

Scientific Research Report

Medication Prescribing Practices in Croatian Dental Offices and Their Contribution to National Consumption



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ARTICLE INFO

Article history:

Available online 26 February 2021

Key words:

Prescribing
Consumption
Dental medicine
Antibiotics
Analgesics
Medications

ABSTRACT

Objectives: The objective of this study was to analyse the pattern of medication prescribing among dental practitioners in the Republic of Croatia and to compare it with general medical practice patterns at the national level.

Methods: Data on drug prescriptions were obtained from the Croatian Health Insurance Fund. The number of dentist prescriptions, the cost of medicine denominated in the national currency (Croatian Kuna [HRK]), and the number of packages and days prescribed have been included in the analysis.

Results: Results indicate that there was an increase in medication prescribing (+5.7%) by dentists, with antimicrobials comprising the majority, whereas national medical antimicrobial prescribing had slightly decreased. Antibiotics accounted for 80% of all dentists' prescriptions, with penicillins being the most commonly prescribed. In particular, amoxicillin with clavulanic acid accounted for 56.4% of all antibiotics prescribed. Such broad-spectrum antibiotics were prescribed more frequently than those of narrow-spectrum. Antibiotics were followed by nonsteroidal anti-inflammatory drugs, with prescribing frequency for ibuprofen increasing by 75%.

Conclusion: Current trends show an increase in the overall prescription rate for all medications prescribed by dentists. The largest increase was observed for the broad-spectrum amoxicillin with clavulanic acid, and ibuprofen. As the apparent widespread use of broad-spectrum antibiotics by dentists in Croatia is in contrast to national and international recommendations for antibiotic stewardship, there is a need for further prospective investigation and possible provider education and guidelines.

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Introduction

Prescribing medications is a regular part of daily dental practice. Although studies regarding drug prescription in general medicine have been available since the early days of pharmacotherapy, the importance of drug use in dentistry was not recognized until a few decades later.^{1,2} Interest in drug prescribing in dentistry, antibiotics in particular, recently

increased with the emergence of bacterial resistance throughout the world.^{3,4} This issue created the need for better regulation and stewardship of antibiotics, aimed primarily at rationalising consumption.⁵ Rational drug prescription is defined as using the least possible amount of the most appropriate drug to obtain the best possible effect in the shortest period of time and at a reasonable cost.⁵

Use of antibiotics in dentistry is generally regulated by evidence-based guidelines. Most common infections requiring antibiotic therapy in dentistry are odontogenic and periodontal. Systemic antimicrobial therapy commonly serves as an adjunct to mechanical treatment. Indications for systemic

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<https://doi.org/10.1016/j.identj.2021.01.004>

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antibiotic therapy in endodontic and odontogenic infections are acute apical abscess with systemic involvement, rapid onset of a severe infection, spreading infection, osteomyelitis, replantation of avulsed permanent teeth, and soft tissue trauma requiring treatment or use in patients who are medically compromised.⁶ In these cases, beta-lactam antibiotics (penicillin V and amoxicillin) are recommended as the first-choice antibiotic. If penicillin V alone is not effective after 48-72 hours, metronidazole can be used in combination with penicillin V, or penicillin V is switched to amoxicillin with clavulanic acid. In case of allergy to penicillin, clindamycin is the drug of choice.⁷ In cases of severe periodontitis, systemic antimicrobials can be used as adjunctive therapy to scaling and root planing, and antibiotic treatment may also be indicated in cases of localized deep sites with persistent or recurrent disease if the periodontal infection needs to be rapidly suppressed in early-onset disease or in patients with uncontrolled diabetes.⁸ According to the latest systematic review/meta-analysis, the first choice of therapy that demonstrated significant benefits on different clinical outcome measures when antibiotics were used was a combination of amoxicillin and metronidazole and, to a lesser extent, metronidazole and azithromycin.⁹

The first step in the rationalisation of medication use is to screen its consumption on a national level. Analysis of prescription patterns is helpful in providing feedback on rational prescribing, especially of antibiotics, to raise the quality standards of clinical pharmacotherapy in dental medicine. Surveys of dentists' prescribing patterns have raised awareness of rationalisation in many developed countries.¹⁰ Because there are currently no studies available in Croatia presenting data on drug use in dentistry, it is not possible to propose measures for improvement or indeed even assess if improvements are needed. The aim of this study was to assess the prescription pattern for all medications prescribed by Croatian dental practitioners over a 5-year period and to compare it with general medical use at the national level.

Methods

The overall data on medications prescribed by dentists in the period between January 1, 2014, and December 31, 2018, were obtained from the Croatian Health Insurance Fund (CHIF). Data contained the number of prescriptions, the cost of medicines denoted in the national currency (Croatian Kuna [HRK]), and the number of packages prescribed. The data did not include private prescriptions or medicines dispensed to in-hospital patients as data on private prescriptions are registered and stored only at the pharmacies where they are filled. According to official public drug use reports of the Agency for Medicinal Products and Medical Devices of Croatia, the majority (87.5%) of general prescriptions in Croatia over the 5 years covered by this study were funded by the CHIF, so the analysis of medication consumption based on the CHIF data should represent a realistic consumption rate. However, the reports do not show actual consumption of some anti-inflammatory and analgesic medications that can be purchased without a prescription, so the data on use of such drugs in dentistry are incomplete.

Official national population statistics were obtained from the Croatian Bureau of Statistics website and the First Results publication. These are short and concise statistical information sheets issued in accordance with the regular survey schedule.¹¹ The number of licensed dentists, patients, and dental procedures was obtained from the Croatian Institute for Public Health (CIPH).¹² The CIPH was also used as the source for data on the incidence of dental diseases registered under the International Statistical Classification of Diseases and Related Health Problems, 10th edition (ICD-10) codes¹³ for which medication is commonly prescribed. The CIPH acts as a statistical authority that maintains national public health registries, supervises data storage, and coordinates the work of other health registers.

For the analysis of prescription data the World Health Organization (WHO) anatomical-therapeutic-chemical (ATC) classification standard codes were used for the classification of medications and the defined daily dose (DDD). The defined daily dose per 1000 inhabitants per day (DID) was used to calculate a standardized measure of medicine consumption at the national level. The DDD is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults, and this standard value for each drug was obtained from the WHO Collaborating Centre for Drug Statistics Methodology website.¹⁴ The DDD has become a standard dose unit in most of the pharmacoepidemiologic studies because it provides a fixed unit of measurement independent of dosage form, package size, or price.

The data did not contain any personal information on either the practitioners or the patients, and the Ethical Board of the School of Dental Medicine, University of Zagreb, independently reviewed and approved the study under approval No. 05-PA-30-XI-11/2019. The data was analysed using Microsoft Excel software, and the results are presented using descriptive statistics including means and percentages. Quantitative analysis was undertaken using a methodology based on DID and ATC classification according to WHO standards.

Results

During the analysed period, the average annual number of all prescriptions issued by dentists was 446,204 with an increase of 5.7% between 2014 and 2018. The total number of dentist prescriptions of antibiotics increased by 21,971 (6.3%), while total expenditures by the CHIF for those medications

Table 1 – Croatian medication prescribing in dentistry between 2014 and 2018 and its contribution to the overall national drug consumption.

Year	Cost*/Contribution to the national financial burden	Number of issued prescriptions
2014	15,887,518.50 (0.46%)	425,385
2015	14,265,567.85 (0.41%)	439,737
2016	14,197,660.64 (0.39%)	459,718
2017	13,306,581.12 (0.35%)	456,499
2018	12,605,054.61 (0.30%)	449,683

* Croatian Kuna (HRK).

decreased by 20% over the same period, reflecting reduced prices (Table 1). On average, each dentist issued 181 prescriptions annually with an average number of 3.6 prescriptions per insured patient who received some kind of dental service. The average number of licensed dentists in Croatia during the same period was 2465 with the number of dentists increasing by 5% during the period under observation. The number of patients that used dental services was, on average, 1,633,710 per year with minimal annual fluctuations. The Croatian Health Statistics Yearbook Annual CIPH Reports show the number of odontogenic infections by the International Classification of Diseases-10th edition classification (K04) and periodontal infections (K05.2-K05.4) decreased during the observed time period by 17% and 11.5%, respectively. In numbers, this decrease went from 993,195 to 822,875 cases and from 128,820 to 113,072 cases, respectively. In 2014, Croatia had 4,225,310 inhabitants, and the population decreased by 3.5% over the 5 years.¹¹

Analysis of prescriptions by ATC classification per number of prescriptions issued show that the antibacterials (J01) were by far the most frequently prescribed drugs, averaging 72% of all prescriptions (Table 2). This accounts for 3.5% of overall national antibiotic use and 9.4% of national outpatient use.¹⁵ To put this in context, dentists comprise approximately 15% of the Croatian health care workforce that has prescribing authority. The number of prescriptions for all antimicrobial drugs (J01 and P01) accounted for an average of 80% of all dental prescriptions issued annually. In the top 10 prescribed drugs, antimicrobials clearly predominate (Table 3). The same was true by number of prescriptions (DDD) and length

of use (DID) (Table 4). Among antibacterials, amoxicillin with clavulanic acid (amoxiclav) was the most prescribed drug, averaging 56% of all antibiotic prescriptions, followed by amoxicillin (13.9%), clindamycin (12.5%), and metronidazole (10%). Dentists' prescriptions accounted for 18% of the total national consumption of amoxiclav, with the DID growing from 1.15 to 1.36 (18%). This is relatively more than the overall national increase in use of the same drug from 5.00 DID to 5.53 DID (11%) in the period between 2014 and 2018. Dentists' contribution to the national outpatient antibiotic use ranged from the highest proportion of 24.7% for metronidazole, 23% for amoxiclav acid, 17% for clindamycin, and 11% for amoxicillin. The second group of most prescribed medications by dentists were pain relief medications, with ibuprofen as the first choice with an increase of 75% in the number of prescriptions.

Discussion

The present study is the first assessment of the prescribing trends on the national level in dental medicine in Croatia. We noted an overall increase of 5.7% in medication prescribing over the 5-year period, measured in the number of prescriptions per insured person per year. This finding followed the general trend of increase in Croatia, where outpatient consumption in just a 1-year period (between 2017 and 2018) increased by 4.5% according to the DDD and by 5.8% in financial burden.¹⁵ Croatia is also higher in total consumption of antibiotics (DID 23.5) than the European average of 21.8 DID with outpatient consumption of antibiotics at DID 17.^{2,14-16}

Table 2 – The number and cost of the most frequently prescribed classes of drugs by Croatian dentists by ATC classification and year.

Rank	ATC ^{ref}	2014		2015		2016		2017		2018	
		N* % [†]	Cost [‡]	N %	Cost	N %	Cost	N %	Cost	N %	Cost
1	J01 Antibacterial drugs	312,895 73.5%	12,230,227	317,120 72%	10,302,030	327,184 71%	9,960,259	326,233 71%	9,979,581	323,912 72%	9,798,492
2	M01 Anti-inflammatory and antirheumatic drugs	46,937 11%	651,676	53,145 12%	712,440	60,022 13%	805,649	64,700 14%	871,004	68,597 15%	940,121
3	P01 Antiprotozoal drugs	33,400 7%	1,039,827	35,126 7%	1,156,954	37,021 8%	1,213,363	37,410 8%	1,238,056	38,456 8%	1,275,264
4	D08 Antiseptics and disinfectants drugs	13,783 3%	267,334	14,693 3%	284,945	16,184 3.5%	317,320	9649 2%	188,258	294 0.06%	3779
5	A01 Stomatological preparations	8427 1%	1,373,598	8,707 1%	1,436,885	8876 1.9%	1,571,718	7804 1.7%	679,223	7,494 1.6%	228,914
6	D06 Antibiotics and chemotherapeutics for dermatological use	12,93 0.3%	40,383	1,324 0.3%	42,333	1404 0.3%	46,418	1344 0.3%	44,977	1,306 0.29%	44,773
7	S01 Ophthalmological drugs	1246 0.29%	19,266	1275 0.28%	18,521	1212 0.2%	17,183	1306 0.28%	18,250	1576 0.35%	22,108
8	D07 Topical dermatological corticosteroids	1006 0.2%	21,698	1256 0.28%	26,691	1235 0.26%	25,331	1251 0.27%	25,999	698 0.15%	28,318
9	N02 Analgesic drugs	827 0.1%	28,343	940 0.2%	26,494	865 0.18%	26,320	959 0.2%	31,358	1095 0.24%	32,087
10	D01 Antifungals for dermatological use	713 0.1%	10,986	749 0.1%	10,760	647 0.1%	9438	568 0.1%	8327	644 0.1%	9119

ATC = anatomic-therapeutic-chemical.

* Number of prescriptions.

† Percentage of all Croatian prescriptions).

‡ Croatian Kuna (HRK).

Table 3 – The 10 most frequently prescribed medications by Croatian dentists between 2014 and 2018 by annual number of prescriptions.

Rank	ATC/INN ^{Ref}	Number of prescriptions percentage of all Croatian prescriptions						Change 2014-2018
		2014	2015	2016	2017	2018		
1	J01CR02 Amoxicillin + Clavulanic Acid	186,698 43.8%	194,123 44.1%	205,411 44.4%	209,632 45.9%	212,860 47.3%	+14%	
2	J01CA04 Amoxicillin	52,492 12.3%	50,863 11%	50,349 10.9%	48,077 10.5%	45,712 10.1%	-16%	
3	J01FF01 Clindamycin	44,805 10.5%	45,391 10.3%	46,362 10%	44,544 9.7%	43,699 9.7%	-2%	
4	P01AB01 Metronidazole	33,330 7.8%	35,049 7.9%	36,923 8%	37,254 8.1%	38,284 9.7%	+14%	
5	M01AE01 Ibuprofen	27,133 6.3%	33,084 7.5%	38,757 8.4%	43,477 9.5%	47,906 10.6%	+76%	
6	J01DB01 Cephalexin	18,092 4.2%	16,516 3.7%	15,220 3.3%	13,796 3%	11,475 2.5%	-36%	
7	D08AG02 Povidone Iodine	13,627 3.2%	14,471 3.2%	15,923 3.4%	9487 2%	294 0.06%	-97%	
8	M01AB05 Diclofenac	9791 2.3%	8958 2%	8241 1.7%	7721 1.6%	6985 1.5%	-22%	
9	M01AE03 Ketoprofen	9491 2.2%	10,168 2.3%	11,834 2.5%	11,879 2.6%	11,667 2.6%	+22%	
10	A01AB09 Miconazole	5924 1.3%	6216 1.4%	6340 1.3%	6736 1.4%	7383 1.6%	+24%	

ATC = anatomic- therapeutic-clinical; INN = international nonproprietary name.

Results of our analysis showed that dentists predominantly prescribed antibiotics (80%), which is supported by previous reports.³ The proportion of dentists' prescriptions of total outpatient use was 9.4%, which correlated with the available data on the average participation of dentists in the prescribing of antibiotics worldwide.^{3,17-19} In addition, antibiotic prescriptions increased by 4.7%, but the exact reason could not be determined because the information on indications was not available. Our results show that as the most prescribed (56%) among antibiotics, amoxiclav was by implication the first-choice antibiotic. These findings were corroborated by the prospective studies done in Croatia by Bjelovučić et al²⁰ and Perić et al.²¹ Moreover, use of amoxiclav grew by 18% in 5 years,

measured both in the number of prescriptions and the DID. The increase in dental prescriptions of amoxiclav and metronidazole is one of the main causes of its increase at the national level because the share of dental prescriptions of amoxiclav and metronidazole in national outpatient antibiotic consumption was 24% and 23.7%, respectively.²² The predominant use of amoxiclav is contrary to current guidelines on the use of antibiotics in dental medicine.^{6,7,9,23,24} It is also contrary to recently reported practices in other countries, where treatment normally starts with a narrower-spectrum antibiotic.^{17,25-28} This increase could not be explained by the disease incidence trends officially reported by the CHIP, where the incidence of odontogenic infections and periodontal infections actually showed a

Table 4 – The 10 most frequently prescribed medications by Croatian dentists in defined daily dose and defined daily dose per 1000 inhabitants per day between 2014 and 2018.

Rank	ATC ^{Ref}	Prescribed Medication	2014		2015		2016		2017		2018		Change 2014 to 2018
			DDD	DID	DDD	DID	DDD	DID	DDD	DID	DDD	DID	
1	J01CR02	Amoxicillin + Clavulanic Acid	1,783,758	1.15	1,855,588	1.22	1,961,997	1.28	2,001,626	1.33	2,034,545	1.36	+18%
2	J01CA04	Amoxicillin	307,066	0.19	293,290	0.19	289,616	0.19	274,848	0.18	260,869	0.17	-15%
3	J01FF01	Clindamycin	197,216	0.13	199,884	0.13	204,652	0.13	197,016	0.13	193,544	0.13	-2%
4	P01AB01	Metronidazole	104,496	0.07	109,446	0.08	116,868	0.08	116,115	0.08	119,520	0.08	+14%
5	M01AE01	Ibuprofen	285,590	0.19	346,740	0.23	404,700	0.27	452,060	0.30	497,820	0.33	+74%
6	J01DB01	Cephalexin	83,820	0.05	75,504	0.05	70,348	0.05	67,276	0.04	56,156	0.04	-33%
7	D08AG02	Povidone Iodine	148,170	0.10	158,390	0.10	175,910	0.11	164,230	0.11	151,300	0.10	-52%
8	M01AB05	Diclofenac	236,240	0.15	214,680	0.14	196,300	0.13	181,900	0.12	165,420	0.11	-30%
9	M01AE03	Ketoprofen	201,640	0.13	217,000	0.14	250,860	0.17	251,260	0.17	247,480	0.17	+23%
10	A01AB09	Miconazole	28,776	0.02	30,584	0.02	31,104	0.02	33,132	0.02	36,740	0.02	+28%

ATC = anatomic- therapeutic-clinical; DDD = defined daily dose; DID = dose per 1000 inhabitants per day.

decrease in the time period under observation by 17% and 11.5%, respectively.¹² The same trend was noted for the number of patients seeking dental treatment, which decreased by 4.4%, and the number of people in the general population, which decreased by 3.5%.^{11,12} At the moment there are no studies available that would offer an explanation for this phenomenon. These results may serve as a preliminary indication of disease incidence trends or a national (patient) trend, but they do not represent precise information on the incidence of specific indications or explain the reason for that increase. This subject needs to be studied further.

For metronidazole, as the most commonly prescribed antibiotic combination in dentistry with amoxicillin,⁷⁻⁹ the increase in consumption (14%) followed the increased usage of amoxiclav. Metronidazole use is irreplaceable in the treatment of anaerobic pathogens in periodontal and some advanced odontogenic infections and is commonly used in combination with amoxicillin.^{6,7} The similar increasing use trends as amoxiclav may indicate that dentists in Croatia use wider-spectrum penicillin drugs in antimicrobial therapy instead of the recommended narrower-spectrum drugs, but prospective studies need to be performed to verify this assumption. A recent systematic review and meta-analysis of the use of systemic antimicrobials in periodontitis therapy indicated that the best treatment outcomes were achieved when a combination of amoxicillin plus metronidazole was used, followed by metronidazole alone, and then azithromycin alone.⁹ This recent data corroborate previous findings that amoxicillin with metronidazole is the most efficient treatment regimen in patients with periodontitis. The increased use of amoxicillin with clavulanic acid also has no support in the scientific literature and could actually be considered as *vitium artis*.

There are some differences between the recommended antimicrobials used in endodontic and periodontic treatment. According to the European Society of Endodontology Position Statement on the Use of Antibiotics in Endodontics, the recommended antimicrobials are first the beta-lactam antibiotics (penicillin V and amoxicillin) followed by amoxiclav. A combination of amoxicillin and metronidazole is recommended if the penicillin therapy is ineffective.⁶ On the other hand, in patients with periodontitis and advanced, severe defects, systemic administration of amoxicillin plus metronidazole significantly enhanced the effects of scaling and root planing, decreasing the need for surgical intervention, especially on molar teeth.^{29,30} However, a recent European Federation of Periodontology (EFP) S3 Level Clinical Practice Guideline, the consensus was that the routine use of systemic antimicrobials as an adjunct to subgingival debridement was not generally recommended in patients with periodontitis, although it could be considered for specific patient categories such as young adults with generalized periodontitis stage III.³¹ Therefore, there is a clear difference in the recommended antimicrobial regimens and administration between these 2 conditions.

As the second most frequently used class of medication in dental medicine, the pain relief nonsteroidal anti-inflammatory drugs (ie, ibuprofen, ketoprofen, and diclofenac) were also recorded in the top 10 prescribed medications. Our analysis showed a decline in prescribing over

time only for diclofenac, and use of the other 2 nonsteroidal anti-inflammatory drugs has been continuously increasing. Reduction of diclofenac use can, perhaps, be explained by its frequent elicitation of patient complaints of irritation to the gastric mucosa. Another aspect of this decrease is likely reflected in the increased use of ibuprofen, which has become the first-choice analgesic in dental medicine. We found ibuprofen use increased by 75%. Such a high frequency of dental ibuprofen prescription is, besides Croatia, seen only in Germany³² and the United Kingdom.³³ However, several recent studies do show an increased consumption of analgesics worldwide.^{32,34-36} There also seems to be a rising global trend for prescribing more opioid analgesics in dental medicine, which prompted an appeal for better control in their prescribing. That increase was not noted in this study.^{37,38} The global increase in consumption of analgesics is probably due to the easy availability of this group of pharmaceuticals and relatively low incidence of adverse side effects.

Lack of easily accessible and clearly visible guidelines on the use of antibiotics in dental medicine in Croatia is perhaps the most important factor contributing to the increase in prescribing of these medications, and studies are currently under way to detect reasons for these findings. Countries such as England and Germany, with strict guidelines and a long history of providing recommendations for different health care measures, have achieved encouraging rationalisation of medication use in dentistry, as a result of their efforts in updating, controlling, and periodically revising guidelines.^{20,25,26} On the other hand, in transition countries where many guidelines are often just adapted and not developed for their own purposes, an increased number of prescriptions or a high proportion of uncritically prescribed medications has been reported.^{17,39} To the best of our knowledge this study is the first report on medication prescription habits in dental medicine in Croatia. It is also the first report using the WHO-defined drug measurement units of DDD and DID to assess the utilisation rate and the length of medication use in dental practice set to international norms. Prescription pattern monitoring studies are a tool for assessing the prescribing, dispensing, and distribution of medicines. The main aim is to facilitate the rational use of medicines and adherence to established medical (or dental) prescription practices and current recommendations or guidelines.⁴⁰

The main limitation of this study is the general lack of information on accompanying diagnoses (indications) relevant for the prescription of a given drug. The problem seems to be structural in nature because the data on illnesses and diagnoses are collected by the CIPH, while the data on drugs is collected by the CHIF. Merging or cross-referencing these 2 databases at the national level could resolve this issue in the future. There is also a general lack of information on private prescriptions, although their participation at the national level seems minimal. Another limitation is the impossibility of tracking consumption of nonprescription, over-the-counter (OTC) drugs, which would provide better insight into general consumption.

The finding of increased medication consumption is a consequence of the underlying problem, which is poor oral

health. Oral diseases, as a preventable global health problem, are often a neglected issue and rarely seen as a priority in health policy.⁴¹ The WHO recognized the need to move from current clinical approaches to policy initiatives that tackle oral health inequalities at the structural level. Dental care systems should focus more on promoting and maintaining oral health and achieving greater oral health equality to minimise medication prescribing and increase quality of life.^{42,43}

Conclusion

This study showed an increase in the overall medication prescribing rate by dentists in Croatia. The highest increase was observed in the use of the broad-spectrum amoxicillin with clavulanic acid, and ibuprofen. Dental prescriptions significantly contributed to the consumption increase at the national level for amoxiclav and metronidazole. As the proportion of correctly and incorrectly indicated antibiotic prescription by dental practitioners could not be determined from the CHIF database, additional study is needed to identify the reasons for this increase and to target areas of possible intervention and improvement, including rational prescribing guidelines and training for dentists.

Conflict of interest

None disclosed.

Acknowledgements

We thank the Croatian Health Insurance Fund for providing the data. Authors also wish to thank Professor Frank A. Roberts for his valuable advices in manuscript preparation.

Author contributions

Ivana Šutej was primarily responsible for data collection and the study conception and design. Material preparations were performed by Ivana Šutej and Katja Pernarić. The first draft of the manuscript was written by Ivana Šutej. Dragan Lepur and Darko Božić conducted the analysis and critically revised the manuscript. All authors read and approved the final manuscript.

Funding

None disclosed.

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