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Letter to the Editor

Effect of the coronavirus disease 2019 pandemic on antibiotic use in primary care

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To the Editor,

During the coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), disruption of antimicrobial stewardship interventions has become a matter of concern. Antimicrobial resistance and the many unintended negative clinical consequences resulting from antibiotic misuse and overuse will persist and may potentially be aggravated by the pandemic, making it necessary to measure its impact on antibiotic use in all health-care settings [1].

Antibiotic consumption increased in hospitals during the pandemic [2,3]; however, no study has reported the effect on antibiotic use in the community. Our objective was to assess the impact of the COVID-19 pandemic on antibiotic prescribing in primary care in a region with an existing comprehensive antimicrobial stewardship programme for hospitals and primary-care centres, the PIRASOA programme [4].

We conducted a before and after cross-sectional study comparing antibiotic use in the community in the first and second quarters (Q) of 2019 and the same quarters in 2020 (COVID-19 period). A lockdown was in force in the region from 14 March to 21 June 2020. Outpatient antibiotic use was assessed for the whole public primary health-care system of Andalusia, Spain, with 8069 physicians distributed in 1516 primary-care centres clustered in 26 health districts, serving a population of 8.4 million people. We calculated quarterly antibiotic use as defined daily doses per 1000 inhabitants per day (DID) for overall antibacterials for systemic use (WHO's ATC Classification System group J01), six antibiotic groups: J01A (tetracyclines), J01C (penicillins), J01D (other β-lactam antibacterials), J01E (sulphonamides and trimethoprim), J01F (macrolides, lincosamides and streptogramins) and J01M (quinolones), and five antibiotics considered as strategic for respiratory infections: amoxicillin-clavulanate, amoxicillin, cefuroxime, levofloxacin and azithromycin. Data were collected from the computerized pharmacy records of reimbursed and dispensed drugs, hosted by the Pharmacy Service of the Andalusian Health Service. Patient data were anonymized. The pooled DID for each variable was calculated as total defined daily dose prescribed to the total population. To assess the statistical significance of the differences between quarters, means or medians were compared for the 26 health-care districts data using paired Student's ***t***-test or Wilcoxon log-rank test, as appropriate after checking for

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normality, using the IBM SPSS Statistics software, version 23.0 (IBM, Armonk, NY, USA).

We found that the overall use of antibiotics in the community decreased in the COVID-19 period compared with the pre-COVID-19 period. The mean reduction of total antibiotic consumption was −1.30 ± 1.18 DID between 2020Q1 and 2019Q1 (−7.6% pooled DID reduction; p <0.0001), whereas the mean reduction was −5.14 ± 1.31 DID between 2020Q2 and 2019Q2 (−36.8% pooled DID reduction; p <0.0001). The magnitude of this reduction was significantly greater between the second quarters than between the first quarters (mean difference 3.84 ± 1.40 DID; p <0.0001). Larger reductions were also observed between the second quarters in most antibiotic groups: penicillins (−9.6% difference between 2020Q1 and 2019Q1 versus −41.3% difference between 2020Q2 and 2019Q2), cephalosporins (−3.8% versus −24.6%), macrolides (−6.9% versus −48.6%) and quinolones (−9.3% versus −30.5%). Except for azithromycin, which remained stable, consumption of strategic antibiotics decreased between the first quarters, ranging from −6.7% (p 0.001) for cefuroxime to −10.8% (p <0.0001) for amoxicillin. Larger reductions were found between the second quarters for all the individual antibiotics under study, azithromycin included, ranging from −27.0% (p <0.0001) for amoxicillin-clavulanate to −55.6% (p <0.0001) for amoxicillin (Table 1). The quarterly time-series evolution of antimicrobial consumption since 2014, the starting year of the PIRASOA programme, shows a decreasing trend that is consolidated during the first two quarters of 2020 (Fig. 1).

Concomitantly, primary-care consultations dropped from 9 556 575 in 2019Q1 to 9 412 596 in 2020Q1 (−1.5%), and from 9 307 171 in 2019Q2 to 8 637 335 in 2020Q2 (−7.2%).

Our findings show that antibiotic use in primary care decreased during the COVID-19 pandemic period in our region, with the sharpest decline occurring in the second quarter of 2020, when the lockdown was more extensive. These data contrast with the increase reported in hospitals [2,3]. Interestingly, azithromycin use remained stable between 2020Q1 and 2019Q1, dropping markedly in 2020Q2 compared with 2019Q2 (−49.4%). Such different behaviour from that of other antibiotics may have been due to changes in the indication for the use of azithromycin, which in the early stages of the pandemic

Table 1
Differences in antibiotic use in primary care in the Andalusian Public Health System 2019 versus 2020

Antibiotic	Quarter 1 (January–March) (n = 26)				Quarter 2 (April–June) (n = 26)			
	2019 (DID)	2020 (DID)	Difference (%)	p value[a]	2019 (DID)	2020 (DID)	Difference (%)	p value[a]
Total antibiotics (J01)	15.77	14.58	−7.6	<0.0001	12.80	8.10	−36.8	<0.0001
Tetracyclines (J01A)	0.51	0.55	8.1	0.017	0.45	0.39	−12.4	0.34
Penicillins (J01C)	9.34	8.45	−9.6	<0.0001	7.74	4.54	−41.3	<0.0001
Amoxicillin	4.91	4.38	−10.8	<0.0001	3.88	1.72	−55.6	<0.0001
Amoxicillin-clavulanate	4.09	3.74	−8.4	<0.0001	3.49	2.55	−27.0	<0.0001
Other β-lactam antibacterials (J01D)	1.32	1.27	−3.8	0.17	1.10	0.83	−24.6	<0.0001
Cefuroxime	1.00	0.93	−6.7	0.025	0.82	0.58	−29.1	<0.0001
Sulphonamides and trimethoprim (J01E)	0.18	0.20	9.5	0.016	0.18	0.20	8.5	0.007
Macrolides. lincosamides and streptogramins (J01F)	2.26	2.11	−6.9	0.002	1.62	0.83	−48.6	<0.0001
Azithromycin	1.64	1.61	−2.3	0.20	1.14	0.58	−49.4	<0.0001
Quinolones (J01M)	1.70	1.54	−9.3	<0.0001	1.25	0.87	−30.5	<0.0001
Levofloxacin	0.91	0.83	−8.5	0.001	0.56	0.26	−53.4	<0.0001

Abbreviation: DID, defined daily doses per 1000 inhabitants; 2019 and 2020 DID are presented as pooled data.
[a] p values show the statistical significance of means or medians comparison for the 26 health-care districts data using the paired Student's ***t***-test or the Wilcoxon log-rank test, as appropriate, after testing for normality by means of the Kolmogorov–Smirnov test.

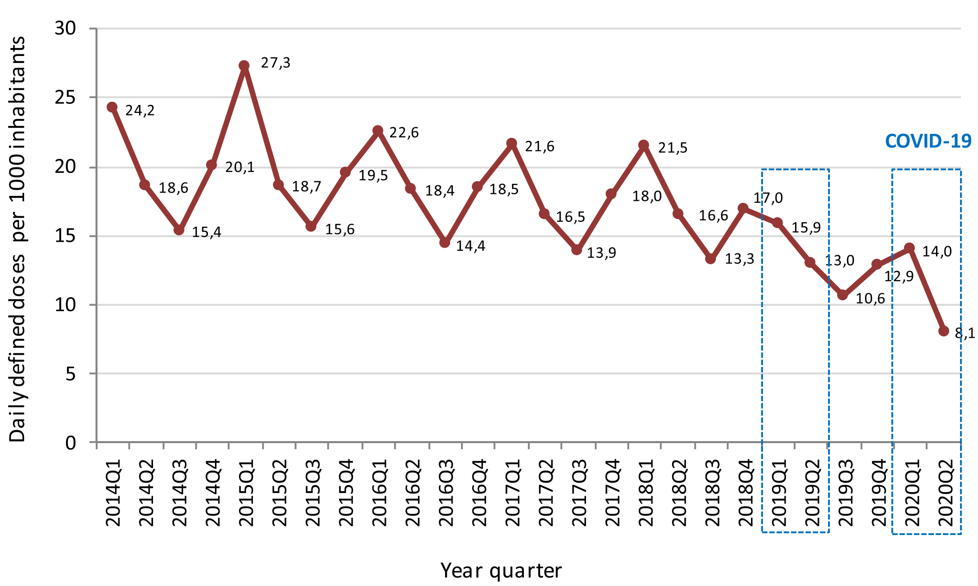

Fig. 1. Total antimicrobial consumption in primary Care in Andalusia, Spain. Total antimicrobial consumption values are presented as mean defined daily doses (DDD) of total systemic antibiotics (J01) and antifungals (J02) per 1000 inhabitants per year-quarter. From 2019Q1 onwards, consumption data were calculated following the WHO's ATC/DDD alterations 2019, available at: www.whocc.no/atc_ddd_index/updates_included_in_the_atc_ddd_index/.

was suggested to be effective in treating individuals with COVID-19 [5].

It would be relevant to know why this decline in total antibiotic consumption in the community happened. Confinement has probably contributed to this reduction because the use of masks and hygienic measures prevented other infections. The lockdown could have hampered outpatients' access to the healthcare system and to antibiotic prescriptions. Although telephone consultations were readily available, patients' worries about using health services might have reduced the demand for appointments related to infectious disease care, or increased the use of alternatives, such as hospital emergency units or the 112 telephone line. However, our results suggest that the decreased antibiotic prescriptions are not entirely explained by decreased primary-care consultations, but to a large part by a sustained change in prescribing patterns due to the long-term effect of the PIRASOA programme [6].

Gaining access to that information may be useful to improve antimicrobial stewardship programmes in primary care. If these results are confirmed in other health systems, further studies are needed to determine whether this reduction in antibiotic use in the community during the pandemic has resulted in a favourable ecological impact.

Transparency declaration

The authors declare no conflict of interests. No funding has been received.

Authors' contributions

JMC and GP conceived, designed and supervised the study, and had full access to all the data; GP, RSB, MAPM, MDPP, APM, JM and JMC collected and interpreted the data; GP analysed the data; JMC and GP wrote the first draft of the manuscript and GP, RSB, MAPM, MDPP, APM, JM and JMC participated in the subsequent critical revisions of the manuscript.

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