ORIGINAL ARTICLE



Dental antibiotic policies, stewardship, and implementation in India: A policy document analysis

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Abstract

Objectives: Dental antibiotic stewardship is crucial in low- and middle-income countries where the burden of antimicrobial resistance (AMR) is high and antibiotic misuse is common. Given that India is the most populous country, the largest antibiotic consumer and has a large dental prescriber population, this study investigated the extent to which current Indian policy and practice for dental antibiotic prescribing and stewardship aligns with the global policy and best practice.

Methods: The READ approach was used to identify and extract data and synthesize the findings. Policy documents on dental antimicrobial stewardship were identified using a systematic search strategy involving nine medical and grey literature databases (Medline, Global Health, Web of Science, Cochrane, CINAHL, Eldis, Global Index Medicus, Proquest and Opengrey), targeted websites (government organizations and dental regulatory bodies) and contact with experts. Framework analysis was used to code extracted data into themes related to dental antimicrobial stewardship. Results: Of the 3039 records screened, 25 documents were included in the final analysis. The analysis showed a lack of guidelines or toolkits for appropriate antibiotic prescribing in dentistry in India. The treatment guidelines for antimicrobial use in common syndromes published by the Indian Council of Medical Research had no section or content for dental practitioners. Furthermore, the undergraduate dental curriculum developed by the Dental Council of India (DCI), included little content on appropriate antibiotic prescribing and no mention of AMR or stewardship. There were no educational resources either for dental practitioners or patients in the documents. Conclusion: This document analysis showed that there was little or no mention of dental antibiotic prescribing guidelines in key policy documents such as the National Action Plan on AMR. In addition, contradictory and subjective information provided in some policy documents could encourage dentists and other health professionals such as general practitioners to prescribe antibiotics for common dental conditions for which they are contra-indicated. There is an urgent need to develop relevant guidelines and include these in Indian policy documents on AMR particularly the National Action Plan on AMR.

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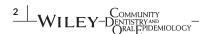
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KEYWORDS

AMR, antibiotic resistance, dentistry, India, policy, prescriptions, stewardship

1 | INTRODUCTION

The need for Antimicrobial Stewardship in dentistry was emphasized in 2019 by experts from the World Dental Federation, the FDI, as antibiotics are often inappropriately prescribed in dentistry. Inappropriate antibiotic prescribing occurs when antibiotics are prescribed unnecessarily (when not needed) or incorrectly (wrong antibiotic, dose and/or duration). Around 80% of antibiotics prescribed in dentistry worldwide are found to be inappropriate, 2.3 adding to the global burden of antimicrobial resistance (AMR). The World Health Organization's (WHO) Global Action Plan provides a framework for development of national action plans (NAPs) to tackle AMR and includes dental prescribers as stakeholders. The FDI's policy statement on antimicrobial stewardship in dentistry and the FDI white paper provide guidance and resources from the WHO for developing stewardship programmes.

Many high-income countries have adopted these gold standards into stewardship measures to tackle AMR including establishing and updating prescribing guidelines for dental practitioners and developing educational resources for consumers. In the United Kingdom, for example, there are antibiotic prescribing guidelines^{7,8} and tools for dentists and patients in the form of desk guides and information leaflets. Additionally, a number of antibiotic stewardship toolkits are available for dental practitioners including self-audit tools, mobile applications and online modules. ⁹⁻¹² The American, Australian and Canadian Dental Associations also provide similar guidelines and resources. ¹³⁻¹⁷ The Centers for Disease Control and Prevention (CDC) provides a checklist for dental practitioners as well as patient resources. ^{18,19}

Stewardship measures are crucial in low and middle income countries (LMICs) and resource constrained settings, which not only bear the brunt of resistant infections but where lack of access to essential antibiotics kills millions.²⁰ The WHO Southeast Asia (SEA) region comprising 11 countries (of which nine are low and lower middle-income countries), is estimated to possess the highest risk of emergence and transmission of antibiotic resistance in healthcare settings and community among all WHO regions.²¹ A high prevalence of oral and dental diseases in this region and poor prescribing practices require that dental practitioners play a vital role in antimicrobial stewardship programmes.^{22,23}

Southeast Asia region member state representatives met in 2011 in Jaipur, India, and expressed commitment towards containing AMR, following which each member state developed its NAP.²⁴ However, an exploration of the publicly available AMR NAPs of the nine low and lower middle-income countries in this region (Supplementary file S1) shows little or no mention of AMR stewardship for dentistry.²⁵ In fact, none of them have a dental representative in their task force or working committee. Moreover, the NAP of eight of

these nine countries available publicly in the WHO website is currently outdated.²⁵ In India; however, the national dental regulatory body and dental association are included as stakeholders responsible for creating awareness and developing guidelines and training modules; nevertheless, information pertaining to surveillance, monitoring, community awareness, research or evidence-based interventions in the dental sector is scarce.

India is the largest global antibiotic consumer by volume with its consumption growth increasing by over a 100% between 2010 and 2015. 26,27 There are approximately 318 dental teaching institutions in the country-both public sector and private sector, producing around 28000 dental graduates each year, the highest in the world.²⁸ As all dental practitioners are potential prescribers, education and training are an important part of any good stewardship programme in dentistry, as are practical prescribing guidelines and implementable stewardship policies. These factors must be considered in light of the large AMR burden in the country, 20,29 high prevalence of dental diseases and antibiotic misuse in dentistry.²² Little is known about dental antibiotic stewardship in India. Despite previous studies attributing antibiotic misuse to a lack of guidelines for dental practice, 22,30-33 there are no robust studies evaluating policies or guidelines for dental antibiotic prescribing in India. The aim of the study was therefore to address this gap in knowledge by undertaking a document analysis to explore the extent to which the current Indian policy and practice for dental antibiotic prescribing and stewardship, aligns with the global best practice. Specific objectives were to:

- Examine if stewardship policies and guidelines for dental antibiotic prescribing exist in India, and to what extent they align with global standards.
- 2. Provide recommendations for policy regarding antibiotic prescribing and stewardship for dental practitioners in India.

2 | METHODOLOGY

THE READ APPROACH: The READ (Ready materials, Extract, Analyse data, Distil findings) approach³⁴ was used to retrieve relevant Indian documents and extract and synthesize emerging data. Ethical approval was not required as the study involved accessing documents available freely in the public domain.

2.1 | Ready materials

A systematic search strategy described below was used to identify relevant documents. As English is the medium of communication in

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medical and dental education in India, only resources published in English were included and those published and/or updated since 2016, when the NAP to tackle AMR was developed in India. All documents were included upon agreement between two researchers (AB, BT), who also agreed on the extracted data. Both researchers have training and significant work experience in dentistry in India and understand the local context and policies.

2.1.1 | Eligibility

Resources that were considered relevant included:

- 1. Policies in public sector such as Antibiotic policy, Oral health policy, etc.
- 2. Action plans at the National and State levels
- 3. Procedural laws and regulations
- 4. Procedures and training manuals
- 5. Clinical practice guidelines, training and educational resources
- Dental (BDS) curriculum formulated by the Dental Council of India
- 7. Antimicrobial stewardship programmes by government organizations relevant to dentistry.

2.1.2 | Information sources and searching

The following search approaches were adopted to ensure resources were not missed.

- Database search: A thorough search for various medical and grey literature databases was performed. Nine databases-Medline and Global Health (through Ovid), CINAHL, Web of Science, Cochrane, Eldis, Global Index Medicus, grey literature databases Proquest and OpenGrey were searched until 31 December 2022 and updated on 31 March 2024. A detailed search methodology and sample search strategies for Medline and ProQuest are given in Supplementary files S2 and S3.
- Google search engine using keywords: Relevant keywords in various combinations (Supplementary file S3) were used on the Google search engine and the first five pages were reviewed for each combination used.
- Targeted website search: Relevant websites of the Indian government, websites of the Dental Council of India (DCI), Indian Dental association (IDA) and other organizations were explored. The list of websites searched is given in Table 1.
- 4. Contacting experts: In order to avoid missing important documents, experts from the DCI, the IDA and dental practitioners in the field of interest were contacted to signpost towards documents or websites relevant to the research question.
- Latest draft dental curriculum formulated by the Dental Council
 of India was critically examined for the extent of coverage of
 knowledge on antibiotics, any references on AMR or 'statement

of intent' on antimicrobial stewardship, and/or recommendations to dentists

All searches including database search, google search and targeted website search were updated again until 31 March 2024.

Two authors (AB, BT) independently reviewed the title and abstract page and excluded all irrelevant resources. Full texts of potentially eligible resources were carefully examined for information pertaining to the research question, and relevant resources were included. Reference list of included documents was examined for further resources. Any disagreement was resolved by involving others in the research team (VA, RK).

Data extraction and analysis

Framework analysis was used to analyse and interpret emerging data given that the objective of this study was to map Indian policy documents related to antibiotic prescribing and stewardship to global best practice.³⁵

The FDI (World Dental Federation's) online library of resources on antibiotic resistance and stewardship³⁶ was used to form a set of 'a priori' codes covering important aspects of dental antibiotic stewardship which in turn mapped on to six broader thematic areas that are essential for good antibiotic stewardship. These are: therapeutic antibiotic prescribing; prophylactic antibiotic prescribing; prescribing resources for dental practitioners; stewardship for dental practitioners; policy and regulatory factors; and patient resources. Initially, general and non-specific codes were given so as not to miss information. New codes were added as new documents were examined. In line with qualitative methodology, the process was iterative and several sets of codes were created and refined after discussion and agreement with all authors. The coding framework is illustrated in Figure 1 and a list of global documents examined to formulate these codes is included in Supplementary file S4.

For each document, specific information pertaining to AMR or stewardship in relation to dentistry and/or specific guidance related to antibiotic prescribing in the dental office was extracted. A matrix was created in an excel spreadsheet, where document names were entered in rows and codes/themes from global documents in columns. The topic, year, type and purpose of the document, and target audience were extracted, along with a general assessment of its credibility (source of the document). Data consistent with our coding framework (Figure 1) were manually charted onto the matrix. As data were extracted, they were analysed and interpreted through an iterative approach. The results are presented according the six key thematic areas identified. Although the approach was largely deductive where prior issues guided the framework, analysis was open to any new themes emerging from the data.

3 | RESULTS

Out of 3039 records identified and screened from all sources, 25 were included for final analysis. Only three of the 25 documents



Source		
number	Indian organization	Website
1	Open government data Platform of India—Open Government Data Portal designed, developed and hosted by the National Informatics Centre (NIC), under the aegis of the Ministry of Electronics & Information Technology Health and Family welfare data Health and Family welfare data—field search	https://data.gov.in https://data.gov.in/sectors/Health%20and%20Family%20wel fare-9312 https://data.gov.in/search/site?query=health&field_search=&item= 100
2	National Health portal National Health Policy 2017	https://www.nhp.gov.in https://www.nhp.gov.in/about-national-health-portal_pg https://www.nhp.gov.in/nhpfiles/national_health_policy_2017.pdf https://www.nhp.gov.in/waaw-2019_pg
3	National Oral Health Programme NOHP	https://www.edantseva.gov.in/content/national-oral-health-programme
4	Department of Health Research	https://dhr.gov.in
5	NCDC—National centre for disease control, under DGHS, MoHFW, Gol. NCDC—AMR page National Rx Guidelines for Antimicrobial Use in Infectious Diseases 2016 National Guidelines on Infection Prevention and Control in Healthcare Facilities National Action Plan on AMR (NAP-AMR 2017–2021) Guidance for State Action Plans for Containment of Antimicrobial Resistance (SAPCAR) Patient Awareness video	https://ncdc.gov.in/index.php https://ncdc.gov.in/index1.php?lang=1&level=1&sublinkid=145& lid=74 https://ncdc.gov.in/showfile.php?lid=649 https://ncdc.gov.in/index1.php?lang=1&level=2&sublinkid=390& lid=348 https://ncdc.gov.in/WriteReadData/l892s/File645.pdf https://ncdc.gov.in/index1.php?lang=1&level=2&sublinkid=389& lid=347 https://ncdc.gov.in/index1.php?lang=1&level=3&sublinkid=810& lid=604 Three short videos in home, school and pharmacy settings respectively (Hindi Language)
6	Niti Aayog—Public policy thinktank	https://www.niti.gov.in https://www.niti.gov.in/documents/reports
7	Integrated Disease Surveillance Project-to monitor disease trends. Central, State and District Surveillance Units (CSU, SSU, DSU)	https://www.idsp.nic.in
8	National Health Mission—for Health System Strengthening in rural and urban areas NOHP	https://www.nhm.gov.in http://qi.nhsrcindia.org/cms-detail/stg-guideline/MTM5 https://nhm.gov.in/index1.php?lang=1&level=2&sublinkid=1044& lid=608
9	Health Management Informations System (HMIS) portal- to monitor the National Health Mission and other Health programmes and provide key inputs for policy formulation and appropriate programme interventions. gives info on health indicators of India, derived from data uploaded by the States/UTs	https://hmis.nhp.gov.in/#!/
10	National Portal of India	https://www.india.gov.in https://www.india.gov.in/topics/health-family-welfare
11	Vikaspedia-online information guide launched by the Government of India. Run by the Department of Electronics and Information Technology, Ministry of Communications and Information Technology	https://en.vikaspedia.in/health/nrhm https://en.vikaspedia.in/health https://vikaspedia.in/health/health-directory/standard-treatment-guidelines https://vikaspedia.in/health/sanitation-and-hygiene/national-guide lines-for-infection-prevention-and-control-in-healthcare-facilities https://vikaspedia.in/health/nrhm/national-health-programmes-1/ national-oral-health-programme https://vikaspedia.in/health/where-there-is-no-dentist
12	Ministry of Health & Family Welfare National Guidelines for Infection control in healthcare facilities	https://main.mohfw.gov.in https://www.mohfw.gov.in/pdf/National%20Guidelines%20for% 20IPC%20in%20HCF%20-%20final%281%29.pdf
13	Clinical Trial Registry	http://ctri.nic.in/Clinicaltrials/advancesearchmain.php
14	Central Drugs Standard Control Organization—a National Regulatory Authority (NRA) of India	https://cdsco.gov.in/opencms/opencms/en/Home/



TABLE 1 (Continued)

TABLE	1 (Continued)	
Source number	Indian organization	Website
15	Directorate General of Health Services (attached to MoHFW)— repository of technical knowledge concerning Public Health, Medical Education and Health Care	https://dghs.gov.in https://dghs.gov.in/content/1352_3_NationalOralHealthProgram me.aspx
16	Indian Dental Association IDA's Emergency Dental Centre IDA's Oral Health Programme	https://www.ida.org.in/Home https://www.ida.org.in/Membership/Details/Dental-Therapeutics https://www.ida.org.in/Membership/Details/DrugsusedinDentistry http://edc-ida.org.in/#/home http://nohp.org.in/#/Home
17	INDIAN COUNCIL OF MEDICAL RESEARCH—the apex body in India for the formulation, coordination and promotion of biomedical research	https://main.icmr.nic.in https://main.icmr.nic.in/content/guidelines-0
18	AMSRN—(India's) Antimicrobial Resistance Surveillance & Research Initiative	https://iamrsn.icmr.org.in/index.php/amsp/amsp-guidelines https://iamrsn.icmr.org.in/index.php/amsp/icmr-amsp
19	PREVENT-IT project Co-funded by the Erasmus+ Programme of the European Union	https://preventit.in/about/antibiotic-resistance-project-abr/
20	ReAct Network	https://www.reactgroup.org https://www.reactgroup.org/news-and-views/news-and-opinions/ year-2017/antibiotic-resistance-national-workshop-in-india-for- voluntary-organizations/
21	Centre for Science and Environment Public interest research & advocacy organization based in New Delhi	https://www.cseindia.org/page/aboutus https://www.cseindia.org/page/antimicrobial-reststance-progr amme https://www.cseindia.org/workshop-on-development-and-imple mentation-of-state-action-plan-on-antimicrobial-resistance-9498
22	Sameeksha ("Review" in Hindi)—a compilation of publications/ resources on AMR, along with a brief summary. It aims to review and share information according to strategic priorities of India's NAP- AMR	https://www.who.int/india/antimicrobial-resistance-sameeksha
23	WHO—Institutional repository for information sharing (IRIS)	https://apps.who.int/iris/discover?scope=10665%2F126384&query=dental+india+antibiotics&submit=
24	IIMAR—Indian Initiative for Management of Antibiotic Resistance	http://save-antibiotics.blogspot.com/2017/08/ http://antibio-resistance.blogspot.com
25	Dental Council of India—DCI portal	https://dciindia.gov.in/Dentistact1948.aspx https://dciindia.gov.in/Rule_Regulation/Gazette_Notification_reg_ DCI_Revised_Dentists_Code_of_Ethics_Regulations_2014_27.06. 2014.pdf https://dciindia.gov.in/Rule_Regulation/Continuing_Dental_Education_Regulations_2018.pdf
26	NABH-National Accreditation Board for Hospitals and Healthcare facilities	https://www.nabh.co/images/Standards/NABH%205%20STD% 20April%202020.pdf

were identified from searching databases (Supplementary file S5). The document search and selection process are illustrated in the PRISMA flowchart (Figure 2).

3.1 | Description of sources

Of the 25 resources, four were action plans $^{37-40}$ six were policy documents, $^{41-46}$ 12 were national and state guidelines, $^{47-58}$ two reports, 59,60 and one dental curriculum 61 (in draft stage). Of the six policies, three 43,44,46 were antibiotic policies from central

government-run public hospitals. Of the 12 guidelines, eight^{47-52,56,58} were national-level and four^{53-55,57} were state-level guidelines involving the states of Uttar Pradesh, Maharashtra, Odisha and Delhi. A search of the Indian Dental Association (IDA) website⁶² was carried out for antibiotic prescribing or stewardship resources. The data from included documents and the draft dental curriculum are presented in Tables 2 and 3. Apart from the dental curriculum, all other documents were general policy or guidance documents, and were non-specific to dental practitioners. Overall, four documents did not have a publication date, ^{46,48,53,55} two had no clear aims ^{43,53} and two documents did not mention the target audience. ^{45,56}

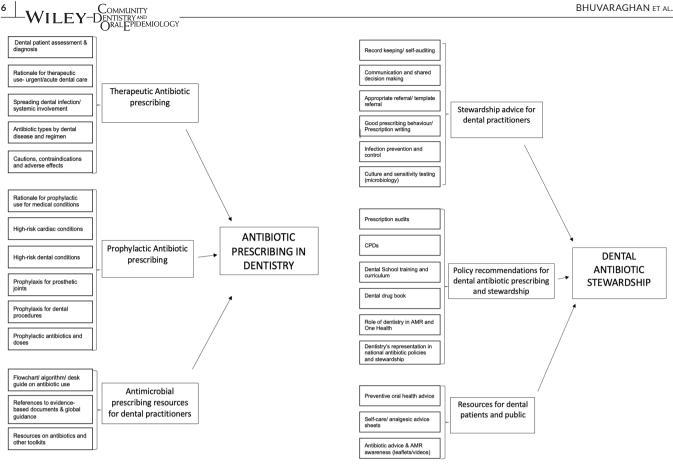


FIGURE 1 Coding framework mapping Indian policy documents on antibiotic prescribing and stewardship in dentistry to global documents.

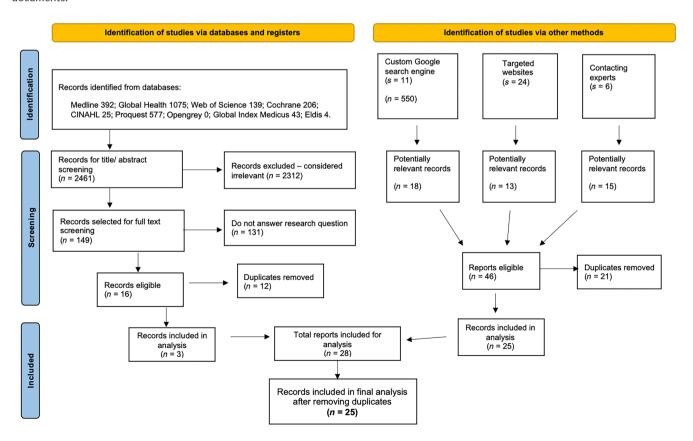


FIGURE 2 Prisma flowchart-search and selection process of Indian policy documents.

TABLE 2 Key data on dental antibiotic prescribing and stewardship identified from the documents.

					ORAL EPIDE	MIOLOGY VVILEY
Usefulness for dental prescribers	A general action plan for the country Not specific to dentistry. No information for dental practitioners on appropriate Ab prescribing	Not specific to dentistry. No information/guidance for dental practitioners on appropriate Ab prescribing	Not specific to dentistry. No information/guidance for dental practitioners on appropriate Ab prescribing	Not specific to dentistry. No information/guidance for dental practitioners on appropriate Ab prescribing	Acknowledges the problem of AMR. No specific information for dental practitioners	No specific information for dental practitioners
Dental information identified	Among other priorities: DCI and dentists added as one of the stakeholders Awareness of prescribers, monitor use in communities e.g. clinics; advised regulatory bodies to review/revise curriculum to incorporate AMR, and develop periodic training (CPD) for practitioners and trainees. Advises professional associations (including IDA) to ratify and disseminate national antimicrobial use guidelines, and also to develop AMS resources	In line with NAP-AMR Advises to develop AMR module for CME/ CPD for relevant professional groups. Advises inclusion of AMR in curricula of professional Universities. Recommends stewardship training for dentists	In line with NAP-AMR Advises professional educational programmes for doctors, including dentists	In line with NAP-AMR Review and revision of professional curriculum, developing and implementing training modules Also acknowledges & identifies challenges in implementing AMS programmes	Strengthening of six professional councils, including dental Calls for standardization of guidelines for antibiotic use, limiting use and otc sale, prescription audit in hospital and community Suggests collaboration with NGOs/private sector for this	To reform and strengthen dental education and training in India. Emphasis on global health. There is no specific mention of antibiotic prescribing or AMS
Target audience	Stakeholders in human health, animal health and agriculture.	Stakeholders in human health, animal health and agriculture	Stakeholders in human health, animal health, agriculture	Stakeholders in human health, animal health, agriculture & environment	Health sector (MoHFW), Gol	national and state level policymakers, health resource planners, researchers, academicians, service providers and service seekers across the country
Author/ formulating authority	Government of India	Government of Kerala state	Government of Madhya Pradesh state	Government of NCT Delhi	монғw, gol	МонҒW, Gol
Goal/purpose	To effectively combat antimicrobial resistance in India, and contribute towards the global efforts to tackle this public health threat	To develop state action plan in alignment with NAP and GAP	To contain AMR in the state in alignment with the NAP	To develop and implement a State Action Plan to address AMR, in alignment with the NAP-AMR and the GAP-AMR	To attain the highest possible level of health and well-being for all through a preventive and promotive health care orientation in all developmental policies, and universal access to good quality health care services without anyone having to face financial hardship as a consequence.	To provide a framework for prevention of oral diseases and promotion of oral health for all.
Main theme	AMS	AMS	AMS	AMS	Health	Oral Health
Document type	Action Plan	Action Plan	Action Plan	Action Plan	Policy	Policy
Year	2017-2021	2018	2019	2020	2017	2021
Title of document	National Action Plan on Antimicrobial Resistance (NAP-AMR)	(Kerala Antimicrobial Resistance Strategic Action Plan—KARSAP)	(Madhya Pradesh State Action Plan for containment of Antimicrobial Resistance MP—SAPCAR)	(State Action Plan to combat AMR in Delhi: SAP-CAR)	National Health Policy	National Oral Health Policy
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	Usefulness for dental prescribers	No specific information for dental practitioners	No separate section for dental diseases Dental aetiology of cellulitis, Ludwig's angina and Vincent's angina overlooked Antibiotic prophylaxis in the dental clinic not discussed	No separate dental section, with emphasis on incision and drainage, and removal of source of infection by way of rct/extraction High risk dental procedures needing antibiotic prophylaxis not listed	No separate dental section, with emphasis on removal of source of infection by way of RCT/extraction in addition to incision and drainage High risk dental procedures needing antibiotic prophylaxis not listed	No separate guidelines for dental settings; however advises HCIs to develop appropriate AMSPs	No clear guidelines on when to/not to prescribe antibiotics (indications for use). Common antibiotic regimen not available
	Dental Information identified	Consider introducing prescription audit and formulary restrictions. CME for hospital staff and for hospitals in surrounding areas Customized antibiotic policy for each hospital including surgical prophylaxis None specific to dentistry	Antibiotic prescribing for cellulitis (non-tooth related) mentioned Ludwig's angina and Vincent's angina are classified under respiratory tract infections and antibiotic regimen given	Prescribing for deep neck space infections/ cellulitis due to dental causes (including suppurative parotitis, peritonsillar abscess, Ludwig's angina) Advocates antibiotic prophylaxis (Infective endocarditis) for high risk dental procedures in high risk cardiac patients. While the high risk cardiac patients. mentioned, which dental procedures fall under high risk category are not listed	Dental source for deep neck space infection acknowledged. Prescribing dose for cellulitis, suppurative parotitis, Ludwig's angina and odontogenic source of space infections given. Drainage of abscess and pus culture advised. Advocates antibiotic prophylaxis (Infective endocarditis) for high risk dental procedures in high risk cardiac patients. While the high risk cardiac conditions are mentioned, which dental procedures fall under high risk category are not listed	Acknowledges that inappropriate antibiotic use is common in dentistry and recommends facility specific clinical practice guidelines	Separate sections for dental caries, gum disease—but prescribing guidelines vague. For e.g. "prescribe antibiotics if needed" for dental pain, gum disease, abscess/swelling
	Target audience	Hospitals and other? healthcare institutions	Clinicians in healthcare settings	Health care professionals	Health care professionals	Health care institutions	State and district program officers and service providers
	Author/ formulating authority	Kamini Walia, ICMR	OMR	ICMR	ICMR	ICMR	National Health Mission, MoHFW
	Goal/purpose	To describes the strategies and recommendations for formulation of AMSP policy for Indian hospitals (? And healthcare settings)	To ensure appropriate antimicrobial treatment and limit inappropriate use in the management of infections by addressing issues like antibiotic selection, dosing, route, duration, adverse drug events, and cost and prevention of unintended collateral damage	To rationalize the usage of antibiotics on National List of Essential Medicines (NLEM) and to establish consistency in the treatment of various infectious conditions-update to 1st ed	n/av (same as that of previous edition?)	To inform, encourage and support health care institutions to initiate the implementation of antimicrobial stewardship initiatives, as well as combating antimicrobial resistance	The aim of these guidelines is to strengthen the delivery of integrated oral health care services in India.
	Main theme	AMS	Antimicrobial Prescribing	Antimicrobial Prescribing	Antimicrobial prescribing	AMS	Oral/dental guidelines
	Document type	Policy	Guidelines	Guidelines	Guidelines	Guidelines	Guidelines
	Year	2019	2017	2019	2022	2018	2020
E 2 (Continued)	· Title of document	Policy document on artimicrobial stewardship practices in India	Treatment Guidelines for Antimicrobial Use in Common Syndromes (1st ed)	Treatment Guidelines for Antimicrobial Use in Common Syndromes (2nd ed)	Treatment Guidelines for Antimicrobial Use in Common Syndromes (3rd ed)	Antimicrobial Stewardship Program Guideline	Operational Guidelines for Oral Health Care at Health and Wellness Centres
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Usefulness for dental prescribers	No specific information for primary care dental practitioners/dental clinics	No specific information for primary care dental practitioners/dental clinics	No specific information for primary care dental practitioners/dental clinics	No separate section for dental diseases. Dental aetiology of cellulitis, Ludwig's angina and Vincent's angina overlooked	Antibiotics advised for inappropriate conditions where dental Rx would suffice	Antibiotics advised for inappropriate dental conditions. Various conditions mentioned under different sections such as Ent, ophthalmology, dental and cardiology, making it difficult to read	Abscess not clarified- localized/spreading infection. Including extractions as class Il wounds thereby wrongly recommending antibiotics for routine extractions (Continues)
Dental information identified	General. No specific information for dentists. Intended for 2* and 3* HCF. Needs adapting for 1*care and CHCs	Recommends formulation of antibiotic policy and standard treatment guidelines for various clinical syndromes	General principles of Ab use. None specific for dentists	Prescribing for cellulitis, Ludwig's angina and Vincent's angina	Abs advised for most dental conditions such as dental caries, reversible and irreversible pulpitis, pulp polyp, apical periodontitis-acute and chronic, acute alveolar abscess, periodontal abscess, jaw osteonwelitis, pericoronitis, ANUG, aggressive periodontitis, impacted third molars and space infections. Advises prescribing for space infections, cellulitis, Ludwig's angina. Advises prophylaxis in patients with cardiac conditions	Has separate section for dental conditions; however, advises antibiotics for dental caries with pain. Antibiotics for dental space infections, orbital cellulitis, sinusitis advised Separate section for antibiotic prophylaxis for IE comprising high risk cardiac conditions, high risk dental procedures and antibiotics. But needs updating	Recommends prophylactic Ab for class II surgical wounds and therapeutic for class III and IV Dental extraction and alveoloplas ty—Class II Dental extraction with abscess—Class IV
Target audience	Hospital administrators, clinical managers, doctors, nurses and allied professionals as well as policy makers	All staff including doctors, nurses, other clinical professionals and managers working in the hospital	Healthcare providers in hospitals	Healthcare practitioners	Medical officers and health care providers from different levels in the public health care system	Healthcare practitioners	NCT Delhi
Author/ formulating authority	NCDC, MoHFW	NCDC, МоНFW	ICMR	Department of MoHFW, Government of Uttar Pradesh	Public Health Department, Government of Maharashtra	Directorate of Health Services, Odisha	State Government, NCT Delhi
Goal/purpose	To support improvement in infection prevention and control at the health care facility level and control hospital acquired infections	To provide evidence-based information in the prevention and control of infection	To prevent the health care workers and the environment from the transmission of infections	n/av	To serve as a comprehensive index of protocols for the common conditions, syndromes and ailments	n/av	To establish standards in prevention, control measures and minimize HAIs, to define policies and procedures for implementing and monitoring of HAIs at the HCF and to establish antibiotic stewardship program with at least yearly updating of evidence based antibiotic policy with monitoring antibiotic policy with monitoring authorities, monitoring antibiotic utilization in various areas of the HCF
Main theme	Infection Control	Infection	Infection control	Antimicrobial Prescribing	General prescribing guidance	General Prescribing guidance	Prescribing and Infection control
Document type	Guidelines	Guidelines	Guidelines	Guidelines	Guidelines	Guidelines	Guidelines
Year	2020	1	2017			2018	2016
Title of document	National Guidelines for Infection Prevention and Control in Healthcare Facilities	Hospital Infection Prevention and Control guideline	Hospital Infection Control guidelines	Antimicrobial Guidelines, Uttar Pradesh	Standard Treatment Protocols Maharashtra-for Medical practitioners	Standard Treatment Guidelines of Odisha	SOP Infection Control 2016 NCT Delhi
Source	13	14	15	16	17	18	19

TABLE 2 (Continued)

Source	Title of document	Year	Document type	Main theme	Goal/purpose	Author/ formulating authority	Target audience	Dental information identified	Usefulness for dental prescribers
50	Antibiotic policy, All India Institute of Medical Science, AllMS, Jodhpur	n/av	Policy	Antimicrobial Prescribing	To provide a simple, best empirical/ specific treatment of common infections, promote safe, effective, economic and rational use of antibiotics and minimize the emergence of bacterial resistance in community	Dept of Microbiology, AIIMS Jodhpur	Healthcare practitioners	Prescribing for celluitis, Ludwig's angina and Vincent's angina	No separate section for dental diseases. Dental actiology of celluitis. Ludwig's angina and Vincent's angina overlooked
21	Antibiotic policy, AIIMS, Bhopal	2017	Policy	Antimicrobial Prescribing	To provide a guiding framework for strengthening the rational us of antibiotics in the institution and help curb the growing menace of AMR	Director, AIIMS & Med Sup, HICC	Healthcare practitioners	Prescribing for cellulitis, Ludwig's angina	No separate section for dental GI diseases. Dental aetiology of Cellulitis not mentioned
22	Antibiotic policy, AIIMS, Rishikesh	2020	Policy	Antimicrobial Prescribing	To improve optimal utilization of antimicrobials, decrease turn-around time for all microbiological diagnosis, reduce hospital acquired infections and achieve 100% vaccination to all health care workers		Healthcare practitioners	Prescribing for cellulitis (non-specific)	No separate section for dental diseases. Dental aetiology of cellulitis not mentioned
53	Establishing Antimicrobial Resistance, Surveillance & Research Network in India: journey so far	2019	Report	AMR surveillance	Reports on the conception and implementation of AMR surveillance network (set up in 2013), whose aim was to understand the extent and pattern of antimicrobial resistance (AMR) and use this evidence to guide strategies to control its spread	Walia K et al, ICMR	Policymakers and healthcare practitioners	Data generated through this Network have been used to develop standard treatment guidelines across the tertiary level healthcare institution Data shows increasing resistance in Gram-negative bacteria. Also increasing resistance to third-generation cephalosporins, fluoroquinolones and carbapenem. The data expose several gaps and lacunae in the ecosystem and highlight opportunities for action by multiple stakeholders.	No specific dental information available
54	A roadmap for addressing antimicrobial resistance in lowand middle-income countries; lessons learnt from the public private participation and co-designed antimicrobial stewardship programme in the State of Kerala, India	2021	Recommendation/ AMS AMS plan	AMS	Reports the collaborative work of multi-professional groups (PPP) in the co-design, development and implementation of AMS plan across Kerala state Disease based clinical treatment guidelines and state-wide infection prevention policy	Singh S et al.	All stakeholders aiming to implement action plans for AMR	Senior office bearers of 14 professional bodies, including the state branch of the IDA were involved in developing antibiotic CTGs. Curriculum change suggested for medical students. CME programmes and awards/incentives suggested. Teaching modules (educational content) developed for HCWs and being piloted. Similar strategy being tried for dental	One of the private institutions (Amrita Institute) introduced AMR and antibiotic use in microbiology & pharmacology syllabi (2nd year) for dental trainess. No antibiotic guidances available for clinical dental practice. This PPP for AMS was initiated for 3" care setting; challenges wrt 1" & 2" care

Abbreviations: Gol, Government of India; ICMR, Indian Council for Medical Research; MoHFW, Ministry of Health and Family Welfare; NAP, National Action Plan; NCDC, National Centre for Disease Control.

(Continues)

TABLE 3 Antimicrobial Resistance and Stewardship in the draft undergraduate Dental curriculum 2022 Bachelor of Dental Surgery (BDS)-India.

			Topic related to antimicrobials covered	to covered		
Subject	Study year	Competency studied	Antibiotics	AMR AMS	Learning mode	Miller's pyramid category ^a
Pharmacology	=	Antimicrobial drugs, cancer chemotherapy $\&$ Immunopharmacology. Knowledge on drugs used for chemotherapy of Infections (bacterial, fungal, viral)	>		Theory/didactic lectures	Υ
		Learn about different classes of drugs, their mechanism of action and adverse effects that enable students to prescribe precise drugs for different oral disease manifestations	>		Theory/didactic lectures	\mathbf{x}
		P drug selection for common diseases Knowledge and understanding of advarce offerts of drugs in general and	> >		Skills	Ŧ A
		Knowledge and understanding of adverse effects of drugs in general and dental practice	>		Ineory	∀
		Pharmacology to Practice in Dental Clinic-knowledge of prescription writing for oral candidiasis, pericoronitis, apical periodontitis, post-extraction medication, xerostomia and oral ulcers.	>		Skills station	v
Microbiology	=	Competent in interpreting the microbiological case reports and antimicrobial susceptibility tests, and judiciously choose and prescribe antibiotics Should be able to follow the aseptic procedures, should be able to demonstrate the proper infection control measures/PPE, hand hygiene measures	>		Skill section Skill section	KH S
Oral Medicine and Radiology	≥	Ability to safely prescribe appropriate drugs as a follow response to medical therapy Evaluation of knowledge on pharmacological management of Oro facial disorders	> >		Skill section Skill section	Do Do
Oral and Maxillofacial Surgery	≥	Knowledge and understanding of principles and techniques of extractions and transalveolar extractions, pathophysiology and management of odontogenic infections, maxillofacial space infections, pathophysiology of maxillary sinus diseases and management. To understand the various therapeutic drugs and their rational prescription. Knowledge on indications, contraindications and identification of adverse effects. Understanding the importance of infection control in the operating area Current evidence based practice in medical management of common maxillofacial disorders. Pharmacological management of orofacial disorders Manage orofacial space infections with prophylactic antibiotics and incision and drainage	>>>		Lecture Lecture Lecture Skills section Skills	-Oral Epidemiology
Paediatric Dentistry	2	Administer appropriate medications to alleviate pain and infection	>		Skill	ОО
aK. know: KH. know how: S. show: SH. show how/Do	: works S:wc	SH. show how/Do.				

^aK, know; KH, know how; S, show; SH, show how/Do.



3.2 | Alignment of policy documents with global standards

Compliance (or not) of Indian documents with key elements of the framework developed from global standards (Figure 1) is as follows:

3.2.1 | Therapeutic dental antibiotic prescribing

The assessment of global guidance showed that antibiotics were not recommended for treating toothache and localized dental infections. Rather, therapeutic antibiotics were only recommended for spreading dental infections with systemic involvement such as fever and lymph node enlargement with the caveat that managing the source of dental infection that is, draining an abscess, extraction or root treatment should be performed in addition to antibiotic prescription.^{7,8,14}

Nine Indian guidelines^{43,44,46,49,50,53–56} advised antibiotic regimen in cellulitis, Ludwig's angina and Vincent's angina, of which only two mentioned treating the dental source of the problem^{47,56} or the need for abscess drainage.^{54,56}

Precise justification for antibiotic prescribing was not identified in the documents. There were recommendations for antibiotic use in toothache, ⁵⁴ and a range of dental conditions from dental caries to periodontitis to osteomyelitis and space infections, ⁵⁵ and one document gave subjective advice to practitioners, such as 'prescribe antibiotics if needed'. ⁴⁷ Dental extraction of a tooth with abscess was classified as class IV surgical wound requiring therapeutic antibiotics, ⁵⁷ and sinusitis of dental origin was only included under the ENT section. ⁵⁴ The antibiotic regimen were found to vary between documents.

Though no comprehensive document included details on therapeutic antibiotic prescribing in dentistry, the dental emergencies section of the Indian Dental Association website included a summary table of dental conditions including management of dental pain. Where antibiotics were advised for therapeutic use in systemic cellulitis, the antibiotic type/regime was not given.

There was also no clear justification for or against antibiotic use contrary to global guidance, and none of the identified documents stated that antibiotics should not be used for localized dental pain.

3.2.2 | Prophylactic dental antibiotic prescribing

Global guidance advises pre-operative prophylactic antibiotics for high-risk dental procedures involving manipulation of gingiva or periapical region, in patients with certain high-risk cardiac conditions such as prosthetic cardiac valve or its repair, previous endocarditis, unrepaired cyanotic congenital heart disease (CHD), completely repaired CHD within 6 months of procedure, repaired CHD with residual defects, and cardiac transplant patients who develop heart valve problems. 16,63,64 Routine prophylaxis is also not recommended for

patients with prosthetic joints, and those undergoing routine dental procedures including minor surgical procedures.^{7,15}

With respect to Indian documents, two documents provided a list of high-risk cardiac conditions^{50,56} and only one⁵⁴ reported high-risk dental procedures. Four guidelines listed out the prophylactic regimen for high-risk cardiac patients.^{50,54-56} Simple dental extractions were classified as class II surgical wounds that required prophylactic antibiotics,⁵⁷ contrary to the global guidelines which advise against prophylactic antibiotics in routine dental extractions and other minor surgical procedures.⁷ The IDA website had a section for prophylactic antibiotic use against infective endocarditis and for dental patients with joint replacement, but not for prophylaxis for other medical conditions or minor surgical procedures.⁶²

3.2.3 | Antimicrobial prescribing resources for dental practitioners

Globally, several toolkits were identified that enable dental practitioners' adherence to guidelines. 19,65 However, there were few practical antibiotic prescribing resources or toolkits for those in India. While the Antimicrobial Stewardship Programme Guidelines framed by the Indian Council for Medical Research (ICMR) made reference to the UK's openly available toolkits such as TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) and SSTF (Start Smart Then Focus) for primary and secondary care respectively, the document does not provide any recommendations for the Indian setting. 58 Several documents emphasized on general principles of antibiotic use and good prescribing 44,49,50,55-57 which could be tailored to dentistry. The IDA's resource centre lists 951 different brands of antibiotics with their drug interactions and adverse effects, 62 although the range of antibiotics required for management of dental infections is limited, especially in primary dental care.

3.2.4 | Stewardship advice for dental practitioners

Global documents, in addition to prescribing guidelines, also provide advice on stewardship components such as: self-evaluating one's prescribing behaviour; antibiotic good prescribing; infection prevention and control in the dental practice; culture and sensitivity testing where required; appropriate specialist referral and communication with patients.^{7,11}

The operational guidance for oral healthcare⁴⁷ advised dental surgeons to ensure good record keeping. Four other general documents^{47,53,57,58} advocated record keeping, electronic prescribing but gave no information on how and if these were being implemented at present, especially with respect to general dental practitioners—who in India are mostly private. The National infection prevention and control guidelines⁵¹ advised educational programmes for all clinicians. In general, information pertaining to microbial culture and sensitivity testing in dental abscesses, appropriate referral to

COMMUNITY
—DENTISTRY AND
ORAL EPIDEMIOLOGY—WILEY—13

specialists or shared decision making with dental patients were not identified.

3.2.5 | Policy recommendations for antibiotic prescribing and stewardship for dental practitioners in India

India's National (2016) and State AMR action plans (2017, 2018 and 2019),³⁷⁻⁴⁰ in which the National Dental Council and Dental Association are included as stakeholders, and the National Health Policy,⁴⁵ advocated reviewing and revising professional education to include AMR in the curriculum. They also recommended that the regulatory bodies develop training programmes on optimal antibiotic use, including continuing professional development (CPD) resources, AMR modules and stewardship training for professionals. The NAP also advised development and use of standard treatment guidelines for antibiotic prescribing, although no guidelines on dental antibiotic prescribing was identified.

The ICMR acknowledged inappropriate antibiotic use in dentistry and recommended facility specific clinical practice guidelines; however, there was no dental section or content included in the ICMR's 'Treatment Guidelines for Antimicrobial use in common syndromes'.⁵⁸ Educating dental trainees through inclusion in the curriculum and improving provider knowledge by way of CPD programmes are important elements reported in the global stewardship framework.^{1,5} However, the analysis of the recent undergraduate draft dental (BDS) curriculum 2022 (Table 3), showed no mention of either antibiotic resistance or antimicrobial stewardship. 61 While this curriculum mentioned about infection control and prescribing knowledge for orofacial and bacterial infections, rational antibiotic use did not feature in important subject areas such endodontics, periodontics, restorative or paediatric dentistry. Antibiotics or AMS also did not feature in the 'Continuing Dental Education Regulations' set forth by the DCI.²⁸ Additionally, no CPD programmes on dental antibiotic prescribing were identified. While the FDI website indicates that the Indian Dental Association is a signatory in the FDI pledge to tackle AMR, no such information is available on the IDA website. Global documents report audit and feedback as key elements of dental stewardship programmes, yet there was no mention of this in the included Indian documents.

3.2.6 | Resources for dental patients and public

Improving patient awareness is an important component of global dental stewardship with posters and leaflets clarifying that toothache cannot be cured by antibiotics. 9,19 Indian policy documents identified in the search did include advice for improving antibiotic awareness among the public, including resources, celebrating antibiotic awareness week, awareness through mass media and in schools and higher educational institutions. 37-40,47,51 However, these were non-specific to dental problems and/or patients. The IDA website

did not contain resources for dental patients, the public or for dental practitioners that could be used to inform and educate on appropriate antibiotic use in dentistry.

4 | DISCUSSION

This document analysis was conducted to assess the robustness of dental antibiotic policies and stewardship in India, where inappropriate antibiotic prescribing by dental practitioners is commonplace. ^{22,66} An understanding of the extent to which such policies exist is essential to make headway into further policy formulation, policy implementation, and to bring about practice change in antibiotic prescribing in dentistry in India. This study is the first of its kind and could serve as a catalyst for engaging key stakeholders including policymakers in discussions about developing future AMS strategies for dentistry in India.

Although overuse of antibiotics in dentistry has been well documented by the ICMR, ⁵⁸ the findings of this study show that there were no dedicated antibiotic prescribing guidelines for dental practitioners in India, and little or no mention of dentistry in key policy documents such as the NAP and Standard Treatment Guidelines. This indicates a huge gap between the need for dental AMS in India and the existing policies for prescribing clinicians. Contradictory and subjective information provided in some policy documents ^{47,54,55,57} could encourage dentists and other health professionals such as general practitioners to prescribe antibiotics for common dental conditions for which they are contraindicated. While a lack of dental guidelines can negatively influence practitioner attitude and awareness, a discrepancy between documents can lead to lack of trust and poor adoption.

There are some limitations to consider in drawing the above conclusions from the current document analysis. The search was conducted using documents in the public domain and therefore may have missed out those currently in draft or those being updated. This risk was mitigated by contacting several key stakeholders including those from dental regulatory bodies, who confirmed that there were no policy documents updates in progress. However, the draft undergraduate curriculum which was accessed through this approach did not contain information on AMR or its relevance to dentistry nor did it signpost to global guidance on appropriate prescribing of antibiotics for dental conditions. Key strengths included the systematic search, which was comprehensive and led to identification of several key policy documents on health, oral health, and AMR. Additionally, several stakeholders were contacted to avoid missing important policy documents.

Dental infections are unique in that they are caused by bacteria yet require no antibiotics when localized and can be managed by dental treatment to remove the source of infection. ^{14,67} Global guidelines specify use of antibiotics for those dental infections which are spreading and associated with systemic involvement, and not for localized dental conditions, toothache, and routine dental procedures. ^{14,67} However, unlike in high income countries, prophylactic use of antibiotics for routine dental procedures such as extractions

and root canal treatments is common in India.²² There is therefore an urgent need to develop guidelines for dental antibiotic prescribing to guide dental practitioners in India and include them in key documents such as the NAP and Standard Treatment Guidelines. It is essential that these guidelines clarify not only on when to prescribe antibiotics, but also when not to, particularly as global guidance does not recommend therapeutic and prophylactic use for routine dental procedures. Considering dentistry's contribution to antibiotic misuse, the ICMR should include comprehensive antibiotic prescribing guidelines for common dental conditions and procedures in future revisions of treatment guidelines for antimicrobial use.

While the Indian Dental Association has joined the FDI pledge to tackle AMR, ⁶⁸ this agenda has not produced implementable policies or usable guidelines, nor is this information accessible on the IDA website. This needs to be made apparent to show IDA's commitment to tackling AMR and motivate dental practitioners. Additionally, the information on antibiotics on the IDA website must be tailored to the needs of general dental practitioners. ⁶²

Poor record keeping has been a problem in primary care in India, and acts as a major barrier to stewardship programmes.⁶⁹ Other stewardship measures such as audit and feedback, reflection and self-evaluation, and evaluating effectiveness of interventions such as guidelines and education, all become redundant without a good record keeping system.⁶⁹ Therefore, implementing good record keeping system needs to be a key element in the policies. This needs to be made mandatory, and prescriber behaviour assessed through regular audits. While several documents speak about general stewardship measures such as strengthening microbiology capacity, ^{51,58} infection prevention and control, ^{48,51,52} principles of good prescribing, ^{44,49,50,55-57} and appropriate referral, ^{47,49,54} none of these were specific to dentists, or adapted to the primary care dental setting.

Upon completion of undergraduate training, dentists in India are fully qualified and have the licence to prescribe any type of antibiotics including fixed dose combination (FDC) antibiotics independently. Although the Indian government imposed a ban on several FDC antimicrobial drugs in 2018, irrational combination antimicrobials continue to be available. Therefore, knowledge on AMR and appropriate antibiotic prescribing is essential in both pre and post qualification training. Antibiotic prescribing behaviour in LMICs results from a complex web of interactions between clinicians, patients, pharmacists, drug sellers and the health system.⁷¹ With lack of access to antibiotics resulting in considerable fatalities in India,²⁰ behaviour change is a challenge. This could be achieved by inculcating the idea of rational prescribing and the importance of stewardship right from the undergraduate training period. The draft undergraduate dental curriculum in India does not include stewardship measures to educate dental students on appropriate use of antibiotics in dentistry.⁶¹ This needs to be addressed by including modules on appropriate dental antibiotic prescribing in the curriculum. The National Dental Commission (NDC), soon to be replacing the DCI should take this into consideration. In addition, reinforcing learning by developing toolkits, job aides and educational programmes including CPD programmes will address knowledge gaps and improve prescribing behaviour. While a combination of such educational interventions along with regulatory enforcements has been shown to improve prescriber behaviour in LMICs, dental policies should consider local contextual factors such as economic constraints, access to dental care and reliance on antibiotics to compensate for poor infection control.^{71–73}

The WHO's action plan for oral health in SEA region recommends that addressing AMR in oral health care is essential.²³ To achieve this, India's Oral Health Policy should include AMR along with other programmes for India's common oral and dental challenges such as oral cancers, caries and periodontal diseases. There is a need for stakeholders from dental regulatory bodies and health care policy makers to work together to include antimicrobial stewardship in dentistry into key policy documents.

Finally, an area of concern from this document analysis was the lack of patient awareness resources for antibiotic use for dental problems. The drivers of over-the-counter antibiotic use for dental problems need to be addressed by Indian policy makers as dental problems do not require antibiotic self-medication but rather dental procedures for management. Even when antibiotics are needed, for example for spreading infections, dental intervention is often required to address the source of the problem. Therefore, complementing prescriber knowledge with public awareness and education is key in Indian policies targeting antibiotic stewardship in dentistry. This will also mitigate dentists succumbing to patient expectations for antibiotics.⁷⁴

This document analysis shows a serious lack of policy guidance for antibiotic prescribing for Indian dentists. The dental regulatory body (Dental Council of India/National Dental Commission) and the ICMR along with other stakeholders should urgently develop clear guidance and AMR strategy for mitigating dentistry's contribution to AMR. The lack of stewardship information in the draft undergraduate curriculum is a real concern and the DCI/NDC should intervene and include relevant modules to educate trainees. Although the Indian Dental Association is not involved in policy development, it can work with the ICMR and the DCI/NDC to endorse and help implement future policies.

5 | CONCLUSION

AMR is a global challenge and the burden in India is very high. Dentistry is a significant contributor to antibiotic overuse in India and this document analysis showed that there were no dedicated antibiotic prescribing guidelines for dental practitioners in India, and little or no mention of such guidelines in key policy documents on AMR such as the NAP on AMR. The draft dental curriculum has no mention of AMR or stewardship. In addition, contradictory and subjective information provided in some policy documents could encourage dentists and other health professionals such as general practitioners to prescribe antibiotics for common dental conditions for which they are not indicated. There is an urgent need to develop antibiotic prescribing guidelines for dental practitioners in India and include these in Indian policy documents on AMR in particular the NAP on AMR.

—Community Dentistry and Oral Epidemiology—WILEY 15

AUTHOR CONTRIBUTIONS

A.B.: Conception and design, search strategy, study screening, data extraction and synthesis of results, writing-original draft preparation and writing-review and editing. R.K.: Conception and design, synthesis of results, critically revised the manuscript. J.W.: Conception and design, relevance of research results to practice, critically revised the manuscript. B.T.: Study screening, data extraction and synthesis, critically revised the manuscript. V.R.A.: Conception and design, synthesis of results, critically revised the manuscript. All authors gave their final approval and agree to be accountable for all aspects of the work.

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The authors declare no conflict of interest.

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Data will be made available upon reasonable request to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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