Saf. 2007;16(11):1234-1243.

15. Orero Gonzalez A, Ripoll Lozano MA, Gonzalez Nunez J. [Analysis of automedication with antibiotics in Spain]. Enferm Infecc Microbiol Clin. 1998;16(7):328-333.

16. Campos J, Ferech M, Lázaro E, de Abajo F, Oteo J, Stephens P, Goossens H. Surveillance of outpatient antibiotic consumption in Spain according to sales data and reimbursement data. J Antimicrob Chemother. 2007;60(3):698-701.

17. Llor C, Cots JM. The sale of antibiotics without prescription in pharmacies in Catalonia, Spain. Clin Infect Dis. 2009;49(10):1345-1349. doi: 10.1086/598183

18. Colomina Rodriguez J, Dominguez Marquez V, Gimeno Vilarrasa F, Sarrio Montes G, Guerrero Espejo A. [Impact of Integrated Model for Rational Use of Antibiotics in a health area (project MIURA)]. Rev Esp Salud Publica. 2010;84(3):281-291.

19. Gastelurrutia MA, Larrañaga B, Ortega B, Puntonet L. [Assessment of the program for rational use of antibiotics in Gipuzkoa. First phase: 1999-2000]. Pharm Care Esp. 2002;2(3):143-157.

20. Gastelurrutia MA, Larrañaga B, Ortega B. [First program on rational use of antibiotics in Gipuzkoa. Assessment of 1999-2000 period]. Pharm Pract (Granada). 2006;4(1):1-8.

21. Franke RH, Kaul JD. The Hawthorne experiments: first statistical interpretation. Am Sociol Rev 1978;43:623-643.

22. Alte D, Weitschies W, Ritter CA. Evaluation of consultation in community pharmacies with mystery shoppers. Ann Pharmacother. 2006;40(6):945-949.

23. Watson MC, Cleland JA, Bond CM. Simulated patient visits with immediate feedback to improve the supply of over-the-counter medicines: a feasibility study. Fam Pract. 2009;26(6):532-542. doi: 10.1093/fampra/cmp061

24. Benrimoj SI, Werner JB, Raffaele C, Roberts AS. A system for monitoring quality standards in the provision of non-prescription medicines from Australian community pharmacies. Pharm World Sci. 2008;30(2):147-153.

25. Watson MC, Norris P, Granas AG. A systematic review of the use of simulated patients and pharmacy practice research. Int J Pharm Pract. 2006;14(2):89-93.

26. Watson MC, Skelton JR, Bond CM, Crot P, Wiskin CM, Grimshaw JM, Mollison J. Simulated patients in the community pharmacy setting. Using simulated patients to measure practice in the community pharmacy setting. Pharm World Sci. 2004;26(1):32-37.

27. Zalmanovici Trestioreanu A, Green H, Paul M, Yaphe J, Leibovici L. Antimicrobial agents for treating uncomplicated urinary tract infection in women. Cochrane Database Syst Rev. 2010;(10):CD007182. doi: 10.1002/14651858.CD007182.pub2
28. Lior C, Rabanaque G, Lopez A, Cots JM. The adherence of GPs to guidelines for the diagnosis and treatment of lower urinary tract infections in women is poor. Fam Pract. 2011;28(3):294-299. doi: 10.1093/fampra/cmq107

29. Lior C, Monnet D, Cots J. Small pharmacies are more likely to dispense antibiotics without a medical prescription than large pharmacies in Catalonia, Spain. Euro Surveill. 2010;15(32). pii: 19635.

30. Gonzales R, Corbett KK, Wong S, Glazner JE, Deas A, Leeman-Castillo B, Maselli JH, Sebert-Kuhlmann A, Wigton RS, Flores E, Kafadar K. "Get smart Colorado": impact of a mass media campaign to improve community antibiotic use. Med Care. 2008;46(6):597-605. doi: 10.1097/MLR.0b013e3181653d2e

31. Goossens H, Guillemot D, Ferech M, Schlemmer B, Costers M, van Breda M, Baker LJ, Cars O, Davey PG. National campaigns to improve antibiotic use. Eur J Clin Pharmacol. 2006;62(5):373-379.

32. Sabuncu E, David J, Bernède-Bauduin C, Pépin S, Leroy M, Boilé PY, Watier L, Guillemot D. Significant reduction of antibiotic use in the community after a nationwide campaign in France, 2002-2007. PLoS Med. 2009;6(6):e1000084. doi: 10.1371/journal.pmed.1000084