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# Antibiotic use by dentists in Germany: a review of prescriptions, pathogens, antimicrobial resistance and antibiotic stewardship strategies

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***Background***: In Germany, 85% of all antibiotics are prescribed in the outpatient care sector, and dentists account for 11% of the total outpatient antibiotic prescriptions. ***Objective and Method***: Summarise published literature on antibiotic use, pathogens and antibiotic resistance in odontogenic infections and German clinical guidelines and interventions for antibiotic use in dental care. ***Results***: In contrast to other outpatient physicians, the volume of antibiotics prescribed by dentists in Germany did not decrease over the last decade. Penicillins and aminopenicillins are the most frequently prescribed antibiotics (70% of all prescriptions), followed by clindamycin (26%). *Streptococcus* spp. and *Staphylococcus* spp. are frequent pathogens isolated from odontogenic infections. However, the infections are often polybacterial with a mixed growth of anaerobic and aerobic bacteria. While the widespread use of penicillin class antibiotics is compatible with German recommendations on empiric antibiotic therapy, there is evidence that pathogens from odontogenic infections frequently exhibit resistance against them. Moreover, the high prescription volume of clindamycin (>25%) appears to be inadequate, since relatively high resistance rates are observed and clindamycin is not recommended as first-line choice in empiric antibiotic therapy. National and international studies show that continuous education of patients and dentists, individual prescription feedback as well as evidence-based guidelines are important measures to improve antibiotic prescription patterns among dentists. ***Conclusion***: To promote rational antibiotic use in outpatient dental care, antibiotic stewardship measures are necessary that include prescription guidelines based on AMR surveillance data as well as continuous education of dentists.

**Keywords**: *Dentists, Antimicrobial resistance, Dental medicine, Odontogenic infections, Antibiotic stewardship*

## Introduction

Antimicrobial resistance in common bacterial pathogens impairs the effectiveness of antibiotics, and is a public health challenge as it is associated with a significant burden to individual patients and healthcare systems. The main driver of antimicrobial resistance is the inappropriate use of antibiotics, including unnecessary prescriptions and the inadequate choice of antibiotic drug when prescription is justified (World Health Organisation, 2014), which applies to both clinical and dental care. In order to limit the spread of antibiotic resistance, two basic strategies are pursued: (i) research and development of novel antibiotic agents overcoming known resistance and (ii) preserving the effectiveness of existing antibiotics by antibiotic stewardship (ABS) as well infection prevention and control (IPC) measures (World Health Organisation, 2014). Antibiotic resistance is a serious concern in both low (Ayobami *et al*., 2022) and high-income countries, such as Germany where greater antimicrobial resistance is observed for several pathogens (Markwart *et al*., 2019; Maechler *et al*., 2017). In Germany, 85% of all antibiotics are prescribed in the outpatient care sector, including dentistry, (Federal Office of Consumer Protection and Food Safety, 2016) underlining the importance of this healthcare setting for ABS and IPC measures as well as evidence-based guidelines.

This review summarises the existing literature and guidelines on antibiotic consumption and antibiotic resistance in the outpatient dental care sector in Germany. We also review national and international studies that have investigated the effectiveness of ABS strategies and interventions tailored to dentistry.

## Method

We carried out a structured literature search using appropriate search strings in the MEDLINE (via PubMed) electronic database, complemented by a hand search for articles published between 2000 and 2021. The search terms are available at https://www.uniklinikum-jena.de/allgemeinmedizin/Publikationen.html. We included publications from Germany, which (i) were published between 2000 and 2021, (ii) provided data for antibiotic resistance proportions in clinical isolates from patients with odontogenic infections, or (iii) provided data for antibiotic consumption/use in the outpatient dental care sector. Moreover, we included studies from, whether from Germany or not, that investigated the effectiveness of interventions to improve rational antibiotic use in dentistry, published between 2000 and 2021. Excluded from this review were studies that did not fulfil these inclusion criteria. We also performed a hand web search to identify relevant German clinical

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guidelines and recommendations for dentists (German Federal Dental Association (*Bundeszahnärztekammer*), German state dental associations (*Landeszahnärztekammern*); all German dental societies as well as the webpage of the German Working Group of the Scientific Medical Societies (*Arbeitsgemeinschaft der Wissenschaftlich-Medizinischen Fachgesellschaften, AWMF*). Antibiotic prescription is rational when the following criteria are met: appropriate (i) clinical indication, (ii) choice of antimicrobial agent, (iii) dosing and (iv) therapy duration (Kern, 2018). In Germany, data on outpatient drug prescription for all patients with statutory health insurance are published in an annual report, including data from the dental sector (Schwabe and Ludwig, 2021).

## Results

From 2012 to 2020 fewer antibiotics (expressed in defined daily doses, DDD) were prescribed by outpatient physicians (relative change: -35%), while no corresponding change was observed for outpatient dentists (Figure 1) (Holstiege *et al*., 2020). Consequently, the proportion of antibiotic prescriptions by dentists among all outpatient prescriptions increased from 7.8% in 2012 to 11.0% in 2020 (relative change: +41%) underlining the importance for ABS and IPC measures in this healthcare sector. The decreased antibiotic prescription volume by outpatient physicians might be explained by greater attention towards the global rise of antibiotic resistance and national programs to limit the spread of antibiotic resistance, such as the German Antibiotic Resistance Strategy 2020 (Deutsche Antibiotika-Resistenzstrategie (DART) 2020) (Bundesministerium für Gesundheit, 2015). Initiated by the German government in 2015 and extended in 2020, DART 2020 is a bundle of different strategies that include improved diagnostic and therapeutic approaches, greater efforts in infection prevention and control, strengthened research and development and greater public awareness (Abu Sin *et al*., 2018). However, while most programs focus on antibiotic use in the hospital sector and/or outpatient physicians, they are typically not tailored for outpatient dentists, which might explain their unchanged antibiotic prescription volume in this sector. Importantly, due to the SARS-CoV-2 pandemic in 2020, the antibiotic prescription volume of outpatient physicians dropped by 21% compared to 2019. This decline can be explained by the fewer outpatient medical consultations (Zentralinstutut für die Kassenärztliche Versorgung in Deutschland, 2022) and COVID-19 measures, which reduced the number of respiratory tract infections as well as gastro-intestinal infections (Tanislav and Kostev, 2022). Notably, although the number of outpatient dental care consultations also fell in 2020 (Kassenzahnärztliche Bundesvereinigung), the dental antibiotic prescription volume did not change compared to 2019, indicating more prescriptions per consultation. One explanation might be that COVID-19-related measures likely did not affect the prevalence of odontogenic infections.

Data from 2020 show that among outpatient dentists, penicillin class antibiotics were the most frequently prescribed (70.1% of the total prescription volume), whereby aminopenicillins alone account for 51.4% of the total (Table 1) (Schwabe and Ludwig, 2021). The second most frequently prescribed antibiotic was clindamycin (26.3 %). Between 2012 and 2015 there was a shift from clindamycin towards amoxicillin as the most frequently prescribed antibiotic agent (Halling *et al*., 2017).

The constant high proportion of clindamycin prescriptions contrasts with the German guideline on odontogenic infections, which recommends penicillin and amoxicillin for empiric antibiotic therapy, with clindamycin only recommended in cases of penicillin allergy (Al-Nawas and Karbach, 2016). Studies from the United States and Northern Ireland showed, that 8-14% of patients reported allergy to penicillin (Macy, 2014; Kerr, 1994), but penicillin allergy testing is not routinely performed in outpatient care and thus, allergy might be overestimated by dentists. It is believed that at least 75% of the patients with penicillin allergy tolerate all β-lactam antibiotics and therefore, allergists call for proper diagnostics to identify patients with true penicillin allergy (Trcka *et al*., 2004).

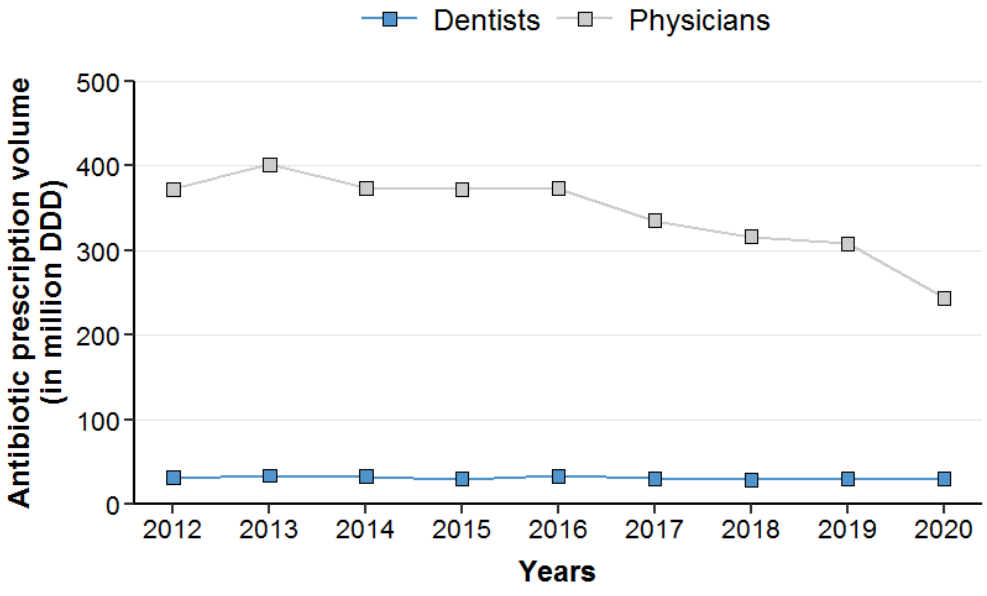


***Figure 1***. *Antibiotic prescriptions by outpatient dentists and physicians in Germany in million DDD (defined daily doses) over time.*

**Table 1**. Antibiotics prescribed by outpatient dentists in Germany.

| | *Antibiotic prescription volume 2020 (in million DDD*)* | *%* |
|---|---|---|
| Amoxicillin | 15.4 | 51.4 |
| Clindamycin | 7.9 | 26.3 |
| Amoxicillin + clavulanic acid | 3.5 | 11.7 |
| Phenoxymethylpenicillin | 2.1 | 7.0 |
| Doxycyclin | 0.6 | 2.0 |
| Metronidazole | 0.3 | 1.0 |
| Cefuroxime | 0.2 | 0,7 |
| Total | 30.0 | 100 |

* DDD = defined daily doses.
Only antibiotics with an annual prescription volume of ≥10,000 DDD included (Schwabe and Ludwig, 2021).

## *Pathogens in odontogenic infections and prevalence of antibiotic resistance*

In a detailed analysis of nationwide surveillance data from the Robert Koch-Institute, Meinen et al. (2021) showed that *Streptococcus* spp. (36%), *Staphylococcus* spp. (12%), *Prevotella* spp. (8%) and *Klebsiella* spp. (5%) are the most frequent bacterial pathogens isolated from patients with odontogenic infections in dental practices. (Table 2).

Meinen et al. reported that antibiotic resistance against penicillin and aminopenicillin in clinical *Streptococcus* spp. isolates from patients treated in German outpatient dental practices is low (≤ 3%) (Table 2). This finding supports the clinical recommendation for penicillin and aminopenicillin in first line antibiotic therapy. However, about 18% of the *Streptococcus* spp. isolates showed resistance against clindamycin, the secondly most prescribed antibiotic in dental practice. In *Staphyloccus aureus*, which accounts for >75% of all *Staphylococcus* spp. infections, penicillin and aminopenicillin are not effective (>65% resistance proportions). Additionally, high resistance proportions (>20%) in *S. aureus* were observed for therapeutic alternatives, such as clindamycin and macrolides (e.g., erythromycin and clarithromycin), which underlines the clinical relevance of antibiotic resistance in this common odontogenic pathogen.

A German study on the microbiological spectrum in patients with periodontitis showed the presence of a typical mixed polymicrobial subgingival biofilm (Jepsen *et al*., 2021). While in 2008, in 37% of screened patients at least one pathogen with relevant antibiotic resistance was detected, this proportion increased to 70% in 2015. Fortunately, the frequency of resistance against the typically used antibiotics in periodontitis, such as amoxicillin or metronidazole, showed a persistently low level. For example, in 2008 and 2015 only 0.11% and 0.17% respectively of the isolated *Porphyromonas gingivalis spp.* were not susceptible to amoxicillin,. These findings are somewhat contrary to studies from 2002 (Müller *et al*., 2002) and 2010 (Cachovan *et al*., 2011), which reported increasing penicillin and clindamycin resistance in periodontopathogens. The typical mixed growth of anaerobic and aerobic bacteria in odontogenic infections enhances antibiotic resistance potential. Karbach et al. (2007) compared clinical isolates with polymicrobial growth from patients with peri-implantitis and found that 37% of the mixed cultures were non-susceptible to all tested antibiotic agents (i.e., penicillin, ampicillin, ampicillin/sulbactam, azithromycin, moxifloxacin). When examined alone, single pathogens showed lower resistance than the combined biofilm.

**Table 2**. Pathogens and associated antibiotic resistance proportions in isolates from outpatient dental practices in Germany (Meinen *et al*., 2021).

| Pathogen spectrum | | Antibiotic resistance | |
|---|---|---|---|
| Pathogen | Proportion | Antibiotic drug | Resistance proportion |
| *Streptococcus* spp. | 36 % | Penicillins (e.g. penicillin V) | 3 % |
| | | Aminopenicillins (e.g. amoxicillin) | 2 % |
| | | Clindamycin | 18 % |
| | | Second-generation cephalosporins (e.g. cefuroxime) | 2 % |
| *Staphylococcus* spp. | 12 % | - | - |
| *S. aureus* | 9% | Penicillins | > 65 % |
| | | Aminopenicillins | > 65 % |
| | | Oxacillin or flucloxacillin (MRSA) | 6 % |
| | | Clindamycin | 19 % |
| | | Macrolides | 19 % |
| | | Second-generation cephalosporins | 5 % |
| *Prevotella* spp. | 8 % | Penicillins | 50 % |
| | | Clindamycin | 13 % |
| *Candida* spp. | 7 % | - | - |
| *Klebsiella* spp. | 5 % | Second-generation cephalosporins | 9 % |
| Other* | 31 % | - | - |

In sum, odontogenic infections are associated with a wide range of pathogens and are often polymicrobial. Although data are conflicting in some cases, recent studies from Germany indicate that pathogens isolated from odontogenic infections frequently harbour resistance to antibiotics that are widely used in German outpatient dental care, i.e., penicillins, aminopenicillins and clindamycin. The wide range of pathogens and associated resistance patterns make empiric antibiotic treatment difficult and calls for continuous AMR surveillance providing national and regional data.

### *German guidelines for rational antibiotic prescription for dentists*

Four clinical guidelines (Al-Nawas and Karbach, 2016; Deutsche Gesellschaft für Parodontologie; Deutsche Gesellschaft für Parodontologie; Deutsche Gesellschaft für Zahn- Mund- und Kieferheilkunde) and one position paper (Naber and Al-Nawas, 2007) are available, which are relevant for dentists and have recommendations on antibiotic prescriptions. The most important clinical guideline is the S3-guideline "Odontogenic Infections*"* (Al-Nawas and Karbach, 2016), which was published in 1997 but expired in September 2021 and has not been updated (S3 indicates that the guidelines are based on a systematic review and clinical evaluation of the evidence). According to this guideline, in odontogenic infections without subsequent extension, antibiotic therapy is not generally recommended, though it is described as one option if an incision does not drain pus (i.e., gingival inflammatory infiltrate). However, antibiotic therapies are recommended as an adjunct to surgical therapy in infections with risk for subsequent extension. Penicillin and aminopenicillin are given as examples of first-line antibiotics with appropriate effectiveness and tolerability. According to this guideline, clindamycin is only an option in patients with penicillin allergy and the low level of evidence for use of clindamycin in odontogenic infections is highlighted. However, this guideline does recommend doses or duration of treatment.

The German implementation of the European EFP-Guideline (Sanz *et al*., 2020), the S3-guideline "Therapy of periodontitis stage I to III" recommends systemic antibiotic therapy only for selected patients with grade C periodontitis with rapid progression (≥2 mm over 5 years) and in patients without modifiable risk factors. A combination of amoxicillin and metronidazole is described without information on dosing or duration of treatment. The treatment of periodontitis with antibiotics is elaborated in the S3-guideline "Adjuvant systemic antibiotics and subgingival instrumentation as part of a systematic therapy for periodontitis" (Deutsche Gesellschaft für Parodontologie, 2018). In line with the previous documents, this guideline recommends antibiotic use only for selected patients: the usage of systemic antibiotics should be restricted to therapy of grade C periodontitis. The antibiotics are specified (amoxicillin and metronidazole) with dosing and duration of treatment.

The S2k-guideline "Dental treatment before heart valve replacement" (Deutsche Gesellschaft für Zahn-Mund- und Kieferheilkunde, 2022) reports controversial discussions about the use of antibiotics in patients with diseased heart valves, but does not recommend for or against antibiotic prescription. In contrast, the position paper "prophylaxis of infective endocarditis" (Naber and Al-Nawas, 2007) by the German Society of Cardiology includes explicit recommendations for indication, dosing and duration of antibiotic use for dental treatment. This paper proposes the administration of a single-dose aminopenicillin (or clindamycin in cases of apparent allergy) for patients with mechanical or biological heart valve replacement, heart surgery with alloplastic material in the previous six months and recovery from endocarditis or a congenital heart defect in the patient's history.

Taken together, given the expired S3 guideline "odontogenic infections", new or updated evidence-based guidelines on the diagnosis and treatment of odontogenic infections in dental practices are needed. These guidelines should include clear recommendations on: (i) when antibiotics are needed/not needed, (ii) which antibiotics should be prescribed as well as (iii) dosing and duration of antibiotics.

### *Antimicrobial stewardship and the effectiveness of interventions to improve rational antibiotic use in dental care*

Outpatient antibiotic prescription in Germany is often out of step with recommendations regarding indication prescription and choice of antibiotics (i.e., often unjustifiably and/or too broad) (Zweigner *et al*., 2018), but no specific data for dental care are available. Studies from other European countries (Belgium (Mainjot *et al*., 2009), Italy (Bianco *et al.*, 2021), Switzerland (Köhler *et al*., 2013), Spain (Segura-Egea *et al*., 2010)) suggest that there is room better antibiotic prescription behaviour in dentistry. A recent qualitative study among German dentists (Böhmer *et al*., 2021) identified a number of barriers for rational antibiotic use, such as lack of available treatment time and the need for thorough therapy decisions, demanding patients, medico-legal concerns and lack of interprofessional communication.

A systematic review of publications between 2001 and 2016 showed that a combination of audit, feedback, education, local consensus, dissemination of guidelines and/or academic detailing successfully reduced the number of antibiotics prescribed and/or increased the accuracy of the prescription in dental care (Löffler and Böhmer, 2017). In line with this synthesis, more recent studies confirm the efficacy of educational interventions to improve the rational use of antibiotics in dental care (Wilding *et al*., 2021; Kusumoto *et al*., 2021; Gross *et al*., 2019; Teoh *et al*., 2021; Löffler *et al*., 2015; Goulao *et al*., 2021).

In addition, a UK randomised controlled trial showed that an educational, animated short-film improved patients' knowledge on antibiotics and might reduce patient demand for antibiotics (Wilding *et al*., 2021) . Although the exact nature of the interventions differed between studies, they all included one or more of the following components: (i) educational audits on rational antibiotic use provided by experts, (ii) education on guidelines, (iii) feedback on individual prescription behaviour, and (iv) decision-making aids.

The DREAM-study (Löffler *et al*., 2015) conducted amongst outpatient dentists in Mecklenburg-Western Pomerania determined several key barriers for rational antibiotic use, such as limited consultation time (especially

before weekends, holidays and during emergency service), a perceived lack of competence in terms of endocarditis prophylaxis, deliberate overtreatment in fear of medico-legal consequences and pressure exerted by patients who demand fast pain relief. Based on these results and the scientific literature, the DREAM investigators designed a multifaceted intervention to optimize prescription behaviour which included communication training and education of patients (flyer, poster) and dentists. The intervention was investigated in a cluster-randomized study among 60 outpatient dentists where the number of prescriptions decreased in the intervention group, while the prescription rate in the control group remained similar.

Although educational programs can improve antibiotic prescription patterns in dental medicine, it remains unclear whether they have a sustainable positive impact. Evidence from Rauniar et al. (2012) shows that positive effects of educational interventions can dwindle, with more antibiotic prescriptions six months post intervention.

In sum, national and international studies show that continuous postgraduate education of dentists and patients, individual prescription feedback as well as evidence-based guidelines are important measures to improve antibiotic prescription patterns among German dentists.

## Summary and conclusion

The rise of antibiotic resistance is a serious public health problem associated with greater morbidity, mortality and economic burden. In Germany, dentists account for about one in nine outpatient antibiotic prescriptions, underlining their important role in sustaining the effectiveness of antibiotics through rational antibiotic use. While the volume of antibiotics prescribed by outpatient physicians has decreased consistently in the last decade in Germany, no change has been observed for dentists, which calls for greater efforts in antibiotic stewardship in dental practices. Penicillin class antibiotics are the predominantly prescribed antibiotics by outpatient dentists, accounting for more than 70% of the total. While the widespread use of penicillin class antibiotics is compatible with German guidelines on empiric antibiotic therapy, there is evidence that pathogens isolated from odontogenic infections frequently exhibit resistance against them. Moreover, the relatively high prescription volume of clindamycin (>25%) appears to be inadequate, since relatively high resistance rates are observed and clindamycin is not recommended as first-line choice. To promote rational use of antibiotics in outpatient dental care, continuously updated evidence-based recommendations are essential that include clear recommendations on: (i) when antibiotics are needed/not needed, (ii) which antibiotics should be prescribed as well as (iii) dosing and duration of therapy. A continuous and dedicated surveillance of pathogens and antibiotic resistances associated with odontogenic infections is lacking in Germany but would be of great value in the development of national and regional antibiotic treatment recommendations. Evidence from international and national studies shows that education of patients and dentists as well as prescription feedback have the potential to improve antibiotic prescription behaviour of dentists.

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