Guideline on the prudent prescriptions of antibiotics in the dental office

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KCE REPORT 332C

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

SHORT REPORT

GUIDELINE ON THE PRUDENT PRESCRIPTION OF ANTIBIOTICS IN THE DENTAL OFFICE

KCE REPORT 332C
GOOD CLINICAL PRACTICE

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GUIDELINE ON THE PRUDENT PRESCRIPTION OF ANTIBIOTICS IN THE DENTAL OFFICE

ROOS LEROY, JOLYCE BOURGEOIS, LEEN VERLEYE, DOMINIQUE DECLERCK, PIETER DEPUYDT, ANOUK ELOOT, JOANA C CARVALHO, WIM TEUGHELS, RITA CAUWELS, JULIAN LEPRINCE, SELENA TOMA, KATLEEN MICHIELS, SAM ARYANPOUR, ASTRID VANDEN ABBEELE, MIEKE DE BRUYNE

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SHORT REPORT

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AGREE	Appraisal of Guidelines Research and Evaluation
AMSTAR	A MeaSurement Tool to Assess systematic Reviews
ATC	Anatomical Therapeutic Chemical
BAPCOC	Belgian Antibiotic Policy Coordination Committee
BAET	Belgian Association for Endodontology and Traumatology
BAPD	Belgian Academy of Paediatric Dentistry (‘Belgische Academie voor Kindertandheelkunde’/’L’Académie Belge de Dentisterie Pédiatrique (BAPD)’)
BCFI – CBIP	Belgian Centre for Pharmacotherapeutic Information (‘Belgisch Centrum voor Farmacotherapeutische Informatie’/ ‘Centre Belge d’Information Pharmacothérapeutique’)
BVIKM – SBIMC	Belgian society for infectiology and clinical microbiology (‘Belgische Vereniging voor Infectiologie en Klinische Microbiologie’/’La Société Belge d''Infectiologie et de Microbiologie Clinique’)
BVP	Belgian Society of Periodontology (‘Belgische Vereniging voor Parodontologie’/ ‘Société Belge de Parodontologie’)
CEBAM	Belgian Centre for Evidence-Based Medicine (EBM)
CSD	Professional association of dental practitioners (‘Chambre Syndicale Dentaire’)
ESC	European Society of Cardiology
FAGG – AFMPS	Federal Agency for Medicines and Health Products (‘Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten’/’Agence Fédérale des Médicaments et Produits de Santé’)
GDG	Guideline Development Group
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
IE	Infective endocarditis
KBVSMFH - SRBSCMF	Scientific association of oral maxillofacial surgeons (’Koninklijke Belgische Vereniging voor Stomatologie en Maxillo-Faciale Heelkunde’/‘Société Royale Belge de Stomatologie et de Chirurgie Maxillo-Faciale’)

KCE	Belgian Health Care Knowledge Centre
MA	Meta-analysis
PICO	Population – Intervention – Comparator – Outcome
p.o.	*Per os* (oral intake)
RCT	Randomized controlled trial
RIZIV – INAMI	National Institute for Health and Disability Insurance (‘Rijksinstituut voor Ziekte- en Invaliditeitsverzekering’/’Institut National d’Assurance Maladie-Invalidité’)
ROBINS-I	Risk of bias in non-randomized studies of interventions
SMD	Professional association of dental practitioners (‘Société de Médecine Dentaire’)
SR	Systematic Review
VBS-MKA – GBS-OMF	Professional association of oral maxillofacial surgeons (‘Belgische beroepsvereniging van de geneesheren-specialisten in de Stomatologie, Mond-, Kaak- en Aangezichtschirurgie’/’Union professionnelle des médecins belges spécialistes en stomatologie et chirurgie orale et maxillo-faciale’)
VBT	Professional association of dental practitioners (‘Vlaamse Beroepsvereniging Tandartsen’)
VVT	Professional association of dental practitioners (‘Verbond der Vlaamse Tandartsen’)
VWVT	Scientific association of dental practitioners (‘Vlaamse Wetenschappelijke Vereniging voor Tandheelkunde’)

1. INTRODUCTION

1.1. Background

1.1.1. Why a guideline on the prudent use of antibiotics in the dental office is needed

Since the 1940s, when penicillin was made available for medical use, antibiotics have made major contributions to public health.[1] However, the use of antimicrobials can result in **antimicrobial resistance**, undermining many of these advances. It is important to realise that the risk of antimicrobial resistance increases if antimicrobials are used in a non-prudent way, e.g. unnecessarily prescribed/used, at sub-therapeutic doses, suboptimal spectrum, for inappropriate periods of time, or when they are used against non-susceptible microorganisms.[2, 3] Therefore, the **prudent use**[a] of antimicrobials is one of the main axes in tackling antimicrobial resistance. Prudent use of antimicrobials should lead to more rational and targeted use, thereby maximising the therapeutic effect and minimising the development of antimicrobial resistance.[2]

The **prudent prescription of antibiotics starts with evidence-based guidelines**, which clearly outline for each indication whether antibiotics are indicated, and if so, which antibacterial agent, dose and duration are preferred. As was also mentioned in KCE Report 311, anno 2020 there is still no guideline on the prudent use of antibiotics for dentists, and for certain indications the available guidance misses consistency.[5]

1.1.2. Current use of antibiotics prescribed by dentists

A retrospective analysis of reimbursement data, provided by the National Institute for Health and Disability Insurance (RIZIV – INAMI), revealed that in 2016 **5.8% of the total antibacterial use in the Belgian ambulatory setting** was **prescribed by dentists**.[6] The relative 'contribution' to the total antibiotic use in ambulatory care was especially high for amoxicillin (10.5% of all amoxicillin used in Belgian ambulatory care was prescribed by dentists), amoxicillin with an enzyme inhibitor (e.g. amoxicillin with clavulanic acid; 8.4%), clindamycin (20.1%) and metronidazole[b] (11.6%). In contrast, the relative contribution of penicillin V was very low (0.3%). The ratio amoxicillin to amoxicillin in combination with clavulanic acid was 1.273.[6]

1.2. Scope

The focus of the present guideline is limited to **systemic antibiotics** which are **administered per os**; the rationale being that Belgian dentists are not qualified to deliver drugs intravenously. In addition, locally delivered antimicrobials (e.g. in gels, root canal sealers, fibres, controlled-release products or ointments) were not considered, neither were antimicrobial molecules used with non-antimicrobial purposes (e.g. low-dose doxycycline). Thus, in this guideline 'antibiotic(s)' should be read as 'systemic antibiotic(s) which are administered per os'; antimicrobial photodynamic therapy[c] was also considered out of scope for the present guideline.

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[a] Several synonyms have been used for 'prudent' use of antibiotics, e.g. 'appropriate', 'rational', 'judicious' and 'responsible'. In the European Union, the term 'prudent use' is preferred, defined by the European Commission as a use which benefits the patient while at the same time minimises the probability of adverse effects and the emergence or spread of antimicrobial resistance.[4] 'Prudent' is thus used with the same purpose as rational, adequate or correct use of antibiotics.

[b] Metronidazole is stricto senso an antiprotozoal (Anatomical Therapeutic Chemical (ATC) code P01AB), yet it is also active against anaerobic bacteria.

[c] Antimicrobial photodynamic therapy or photodynamic inactivation has been suggested to eradicate pathogenic microorganisms such as Gram-positive and Gram-negative bacteria, yeasts and fungi. The principles of photodynamic therapy involve the use of a non-toxic light-sensitive dye called a 'photosensitizer' combined with harmless visible light (low energy)

The different indications under study in this guideline are listed in section 2.2.

1.3. Remit of the guideline

1.3.1. Overall objectives

This clinical practice guideline provides evidence-based recommendations for the prudent use of antibiotics in 12 situations frequently encountered in the dental office. Clinicians are encouraged to interpret these recommendations in the context of the individual patient situation, values and preferences. The main objective of the present guideline is to **reduce the non-prudent prescription of antibiotics by dentists** (and to a lesser extent by general practitioners), and ultimately to reduce antibacterial resistance. Another objective of this guideline is to reduce the variability in clinical practice and to improve the communication between care providers and patients (e.g. to explain why antibiotics are not indicated in certain situations).

1.3.2. Population for which the guideline is meant

The target population of this guideline are **medically fit patients** who present in the dental office with one of the indications specified in section 2.2. In case a dentist has doubts whether the patient in front of him can be considered medically fit and can be treated as is indicated in the guideline, he is advised to contact the physician of the patient and discuss the optimal treatment pathway.

1.3.3. Target users of the guideline

This guideline is primarily developed for **dentists**. In the second place, this guideline is also intended for **general practitioners** who are confronted with patients suffering from infections in the oral cavity. The literature review on which this guideline is based, provides the evidence that in case of infection, source control (through dental treatment) should be the first choice of treatment and that adjunctive antibiotics are rarely indicated. In case a patient consult his GP with complaints which may indicate an acute pulpitis, peri-apical periodontitis, an acute peri-apical or periodontal abscess without systemic involvement, the GP should refer this patient to a dentist so that the **correct diagnosis** can be made and the **necessary dental treatment** can be started.[d] If indicated, pain medication can be initiated.

In addition, the authors hope that the content of this guideline will be incorporated in the academic teaching base on the prudent prescription and use of antibiotics in the Belgian dental schools, as well as in the continuous education programmes for dental professionals and general practitioners.

Last, this guideline may be of interest to patients and their families, and to policy makers.

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of the appropriate wavelength to match the absorption spectrum of the photosensitizer. This procedure stimulates the dye to form free radicals of singlet oxygen that will act as toxic agents to the bacteria/cell.[7]

[d] During weekends and public holidays, the general dentist's on-call service can be reached at 0903 39969 (Flanders), http://www.gardedentaire.be/ (Brussels) or https://www.dentistedegarde.be/ (Wallonia). Currently, there is a shortage of dentists in certain parts of Belgium, which may jeopardise the continuity of care. However, solving this problem is beyond the scope of this guideline.

2. METHODOLOGY

2.1. The Guideline Development Group

This guideline was developed by KCE researchers, in close collaboration with a multidisciplinary group of practicing clinicians and academic experts teaching in the Belgian dental schools (see list of authors). For the discussion of the indications 'Antibiotic prophylaxis in patients at (high) risk of infective endocarditis undergoing dental procedures' and 'Antibiotic prophylaxis in patients with orthopaedic joint implants undergoing dental procedures' the Guideline Development Group (GDG) was enlarged with representatives of the Belgian Association of Orthopaedics and Traumatology, the European Bone and Joint Infection Society, the Belgian Society of Cardiology, the Belgian society for infectiology and clinical microbiology (BVIKM – SBIMC) and the Belgian Antibiotic Policy Coordination Committee (BAPCOC) in order to come to recommendations supported by a multidisciplinary group of health professionals. Guideline development and literature review expertise, support, and facilitation were provided by the KCE expert team. The writing of the report, the conclusions and the recommendations remain the sole responsibility of the KCE team.

2.2. Marking out the scope of the guideline

Currently, prescribers in the ambulatory sector do not have to specify for which indication they prescribe antibiotics, so it is impossible to unravel whether antibiotics are prescribed in a prudent way. Hence, we had to rely on surveys among dentists to identify the indications for antibiotic therapy in the dental office.[8-11] An initial list of 33 indications was reduced to 12 through in-depth discussions with some members of the GDG. This list was then presented to all members of the GDG and the dentists among the stakeholders (see colophon) in an online survey. The results were discussed with the GDG and stakeholders during the first joint meeting. Finally, it was decided that the indication 'Periodontal regenerative surgery' was deleted from the list of indications as this type of surgery is primarily performed by periodontists and not by general dentists. On the other hand, the indication 'Symptomatic irreversible pulpitis in primary teeth' was added, leading to a final list of 12 indications:

1. Symptomatic irreversible pulpitis in primary teeth
2. Odontogenic abscess in primary teeth
3. Symptomatic irreversible pulpitis in permanent teeth
4. Symptomatic apical periodontitis in permanent teeth
5. Symptomatic acute apical abscess in permanent teeth
6. Replantation of avulsed permanent teeth
7. Periodontal treatment of aggressive periodontitis in the permanent dentition
8. Periodontal abscess in permanent teeth
9. Dental implant placement
10. Extraction of permanent teeth
11. Antibiotic prophylaxis in patients at (high) risk of infective endocarditis undergoing dental procedures
12. Antibiotic prophylaxis in patients with orthopaedic joint implants undergoing dental procedures

In a following step, the research questions were further developed and the inclusion and exclusion criteria were defined using the PICO (Participants – Interventions – Comparator – Outcomes) framework (see Scientific Report, Appendix 3). This was discussed in depth with the members of the GDG and the stakeholders.

2.3. Systematic review of the literature

In the scoping phase, a literature review was conducted, with special focus on guidelines, Health technology assessments and systematic reviews (Medline, Embase and dedicated websites**).** In addition, for each indication, a dedicated search was done for SRs, randomized controlled trials (RCTs) and, if indicated, other (primary) studies in Medline, the Cochrane Library and Embase. The search strategies are outlined in the Supplement[LR1]. Members of the GDG were also consulted to identify relevant network that might have been missed during the search process. For all but one indication (i.e. non-surgical treatment of aggressive periodontitis), the selection of records was done by two KCE researchers (of whom one dentist).

2.4. Quality assessment

The quality appraisal was performed using the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument for guidelines,[12] the AMSTAR 2 checklist for systematic reviews,[13] the Cochrane Collaboration's tool for assessing risk of bias for RCTs,[14] and the risk of bias in non-randomised studies of interventions (ROBINS-I) tool for observational studies.[15] Critical appraisal of each study was performed by a single researcher, and critically revised by a second researcher.

The GRADE approach was used to evaluate the quality of evidence (from very low quality to high quality) for each outcome and study (Table 1); it reflects the extent to which a guideline panel's confidence in an estimate of the effect was adequate to support a particular recommendation. The evaluation was based on the following quality elements: study limitations, inconsistency between studies, indirectness, imprecision and publication bias. For each indication Summary of Findings tables are provided in the Scientific Report, Appendix 11.

Table 1 – Levels of evidence according to the GRADE system

Quality level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect

Source: Balshem et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. 2011;64(4):401-6.[16]

2.5. Formulation of recommendations

To determine the strength of each recommendation, the GRADE methodology was followed (Table 2). The strength of a recommendation depends on the balance between all desirable and all undesirable effects of an intervention (i.e. net clinical benefit), the quality of available evidence, values and preferences, and the estimated cost (resource utilization). For this guideline, no formal cost-effectiveness study was conducted.

Table 2 – Strength of recommendations according to GRADE

Grade	Definition
Strong	The desirable effects of an intervention clearly outweigh the undesirable effects (the intervention is to be put into practice), or the undesirable effects of an intervention clearly outweigh the desirable effects (the intervention is not to be put into practice).
Weak	The desirable effects of an intervention probably outweigh the undesirable effects (the intervention probably is to be put into practice), or the undesirable effects of an intervention probably outweigh the desirable effects (the intervention probably is not to be put into practice).

Source: Andrews et al. GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength. J Clin Epidemiol. 2013;66(7):726-35.[17]

A first draft of recommendations was prepared by the KCE researchers. The whole chapter (including evidence tables, summary of findings tables, recommendations, etc.) was circulated at least one week before the face-to-face expert meetings. During these meetings, the documents were discussed in depth, and, when indicated, revised. This was also applicable to the recommendations. After the meetings, the revised documents (with changes well indicated) were shared with the GDG for final approval. No formal consensus procedure was used. Due to the restrictions imposed by the national Security Council due to the Covid-19 pandemic, the last expert meeting had to be replaced by feedback by email.

Given the important harms related to the intake of antibiotics, and given the fact that those were barely reported in the studies we included in the systematic reviews, in the Scientific Report a dedicated chapter was devoted to the adverse events associated with the use of antibiotics (Chapter 3). Indeed for antibiotics, the harms are both on an individual level (direct adverse events) and a more long-term societal level (antimicrobial resistance), which can eventually negatively impact the patient. When balancing benefits and risks, both the direct adverse events and antimicrobial resistance were considered. For the benefits, the evidence for most indications was low or very low. If the evidence suggested only minor or unclear (e.g. only proxy outcomes assessed) benefit from taking antibiotics, the recommendation was formulated in the sense of a weak recommendation. In case the evidence suggested no benefit or in case there was no evidence, the recommendation was formulated as a strong recommendation: antibiotics are not recommended.

In a few indications the use of antibiotics is indicated or can be considered. Yet, for most of these indications there is insufficient high level evidence which antibiotic (regimen) is to be preferred. From the perspective of the prudent prescription of antibiotics, the expert group took the view that dental practitioners should at least get some advice on which antibiotic (regimen) could be considered in those situations. Therefore, clinical practice suggestions are given, which are based on indirect evidence. They are presented between blue lines, so that they can easily be distinguished from the recommendations (in red tables), which are evidence based.

2.6. External review

The recommendations prepared by the GDG were circulated to relevant professional and scientific associations (i.e. Belgian Association for Endodontology and Traumatology (BAET), Belgian Academy of Paediatric Dentistry (BAPD), professional and scientific associations of oral maxillofacial surgeons (VBS-MKA - GBS-OMF, KBVSMFH - SRBSCMF), Belgian society for infectiology and clinical microbiology (BVIKM-SBIMC), Belgian Society of Periodontology (BVP), professional associations of dental practitioners (CSD, SMD, VVT, VBT), professional associations of general medical practitioners (Domus Medica, SSMG), scientific association of dental practitioners (VWVT)), the sickness funds and other patient representatives (Test Aankoop – Test Achats, Ligue des Usagers des Services de Santé and Vlaams Patiëntenplatform), as well as to representatives of the Federal Agency for Medicines and Health Products (FAGG – AFMPS; feedback received), the National Institute for Health and Disability Insurance (RIZIV – INAMI; feedback received), the Federal Public Service Health, Food Chain Safety and Environment (FOD VVVL – SPF SPSCAE), the Belgian Antibiotic Policy Coordination Committee (BAPCOC) and the national One Health Advisor and Antimicrobial Resistance Coordinator for their feedback.

Declarations of interest of GDG members, validators and stakeholders were formally recorded and listed in the colophon.

2.7. Final validation

As part of the standard KCE procedures, an external scientific validation of the report was conducted prior to its publication. This validation was done in two phases. First, the scientific content was assessed by two academic experts in the dental field on 11 September, 2020 (Vibeke Baelum and Ivor G. Chestnutt; see colophon for affiliation). Second, the methodology was validated making use of the AGREE II checklist. This validation process was chaired by the Belgian Centre for Evidence-Based Medicine (CEBAM) on 16 September, 2020 (Martine Goossens, Patrick Vankrunkelsven, Gerda Wauman).

3. CLINICAL RECOMMENDATIONS

The systematic review of the literature which formed the basis for the clinical recommendations, revealed that in most trials the primary outcomes related to efficacy rather than harm. In order to compensate somehow for this underreporting, a special chapter was devoted to the side effects of antibiotics. It is intended for dental practitioners and other health care workers who consider the prescription of antibiotics for a dental problem, to give thought to the potential deleterious effects carried with the use of antibiotics.

Adverse events associated with the use of antibiotics may range from dizziness, nausea, vomiting, diarrhoea, candidiasis and headache to serious adverse events like major allergic reactions (including anaphylaxis), severe toxicities and sudden death.[18] Antimicrobials are able to harm patients by various mechanisms. From a public health perspective, the development of antimicrobial resistance is the greatest concern. But antimicrobials are also associated with disruption of microbiomes, drug hypersensitivity reactions and toxicities. The interested reader is referred to the Scientific Report, Chapter 3.

The details of the evidence used to formulate the recommendations are available in the Scientific Report, Chapter 4 and the related Appendices.

3.1. Symptomatic irreversible pulpitis in the primary dentition

Recommendation[e]	Strength of Recommendation	Level of Evidence
• Given the fact that the administration of preoperative antibiotics in case of pulpitis in permanent teeth is not beneficial, the use of antibiotics is **not recommended** in the pre-operative phase of pulpitis in primary teeth.	Strong	Very low

[e] During weekends and public holidays patients with urgent or emergency dental conditions can contact the out of hours emergency dental service at 0903/39969 (Flanders), http://www.gardedentaire.be/ (Brussels) or https://www.dentistedegarde.be/ (Wallonia).

3.2. Odontogenic abscess in the primary dentition

Recommendations[e]	Strength of Recommendation	Level of Evidence
• Given the lack of any scientific evidence, the use of antibiotics is **not recommended** in children who present with an odontogenic abscess without systemic involvement (e.g. fever, facial cellulitis, lymphadenopathy).	Strong	Very low
• In order to prevent the further systemic spread of pathogens, the use of antibiotics **can be considered** in children who present with an odontogenic abscess with **systemic involvement** (e.g. fever, facial cellulitis, lymphadenopathy).	Weak	Very low

Clinical practice guidance:

In case antibiotics are considered, the following regimen is an option:

- Amoxicillin 75 - 100 mg/kg body weight*/day, administered in 3 doses, for 5 days, or,
- In case of non-IgE mediated penicillin allergy: cefuroxime axetil (a second generation oral cephalosporin) 30 – 50 mg/kg body weight/day, administered in 3 doses, for 5 days, or,
- In case of IgE mediated penicillin allergy: azithromycin 10 mg/kg body weight/day, administered in 1 dose, for 3 days.

Children who present with a dental abscess at their general practitioner should be referred to a dentist for proper dental treatment (source control).

**: It is best to switch to the adult dosing regimes when when the single or daily "adult" dose is exceeded.*

3.3. Symptomatic irreversible pulpitis in the permanent dentition

Recommendation[e]	Strength of Recommendation	Level of Evidence
• The administration of antibiotics in patients with irreversible pulpitis in permanent teeth awaiting dental treatment, is **not recommended.**	Strong	Low

3.4. Symptomatic apical periodontitis and acute apical abscess in the permanent dentition

Recommendations[e]	Strength of Recommendation	Level of Evidence
• The administration of antibiotics in patients with symptomatic apical periodontitis or acute apical abscess in combination with dental treatment, is **not recommended.**	Strong	Very low
• Patients who present with symptomatic periapical periodontitis or an acute periapical abscess without systemic involvement (e.g. fever, facial cellulitis, lymphadenopathy) should **receive dental treatment** without any delay. Currently, there is no scientific evidence on the added value of systemic antibiotics in the meantime.	Strong	Very low
• In order to prevent the further systemic spread of pathogens, the use of antibiotics **can be considered** in patients who present with a periapical abscess with **systemic involvement** (e.g. fever, facial cellulitis, lymphadenopathy).	Weak	Very low

Clinical practice guidance:

When antibiotics are considered in case of systemic involvement, the following regimen is an option:

- Amoxicillin 500 mg, three times a day for 3 - 7 days, or,
- In case of penicillin allergy[f]: azithromycin 500 mg, once a day for 3 days or clarithromycin 500 mg, twice a day for 3 - 7 days.

The administration of antibiotics without proper endodontic treatment should be avoided.

Patients who present with a dental abscess at their general practitioner should be referred to a dentist for source control.

[f] In case of penicillin allergy, the macrolides azithromycin or clarithromycin can be considered. The rationale is that macrolides are less associated with Clostridioides difficile infection than clindamycin (OR for clindamycin: 20.43, 95% CI: 8.50-49.09 vs. for macrolides: 2.55, 95% CI: 1.91-3.39),[19] which has been suggested in other guidelines. In addition, the susceptibility of oral streptococci to macrolides is similar to that of clindamycin and macrolides are also quite active against oral anaerobes.[20] Yet, it is important to mention that Azithromycin and Clarithromycin may cause QT interval prolongations, which increases the risk of sudden cardiac death due to torsades de pointe.

3.5. Replantation of avulsed permanent teeth

Recommendation[e]	Strength of Recommendation	Level of Evidence
• The administration of systemic antibiotics at replantation of avulsed permanent teeth, is **not recommended.**	Strong	Very Low

3.6. Non-surgical treatment of aggressive periodontitis

Recommendation	Strength of Recommendation	Level of Evidence
• The use of systemic antibiotics in combination with the non-surgical treatment of aggressive periodontitis **can be considered.**	Weak	Low

Clinical practice guidance:

In case adjunctive antibiotics are considered, the following regimen is an option:

- The combination of amoxicillin 500 mg and metronidazole 500 mg, three times a day for 3 - 7 days, or,
- In case of penicillin allergy: metronidazole 500 mg, three times a day for 3 - 7 days.

The administration of antibiotics without proper periodontal treatment should be avoided.

3.7. Periodontal abscess in the permanent dentition

Recommendations[e]	Strength of Recommendation	Level of Evidence
• The use of antibiotics is **not recommended** in patients who present with a periodontal abscess without systemic involvement (e.g. fever, facial cellulitis, lymphadenopathy). Also after adequate periodontal treatment the use of antibiotics is not recommended.	Strong	Very low
• The use of antibiotics is **not recommended** in patients who present with pericoronitis without systemic involvement (e.g. fever, facial cellulitis, lymphadenopathy). Also after adequate periodontal treatment the use of antibiotics is not recommended.	Strong	Very low
• In the rare event that a patient presents with a periodontal abscess with **systemic involvement** (e.g. fever, facial cellulitis, lymphadenopathy), the use of antibiotics **can be considered.**	Weak	Very low
• In order to prevent the further systemic spread of pathogens, the use of antibiotics **can be considered** in patients who present with pericoronitis with **systemic involvement** (e.g. fever, facial cellulitis, lymphadenopathy, trismus, difficulty swallowing).	Weak	Very low

Clinical practice guidance:

In case antibiotics are considered, the following regimen is an option:

- Amoxicillin 500 mg, three times a day for 3 - 7 days, or,
- In case of penicillin allergy[f]: Azithromycin 500 mg, once a day for 3 days or Clarithromycin 500 mg, twice a day for 3 - 7 days.

In the absence of trismus, the administration of antibiotics without proper (periodontal) treatment (e.g. debridement under local anaesthesia) should be avoided.

3.8. Dental implant placement

Recommendation	Strength of Recommendation	Level of Evidence
• In order to reduce the number of (early) implant failures, the administration of preoperative antibiotics (i.e**. a single dose of 2 gram of amoxicillin 1 hour prior to surgery**, if there is no known allergy) **should be considered** in case of dental implant placement.	Strong	Low

Clinical practice guidance:

In case of penicillin allergy, the following regimen is an option:

- a single dose of 600 mg clindamycin prior to surgery.

3.9. Extraction of permanent teethg

Recommendation	Strength of Recommendation	Level of Evidence
• The prophylactic administration of antibiotics in patients having a permanent tooth* extracted is **not recommended.**	Strong	Very low

** Two of the three included studies excluded wisdom teeth*

3.10. Antibiotic prophylaxis in patients at (high) risk of infective endocarditis undergoing dental procedures

Recommendation	Strength of Recommendation	Level of Evidence
• Prophylactic antibiotics **can be considered** in patients at high-risk of infective endocarditis undergoing invasive dental procedures. **Invasive dental procedures*** are those dental procedures that involve the manipulation of the gingival tissue or the periapical region of teeth or the perforation of the oral mucosa. The following patients are considered **at high risk of infective endocarditis**: o Patients with a prosthetic valve or a prosthetic material used for cardiac valve repair; o Patients with a history of infective endocarditis; o Patients with congenital heart disease: - Cyanotic congenital heart disease, without surgical repair, or with residual defects, palliative shunts or conduits; - Congenital heart disease with complete repair with prosthetic material whether placed by surgery or by percutaneous technique, up to 6 months after the procedure; - When a residual defect persists at the site of implementation of a prosthetic material or device by cardiac surgery or percutaneous technique.	Weak	Very low

**According to the European Society for Cardiology (ESC) at risk dental procedures involve the manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa (including scaling and root canal procedures). Antibiotic prophylaxis is according to the ESC not recommended for local anaesthetic injections in non-infected tissues, treatment of superficial caries, removal of sutures, dental X-rays, placement or adjustment of removable prosthodontic or orthodontic appliances or braces, or following the shedding of deciduous teeth, or trauma to the lips and oral mucosa. Last, the ESC remarks that there is no evidence to contraindicate implants in all patients at risk.[21] Prophylactic antibiotics are not indicated in cardiac transplant recipients who develop cardiac valvulopathy,[21] in patients who had a coronary artery bypass graft, nor in patients who had coronary artery stents.*

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g As the current guideline focuses on the (prophylactic) administration of antibiotics within the frame of procedures performed in the general dental practice, third molar extractions were considered out of scope.

Clinical practice guidance:

In case antibiotic prophylaxis is provided, the following regimen is advised in **adults**:

- A single dose of 2 g amoxicillin or ampicillin 30 - 60 minutes before the dental procedure, or,
- In case of penicillin allergy: 600 mg clindamycin* 30 - 60 minutes before the dental procedure.

In case antibiotic prophylaxis is provided, the following regimen is advised in **children**:

- A single dose of 50 mg/kg amoxicillin or ampicillin 30 - 60 minutes before the dental procedure, or,
- In case of penicillin allergy: 20 mg/kg clindamycin 30 - 60 minutes before the dental procedure.

**: The risk of Clostridioides difficile infection after one single dose is very small.*
Source: European Society for Cardiology (ESC)[21]

3.11. Antibiotic prophylaxis in patients with orthopaedic joint implants undergoing dental procedures

Recommendation	Strength of Recommendation	Level of Evidence
• The administration of prophylactic antibiotics in patients with an orthopaedic joint implant who undergo dental procedures, is **not recommended.**	Strong	Very low

4. ONGOING TRIALS AND RESEARCH RECOMMENDATIONS

Chapter 5 of the Scientific Report provides a list of ongoing trials on the indications under study. In addition, for each indication the evidence gaps are listed and research recommendations are formulated.

5. DISSEMINATION, IMPLEMENTATION AND UPDATE OF THE GUIDELINE

5.1. Dissemination & implementation

The content of this guideline is intended to be disseminated by national and international scientific and professional (dental) associations. Domus Medica and the Société Scientifique de Médecine Générale (SSMG) were both invited to the stakeholder meeting so that they can spread the content of the guideline to general practitioners. The sickness funds and other patient representatives (Test Aankoop – Test Achats, Ligue des Usagers des Services de Santé and Vlaams Patiëntenplatform) were also invited so that they can inform their clients (i.e. potential patients) about the content of the guideline. As all (but one) Belgian dental schools were represented in the GDG, it is hoped that the content of this guideline will be incorporated in the academic teaching base on the prudent prescription and use of antibiotics, as well as in the continuous education programmes for dental professionals and general practitioners.

Organisations can make attractive and user-friendly tools tailored for implementation purposes. Yet, it is well known that the implementation of guidelines on the prudent use of antibiotics is not easy to accomplish. Evidence suggests that health care professionals are well aware of the threat of antibiotic resistance, but for many this theoretical awareness is difficult to translate in actual prudent prescribing behaviour.[22, 23] Other determinants are decisive in the decision to prescribe: e.g. perceived clinical risks, the relationship with the patient, the perceived patient demand for antibiotics (while research indicates that this demand is overrated),[24-29] uncertainty avoidance, diagnostic uncertainty, time pressure, the idea that over-using antibiotics presents fewer risks than limiting its use ('it's better to prescribe too much than too little'), the importance attached to therapeutic freedom and clinical autonomy, the lack of confidence in existing guidelines and even the opposition to evidence-based medicine ('each patient being unique').[25, 27, 29-32] From the perspective of the patient and the general public at large, qualitative and quantitative research indicates that the demand for quick fixes, difficulties with accepting to manage self-limiting infections with simple rest and symptomatic treatment, the societal pressure to be healthy and performing, and presenteeism are into play.[24, 28, 33]

Implementation strategies should take psychological, social and institutional determinants of behavioural change into account. Improvement strategies only have a chance of success when all types of barriers are targeted.[34] For this purpose, collaboration with the implementation cell of the Evidence Based Practice network is envisaged. In addition, the Belgian Centre for Pharmacotherapeutic Information (BCFI – CBIP) and the Federal Agency for Medicines and Health Products (FAGG – AFMPS) will be contacted to see how this guideline can be disseminated through their channels (e.g. website). Last, it will be discussed with the Research, Development & Quality service of the National Institute for Health and Disability Insurance (RIZIV – INAMI), whether this guideline can be integrated in the following feedback to dentists. The feedback informs healthcare workers about their prescription behaviour; the feedback enables them to compare their own prescription behaviour with their peers.

5.2. Guideline update

In view of the fact that several clinical trials are running and that insights in antimicrobial resistance may change over time, this guideline should ideally be updated every 5 years.

POLICY RECOMMENDATIONS[h]

To the attention of the Minister of Health, the Federal Agency for Medicines and Health Products and the National Institute for Health and Disability Insurance

Given the fact that the packages of antibiotics available on the Belgian market are larger than what is needed for one treatment and in order to decrease the risk of keeping leftovers at home and of subsequent self-medication, the recommendation "Put into practice the delivery of the exact number of antibiotic tablets in pharmacies open to the public" raised in KCE report 311, fully applies here.

To dentists and general practitioners, to their professional and scientific associations, the universities, as well as to EBP-network:

Implement this guideline (o.a. through dissemination, promotion, inclusion in the teaching base and continued education) and invest in a thorough communication between health care provider and the patient.

To the Belgian Commission for the Coordination of Antibiotic Policy (BAPCOC):

Integrate this guideline in the BAPCOC AB guideline for ambulatory practice and in the BAPCOC action plan 2020-2024.

[h] The KCE has sole responsibility for the recommendations.

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COLOPHON

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