

Review

A Review of Guidelines for Antibiotic Prophylaxis before Invasive Dental Treatments

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Abstract: Bacteraemia associated with invasive dental treatments can propagate infective endocarditis in high-risk cardiac patients. Over the past decade, antibiotic prophylaxis before dental treatment has been questioned. This review aims to compare the variations between the UK, European and American antibiotic prophylaxis guidelines before dental treatments. Antibiotic prophylaxis guidelines by the National Institute for Health and Care Excellence (NICE)—Clinical Guideline 64, Scottish Dental Clinical Effectiveness Programme (SDCEP), American Heart Association (AHA), European Society of Cardiology (ESC), European Society of Endodontology (ESE) and Belgian Health Care Knowledge Centre (KCE) position statements were compared regarding the indications, high-risk patients and prophylaxis regimens before dental treatments. In the United Kingdom, the NICE—Clinical Guideline 64 and SDCEP—Implementation Advice do not advise the prescription of prophylactic antibiotics for the majority of high-risk cardiac patients undergoing routine dental treatments. On the contrary, the AHA, ESC and KEC recommend the prescription of antibiotics prior to invasive dental procedures in high-risk cardiac individuals. The ESE also indicates prophylaxis before endodontic procedures for patients with other conditions, including impaired immunologic function, prosthetic joint replacement, high-dose jaw irradiation and intravenous bisphosphonates. Among these guidelines, there are variations in antibiotic prophylaxis regimens. There are variations regarding the indications and antibiotic prophylaxis regimens before invasive dental treatments among these available guidelines.

Keywords: antibiotic prophylaxis; endocarditis; dental treatment; dentistry



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1. Introduction

Infection of the heart lining (usually a heart valve), also known as infective endocarditis, is usually a life-threatening condition which affects 3.6 in every 1,000,000 individuals per year in the general population [1]. It can cause several consequences or complications such as heart murmurs, pyrexia, petechiae, embolic phenomena, anaemia and endocardial vegetations leading to valvular incompetence, myocardial abscess or mycotic aneurysm. It is also reported to affect the central nervous system (CNS), including toxic encephalopathy, stroke, brain abscess, transient ischemic attack and subarachnoid haemorrhage. Thus, clinicians should aim to minimise the risk of infective endocarditis in patients who are at high risk of developing such an infection.

The major predisposing factors for developing infective endocarditis include various cardiovascular diseases which affect the heart and blood vessels, such as bicuspid or calcific aortic valves, prosthetic heart valves, congenital heart defects, rheumatic valvular disease, intracardiac devices, mitral valve prolapse and hypertrophic cardiomyopathy [2].

Furthermore, intravenous drug abusers and immunocompromised patients also have a higher possibility of developing infective endocarditis. Cardiovascular diseases are a cause of global burden as they are the prime cause of death worldwide [3]. By the year 2030, the global economic cost of cardiovascular diseases is estimated to reach \$1044 billion [4].

The pathogenesis of infective endocarditis is thought to be from a bacterial infection arising from transient bacteraemia. In fact, the causes of infective endocarditis are multifactorial, including alteration in the vessels which would cause deposition of platelets and compromise the endothelium of the cardiac valve, or a surgically formulated pulmonary shunt must exist, along with bacteraemia arising from, for example, oral trauma [5]. Bacteraemia could either be low grade but repeated, which occurs from repeated activities such as chewing, toothbrushing or flossing, or it could be high grade caused by invasive dental procedures [6]. Bacteraemia following invasive dental treatment is well documented in the literature. It can occur during tooth extractions or treatment of periodontal and endodontic infections due to the proximity of both infections with the blood circulation [7]. Based on expert opinion as mentioned in the Scottish Dental Clinical Effectiveness Programme (SDCEP)—Implementation Advice [8], invasive dental procedures that can lead to bacteraemia are presented in Table 1.

Table 1. Dental procedures which are considered to be invasive [8].

Invasive Dental Procedures
<ul style="list-style-type: none"> • Matrix band placement • Subgingival rubber dam and clamp • Fixed prosthesis extending subgingivally • Root canal treatment before establishment of an apical stop • Prefabricated metal crowns • Six-point pocket charting in diseased tissue • Surgical subgingival scaling and root planning • Abscess incision and drainage • Tooth extractions • Surgical treatment requiring manipulation of a mucoperiosteal flap or mucogingival area (e.g., apicectomy) • Dental implants involving temporary anchorage devices, mini-implants • Implant substructures uncovering

Endodontic infections are polymicrobial; they are of close anatomic proximity with the bloodstream, which can result in bacteraemia during root canal treatment [9]. Moreover, in contrast to periodontal infections, the epithelial barrier is not found between the highly vascular periapical granulomatous tissue and the necrotic infected root canal. Thus, endodontic infections are an enfolded primary infective focus for dissemination via periapical vasculature of microbes from the root canal during endodontic treatment into systemic environment. Dissemination of microorganisms into the blood stream can occur in a few seconds following an oral procedure and may reach the lungs, heart and peripheral blood capillary system from the infected site [10]. In high-risk patients, some important measures could be taken before invasive dental procedures such as endodontic treatments are carried out. Even though Cahill et al. [11] suggested in their meta-analysis that bacteraemia in patients having dental treatment could be reduced by prophylactic antibiotics, the prescription of antibiotic prophylaxis before dental treatment has become debatable. The risk–benefit analysis has shifted towards the reduced utilisation of antibiotic prophylaxis due to the lack of information on the effectiveness of antibiotic prophylaxis in preventing infective endocarditis and adverse reaction to the drugs. In a recent systematic review, Cervino et al. highlighted the protocols used for antibiotic prophylaxis for extracted teeth and found a variation of protocols and papers which either support or discourage the use of antibiotic prophylaxis [12]. Therefore, this study aims to highlight the variation

between different guidelines (US, UK and Europe) for prophylactic antibiotic use before dental treatment to minimise the risk of developing infective endocarditis.

2. Materials and Methods

2.1. Review of Guidelines

2.1.1. Guidelines for Antibiotic Prophylaxis for Minimising the Risk of Infective Endocarditis in Cardiac Patients Receiving Invasive Dental Treatment

Depending on the practitioner's global location, local guidelines differ. In the United Kingdom, the National Institute for Health and Care Excellence (NICE) in 2008 published Clinical Guideline 64 (CG64), recommending not to prescribe antibiotics prior to dental treatment. Recommendation 1.1.3 suggested that "antibiotic prophylaxis is not recommended for people undergoing dental procedures" [13]. Following the introduction of these guidelines, a significant decrease in antibiotic prescription and a surge in infective endocarditis cases were reported in 2015 (Table 2) [14]. Similarly, in the United States, it was revealed that antibiotic prophylaxis prescription was significantly decreased in both moderate- and high-risk individuals even though this decrease was not complying with American Heart Association (AHA) guidelines [15]. Furthermore, a Canadian study also revealed that a significant reduction in antibiotic prophylaxis prescription in moderate-risk patients and a minor change in individuals of high risk were evident [16]. In 2016, NICE reviewed their guidelines by recommending that "antibiotic prophylaxis is not recommended routinely for people undergoing dental procedures" [13]. However, the definition of which patients should be considered for "nonroutine" dental procedures and what is the appropriate antibiotic regimen(s) for use in dental management was not explained in these amended NICE guidelines, leading to confusion among UK dentists. To address this challenging problem, the Scottish Dental Clinical Effectiveness Programme (SDCEP) [8] developed an implementation advice to enable practice of the NICE guidelines. The NICE recommendation 1.1.1 lists which heart conditions are considered to be at an increased risk of developing infective endocarditis (Table 3). The SDCEP explained that the majority of these high-risk patients undergoing "routine" dental procedures will not require antibiotic prophylaxis and further included a subgroup of high-risk patients requiring special consideration and antibiotic prophylaxis for "nonroutine" dental treatments (Table 3).

Table 2. Incidence of infective endocarditis.

Country	Incidence before Guidelines	Incidence after Guidelines
United States of America [17]	11–12 per 100,000	14–15 per 100,000
Europe [18]	33 per 1,000,000	32 per 1,000,000
United Kingdom [19]	22.2–41.3 per 1,000,000	42–67.7 per 1,000,000

Table 3. High-risk patients for developing infective endocarditis.

Conditions	
National Institute for Health and Care Excellence (NICE) [13]	<ol style="list-style-type: none"> 1. Stenosis or regurgitation of heart valves 2. Cardiomyopathy "hypertrophic" 3. History of infective endocarditis 4. Surgically corrected congenital heart disease or palliated structural conditions, but not including defects of the septal artery, fully repaired ventricular septal defect or patent ductus arteriosus which is fully repaired and endothelialised closure devices 5. Restoration of a valve

Table 3. Cont.

Conditions	
European Society of Cardiology (ESC) [6] and Scottish Dental Clinical Effectiveness Programme (SDCEP) [8]	Special considerations subgroup
	1. The use of a prosthetic valve, such as transcatheter valve, or valve repair with any prosthetic material
	2. History of infective endocarditis
American Heart Association (AHA) [20]	3. Congenital heart defects (CHD)
	a. Cyanotic CHD “any type”
	b. CHD repaired with a prosthetic material, using either surgical or percutaneous techniques, for 6 months following the procedure or lifelong if residual shunt or valvular regurgitation remains
	1. Prosthetic cardiac valves, including transcatheter-implanted prostheses and homograft
	2. Cardiac valve repair using a prosthetic material, such as annuloplasty rings and chords
Belgian Health Care Knowledge Centre (KCE) Report 332 [21]	3. Previous episode of infective endocarditis
	4. Congenital heart disease “cyanotic” or repaired congenital heart disease, with valvular regurgitation or residual shunts at the site of or adjacent to the site of the prosthetic patch or prosthetic device
	5. Valve regurgitation due to abnormal valve in heart transplant patient
Belgian Health Care Knowledge Centre (KCE) Report 332 [21]	1. Valve repair using prosthetic material or a prosthetic valve
	2. History of infective endocarditis
	3. Congenital heart disease such as
	a. Cyanotic with residual defects, palliative shunts or conduits without surgical repair
	b. Congenital heart disease with full reconstruction with prosthesis whether placed surgically or by percutaneous technique up to 6 months after the procedure
	c. Persistence of a residual defect at the site of implementation of a prosthetic material or device by cardiac surgery or percutaneous technique

On the contrary, the American Heart Association (AHA), European Society of Cardiology (ESC) and, most recently, the Belgian Health Care Knowledge Centre (KCE) report 332 [21] recommend that prescription of antibiotic prophylaxis to minimise the possibility of developing infective endocarditis is reasonable before any dental procedure involving the handling of the gingiva as well as the periapical region of teeth and in cases of perforation of the oral mucosa in all patients with a high risk of developing infective endocarditis [6,20–22] rather than just a subgroup of high-risk patients as indicated by the SDCEP. Although these guidelines accept that the evidence base is weak and that an adverse drug reaction risk is present, the rationale for this recommendation is based on the fact that high-risk individuals are more likely to have a poorer outcome from an infective endocarditis event. The conditions associated with high-risk cardiac patients according to the NICE, SDCEP, ESC, AHA and KCE report 332 guidelines are summarised in Table 3.

The NICE guidelines do not recommend antibiotic prophylaxis for the majority of high-risk patients undergoing routine dental procedures. The SDCEP recommends that

cardiac patients from the “special considerations subgroup” (Table 3) may require antibiotic prophylaxis for nonroutine dental management and this should be assessed in consultation with their cardiologists. The AHA, ESC and KCE support antibiotic prophylaxis for their enlisted high-risk cardiac patients (Table 3). Thus, the variations in these recommendations suggest the need for globally accepted consensus guidelines to prevent any confusion among healthcare providers and patients.

2.1.2. Antibiotic Prophylaxis Guidelines against Infection in Patients with Immunosuppressive Conditions Undergoing Endodontic Treatment

Along with cardiovascular diseases, immunosuppressive conditions have also been indicated for antibiotic prophylaxis. Patients with impaired immune response could encounter complications following dental treatment, such as spread of infection. Both non-surgical root canal treatment and endodontic surgery can initiate detectable bacteraemia. It is well documented that the incidence of bacteraemia following root canal treatment and endodontic surgery is up to 20% [23] and 83.3%, respectively [24]. The European Society of Endodontology (ESE) published a position statement on antibiotics in endodontics. Along with cardiac conditions, the authors also mentioned a list of other conditions, including impaired immunologic function, prosthetic joint replacement, high-dose irradiation of jaws and intravenous bisphosphonates, where prophylactic antibiotics are indicated for patients having certain endodontic treatment procedures [25] (Table 4). The abovementioned patient groups, either due to their immune deficiency or decreased tendency of wound healing, are more prone to infections and are thus indicated for antibiotic prophylaxis in endodontics according to the ESE.

Table 4. Antibiotic prophylaxis in endodontics according to the European Society of Endodontology position statement: the use of antibiotics in endodontics [25].

Patient Group	Indications
Immunocompromised patients (Uncontrolled diabetes; dialysis; Leukaemia; end-stage renal disease; HIV/AIDS; patients on chemotherapy, steroids or immunosuppressives following transplant medications; or with inherited genetic defects)	Patients undergoing nonsurgical root canal treatment and, especially, endodontic surgery. The clinician should consider: <ul style="list-style-type: none"> • The state of the infection • Complications related to the infection • Reaction to drugs. If the operator is in doubt, discussion with the physician should be sought prior to treatment.
Patients who are liable to develop infective endocarditis including patients with congenital heart defects, a prosthetic valve or a history of infective endocarditis	Nonsurgical and surgical root canal treatment
Joint replacement	Nonsurgical and surgical root canal treatment During the first 3 months after joint operations
Patients receiving high-dose irradiation	Nonsurgical and surgical root canal treatment
Patients on intravenous bisphosphonate treatment	Surgical root canal treatment

Recently, the American Dental Association (ADA) published guidelines on the use of antibiotics for emergency handling of pulpal and periapical dental pain and oral swelling. They concluded that antibiotics are not recommended in fit and healthy adults diagnosed with symptomatic irreversible pulpitis with or without symptomatic apical periodontitis, pulp necrosis and symptomatic apical periodontitis, but they advised that those patients should be referred for definitive dental treatment. When dental treatment is not feasible and patients’ symptoms get worse, a delayed prescription for amoxicillin or penicillin V potassium administered orally for patients diagnosed with pulp necrosis and symptomatic apical periodontitis is recommended. On the contrary, the expert panel suggested the pre-

scription of antibiotics along with urgent dental treatment in immunocompromised patients diagnosed with pulp necrosis and acute apical abscess with systemic involvement [26].

2.1.3. Guidelines for Antibiotic Prophylaxis Regimens

Antibiotic prophylaxis regimens also vary among different regions of world. There is similarity in the recommendations between the “European Society of Endodontology (ESE) position statement on the use of antibiotics in endodontics” [25] and “The antibiotic Prophylaxis 2017 Update” recommendations by the American Association of Endodontists (AAE) [22], which is based on the 2017 American Heart Association and American College of Cardiology focused update of the 2014 AHA/ADA Guideline (Table 5). The British National Formulary (BNF) [27] lacks information on prophylactic antibiotics for infective endocarditis in dentistry. The SDCEP Antibiotic Prophylaxis Against Infective Endocarditis—Implementation Advice [8] recommends regimens for adults based on the 2006 British Society for Antimicrobial Chemotherapy report [28], while the doses for children are based on the 2015 ESC guidelines [6]. There is a difference between the SDCEP antibiotic prophylaxis regimen and the ESE, AAE and KCE report 332 recommendations (Table 5).

Table 5. Recommendations on antibiotic prophylaxis regimens in endodontics according to the European Society of Endodontology position statement: the use of antibiotics in endodontics [25]; American Association of Endodontics—Antibiotic Prophylaxis 2017 Update [22]; Scottish Dental Clinical Effectiveness Programme—Antibiotic Prophylaxis Against Infective Endocarditis—Implementation Advice 2018 [8]; and the Belgian Health Care Knowledge Centre (KCE) Report 332 [21].

European Society of Endodontology Position Statement: The Use of Antibiotics in Endodontics [25]					
Patient group	Antibiotic	Route	Adult Dose	Child Dose	Timing before procedure
General prophylaxis	Amoxicillin	PO	2 g	50 mg/kg	1 h
Unable to take oral medication	Ampicillin	IV or IM	2 g	50 mg/kg	Within 30 min
Allergic to penicillin	<ul style="list-style-type: none"> • Clindamycin • Cephalexin or cefadroxil 	PO	600 mg	20 mg/kg	1 h
	<ul style="list-style-type: none"> • Clarithromycin or azithromycin 		2 g 500 mg	50 mg/kg 15 mg/kg	
If the patient is allergic to amoxicillin/penicillin/ampicillin and is unable to take the medication orally	<ul style="list-style-type: none"> • Clindamycin • Cefazolin 	IV	600 mg 1 g	20 mg/kg 25 mg/kg	Within 30 min
American Association of Endodontics—Antibiotic Prophylaxis 2017 Update [22]					
Patient Group	Antibiotic	Route	Adult dose	Child dose	Timing before procedure
General prophylaxis	Amoxicillin	PO	2 g	50 mg/kg	One dose 30–60 min
If the patient is unable to take oral medication	<ul style="list-style-type: none"> • Ampicillin • Ceftriaxone or cefazolin 	IV or IM	2 g 1 g	50 mg/kg 50 mg/kg	One dose 30–60 min

Table 5. Cont.

European Society of Endodontology Position Statement: The Use of Antibiotics in Endodontics [25]					
If the patient suffers from allergy to penicillin or ampicillin	<ul style="list-style-type: none"> Cephalexin (or other first- or second-generation oral cephalosporin in equivalent) Clindamycin, clarithromycin or azithromycin 	PO	2 g 600 mg 500 mg	50 mg/kg 20 mg/kg 15 mg/kg	One dose 30–60 min
If the patient is allergic to penicillin or ampicillin and unable to take oral medication	<ul style="list-style-type: none"> Cefazolin or ceftriaxone Clindamycin 	IM or IV	1 g 600 mg	50 mg/kg 20 mg/kg	One dose 30–60 min
Scottish Dental Clinical Effectiveness Programme—Antibiotic Prophylaxis Against Infective Endocarditis—Implementation Advice 2018 [8]					
Patient Group	Antibiotic	Route	Adult dose	Child dose	Timing before procedure
General prophylaxis	Amoxicillin	PO	3 g	6 months to 17 years 50 mg/kg (max dose 3 g)	1 h
Allergic to penicillin	Clindamycin	PO	600 mg	6 months to 17 years 20 mg/kg (max dose 600 mg)	1 h
Allergic to penicillin and unable to swallow capsule	Oral suspension of azithromycin 200 mg/5 mL	PO	500 mg (12.5 mL)	6 months to 11 years 12 mg/kg; max dose 500 mg 12–17 years 500 mg	1 h
Patients requiring intravenous prophylaxis	Amoxicillin	IV	1 g	6 months to 17 years 50 mg/kg (max dose 1 g)	Before procedure or at anaesthetic induction
Patients requiring intravenous prophylaxis and who are allergic to penicillin	Clindamycin	IV	300 mg	6 months to 17 years 20 mg/kg (max dose 600 mg)	Before procedure or at anaesthetic induction
Belgian Health Care Knowledge Centre (KCE) Report 332 [21]					
Patient group	Antibiotic		Dose		Timing before procedure
Patient not allergic to amoxicillin or ampicillin	Amoxicillin or ampicillin		2 g for adults and 50 mg/kg for children		One dose 30–60 min before procedure
Patient allergic to amoxicillin or ampicillin	Clindamycin		600 mg for adults and 20 mg/kg for children		One dose 30–60 min before procedure

The World Health Organisation has emphasised the emergence of microbes with antibiotic resistance. In this regard, it is suggested that if the patient is recommended for antibiotic prophylaxis and is already taking an antibiotic, the clinician should choose an antibiotic from a different class; for example, for a patient already receiving oral penicillin for another condition, beta-lactams-resistant viridans group streptococci are more likely

to be present in the oral cavity, therefore antibiotic from a different class needs to be prescribed for effective prophylaxis [8,22]. In order to encourage best practices, policy makers should make unanimous guidelines globally regarding the drugs, their doses and specific indications to avoid further emergence and spread of antibiotic resistance.

Since at present there are variations in the antibiotic prophylaxis indications and regimens among different guidelines, it is important that these should be discussed in detail with high-risk patients as part of the informed consent prior to any invasive dental treatment, such as endodontic treatment, periodontal treatment and so forth, and the outcome of the discussion should be recorded in patient notes. This would give the patient the opportunity to make an informed decision prior the commencement of invasive dental procedures.

2.1.4. Guidelines for Timing of Dental Screening, Treatment and Favourable Outcome before Invasive Cardiovascular Surgery

The timing of dental screening for oral disease, its treatment and favourable outcome before commencement of cardiovascular surgery is critical. This could significantly reduce the risk of infective endocarditis and systemic inflammatory burden that can trigger vascular events. The need for antibiotic prophylaxis is to prevent the development of such conditions following invasive dental procedures carried out after starting these treatments.

Several studies have linked endodontic infections with systemic diseases, including cardiovascular diseases [29]. This has raised concerns regarding the dental management of patients before undergoing cardiovascular surgery. Dental screening and management of oral infections such as caries, endodontic infections, periodontal infections and so forth, prior to any invasive cardiovascular procedure is controversial due to the available guidelines lacking detailed information in this regard [6]. However, several studies have indicated an extensive preoperative extra- and intraoral examination for the detection of any infection, overall assessment of oral hygiene and sensibility testing for every individual tooth along with radiographic examination for detection of any teeth with irreversible pulpitis, pulp necrosis, apical periodontitis, acute apical abscess and chronic apical abscess requiring endodontic treatment [30].

Available information from the American Heart Association or European Society of Cardiology does not specify how the dental screening should be carried out. These guidelines ignore the fact that it is often challenging to make an accurate diagnosis or a definite conclusion regarding the outcome of dental treatment [6]. Unfortunately, dentists are usually the last to be informed of the timing of the cardiac intervention, which makes it difficult to assess the outcome of the treatment [30]. As reported by the European Society of Endodontology, the favourable outcome of endodontic treatment could be assessed one year after the completion of root canal treatment. Favourable outcome is described as the patient being asymptomatic, the absence of swelling and sinus tracts, functional teeth and radiological evidence of normal periodontal ligament space around the root [31]. If the lesion does not resolve in one year, further review appointments should be considered up to four years. However, if after four years the lesion persists, root canal treatment is considered to have an unfavourable outcome [31]. In a recent consensus report which included cardiologists, endodontists and periodontists, it was concluded that to assess the outcome of endodontic treatment in cases of irreversible pulpitis, pulp necrosis, apical periodontitis, acute apical abscess and chronic apical abscess, follow-up time requires ranges from one week for the patient's symptoms up to one year for radiographic evaluation. The consensus stressed the need for the development of a protocol to aid both cardiologists and dentists during the perioperative preparation phase [30]. Furthermore, in a recent study done to analyse the attitude of cardiologists and cardiovascular surgeons towards the management of endodontic infections and oral health, cardiologists believed that the cardiac health of patients with heart diseases along with endodontic infections could be negatively affected by chronic root canal infection; also, most cardiac specialists emphasised the importance of managing endodontic diseases [32].

3. Discussion

In this review, we have highlighted that there are variations between the use of prophylactic antibiotics globally. Since the introduction of the NICE guidance in the United Kingdom, antibiotic prescriptions have been massively reduced; however, the incidence of infective endocarditis has increased. In the United States, the incidence of endocarditis also increased, but when comparing it with the United Kingdom, the difference was almost doubled following the release of the guidance in 2007. Unlike in the United Kingdom and the United States, the incidence of infective endocarditis in Europe after the introduction of guidelines for the use of prophylactic antibiotics did not have any significant effect, while the prescription of antibiotics has been reduced [33]. Furthermore, variations are present not only in the protocol on whom to give antibiotic prophylaxis but also regarding the doses across different continents; for example, in the United States and Europe, amoxicillin is administered at a dose of 2 g, while in the United Kingdom, it is advised that a dose of 3 g is given as prophylaxis. Guideline variations are thought to be a consequence of the general agreement that there is a lack of evidence to support the effectiveness of prophylactic antibiotics, which could cause confusion among clinicians and put patients' lives at risk [18,34,35].

4. Conclusions

There are variations regarding the indications and antibiotic prophylaxis regimens prior to invasive dental procedures in patients with either cardiac or other immunosuppressive conditions among the available UK, European and American guidelines. Furthermore, there is no defined protocol regarding timings for dental screening, treatment and favourable outcome before commencement of invasive cardiovascular procedure. There is a strong need for global consensus between associations and societies for the development of informative guidelines for the use of antibiotic prophylaxis prior to invasive dental treatment as well as the development of a timeline for the protocol of dental screening, treatment and favourable outcome for cardiologists, physicians and dentists during the pretreatment preparation phase. These unanimous guidelines will be pivotal for healthcare workers around the globe and will provide major health benefits.

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References

1. Thornhill, M.H.; Jones, S.; Prendergast, B.; Baddour, L.M.; Chambers, J.B.; Lockhart, P.B.; Dayer, M.J. Quantifying infective endocarditis risk in patients with predisposing cardiac conditions. *Eur. Heart J.* **2018**, *39*, 586–595. [[CrossRef](#)] [[PubMed](#)]
2. WHO. *Cardiovascular Diseases (CVDs) Fact Sheet*; World Health Organization: Geneva, Switzerland, 2017.
3. WHO. *Global Atlas on Cardiovascular Disease Prevention and Control*; World Health Organization: Geneva, Switzerland, 2011.

4. Bloom, D.E.; Cafiero, E.; Jané-Llopis, E.; Abrahams-Gessel, S.; Bloom, L.R.; Fathima, S.; Feigl, A.B.; Gaziano, T.; Hamandi, A.; Mowafi, M. *The Global Economic Burden of Noncommunicable Diseases*; Program on the Global Demography of Aging; World Economic Forum: Geneva, Switzerland, 2011.
5. Selton-Suty, C.; Celard, M.; Le Moing, V.; Doco-Lecompte, T.; Chirouze, C.; Iung, B.; Strady, C.; Revest, M.; Vandenesch, F.; Bouvet, A.; et al. Preeminence of *Staphylococcus aureus* in infective endocarditis: A 1-year population-based survey. *Clin. Infect. Dis.* **2012**, *54*, 1230–1239. [[CrossRef](#)] [[PubMed](#)]
6. Habib, G.; Lancellotti, P.; Antunes, M.J.; Bongiorno, M.G.; Casalta, J.-P.; Del Zotti, F.; Dulgheru, R.; El Khoury, G.; Erba, P.A.; Iung, B. 2015 ESC guidelines for the management of infective endocarditis: The task force for the management of infective endocarditis of the European Society of Cardiology (ESC) endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur. Heart J.* **2015**, *36*, 3075–3128. [[PubMed](#)]
7. Bender, I.; Seltzer, S.; Yermish, M. The incidence of bacteremia in endodontic manipulation: Preliminary report. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **1960**, *13*, 353–360. [[CrossRef](#)]
8. NHS Education for Scotland. *Antibiotic Prophylaxis against Infective Endocarditis Implementation Advice*; Scottish Dental Clinical Effectiveness Programme; NHS Education for Scotland: Edinburgh, UK, 2018.
9. Debelian, G.J.; Olsen, I.; Tronstad, L. Bacteremia in conjunction with endodontic therapy. *Endod. Dent. Traumatol.* **1995**, *11*, 142–149. [[CrossRef](#)] [[PubMed](#)]
10. Ide, M.; Jagdev, D.; Coward, P.Y.; Crook, M.; Barclay, G.R.; Wilson, R.F. The short-term effects of treatment of chronic periodontitis on circulating levels of endotoxin, C-reactive protein, tumor necrosis factor- α , and interleukin-6. *J. Periodontol.* **2004**, *75*, 420–428. [[CrossRef](#)]
11. Cahill, T.J.; Harrison, J.L.; Jewell, P.; Onakpoya, I.; Chambers, J.B.; Dayer, M.; Lockhart, P.; Roberts, N.; Shanson, D.; Thornhill, M.; et al. Antibiotic prophylaxis for infective endocarditis: A systematic review and meta-analysis. *Heart* **2017**, *103*, 937–944. [[CrossRef](#)]
12. Cervino, G.; Cicciu, M.; Biondi, A.; Bocchieri, S.; Herford, A.S.; Laino, L.; Fiorillo, L. Antibiotic Prophylaxis on Third Molar Extraction: Systematic Review of Recent Data. *Antibiotics* **2019**, *8*, 53. [[CrossRef](#)]
13. NICE. *Prophylaxis against Infective Endocarditis: Antimicrobial Prophylaxis against Infective Endocarditis in Adults and Children Undergoing Interventional Procedures*; NICE Clinical Guidelines, No. 64; National Institute for Health and Care Excellence: London, UK, 2008.
14. Dayer, M.J.; Jones, S.; Prendergast, B.; Baddour, L.M.; Lockhart, P.B.; Thornhill, M.H. Incidence of infective endocarditis in England, 2000–2013: A secular trend, interrupted time-series analysis. *Lancet* **2015**, *385*, 1219–1228. [[CrossRef](#)]
15. Thornhill, M.H.; Gibson, T.B.; Cutler, E.; Dayer, M.J.; Chu, V.H.; Lockhart, P.B.; O’Gara, P.T.; Baddour, L.M. Antibiotic prophylaxis and incidence of endocarditis before and after the 2007 AHA recommendations. *J. Am. Coll. Cardiol.* **2018**, *72*, 2443–2454. [[CrossRef](#)]
16. Garg, P.; Ko, D.T.; Bray Jenkyn, K.M.; Li, L.; Shariff, S.Z. Infective endocarditis hospitalizations and antibiotic prophylaxis rates before and after the 2007 American Heart Association Guideline Revision. *Circulation* **2019**, *140*, 170–180. [[CrossRef](#)] [[PubMed](#)]
17. Pant, S.; Patel, N.J.; Deshmukh, A.; Golwala, H.; Patel, N.; Badheka, A.; Hirsch, G.A.; Mehta, J.L. Trends in infective endocarditis incidence, microbiology, and valve replacement in the United States from 2000 to 2011. *J. Am. Coll. Cardiol.* **2015**, *65*, 2070–2076. [[CrossRef](#)] [[PubMed](#)]
18. Duval, X.; Delahaye, F.; Alla, F.; Tattevin, P.; Obadia, J.F.; Le Moing, V.; Doco-Lecompte, T.; Celard, M.; Poyart, C.; Strady, C.; et al. Temporal trends in infective endocarditis in the context of prophylaxis guideline modifications: Three successive population-based surveys. *J. Am. Coll. Cardiol.* **2012**, *59*, 1968–1976. [[CrossRef](#)] [[PubMed](#)]
19. Quan, T.P.; Muller-Pebody, B.; Fawcett, N.; Young, B.C.; Minaji, M.; Sandoe, J.; Hopkins, S.; Crook, D.; Peto, T.; Johnson, A.P.; et al. Investigation of the impact of the NICE guidelines regarding antibiotic prophylaxis during invasive dental procedures on the incidence of infective endocarditis in England: An electronic health records study. *BMC Med.* **2020**, *18*, 84. [[CrossRef](#)]
20. Nishimura, R.A.; Otto, C.M.; Bonow, R.O.; Carabello, B.A.; Erwin, J.P.; Fleisher, L.A.; Jneid, H.; Mack, M.J.; McLeod, C.J.; O’Gara, P.T. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J. Am. Coll. Cardiol.* **2017**, *70*, 252–289. [[CrossRef](#)]
21. Leroy, R.; Bourgeois, J.; Verleye, L.; Declerck, D.; Depuydt, P.; Eloot, A.; Carvalho, J.C.; Teughels, W.; Cauwels, R.; Leprince, J.; et al. *Guideline on the Prudent Prescription of Antibiotics in the Dental Office—Short Report*; Good Clinical Practice (GCP); KCE Reports 332C. D/2020/10.273/22; Belgian Health Care Knowledge Centre (KCE): Brussels, Belgium, 2020.
22. American Association of Endodontists. AAE Position Statement: AAE Guidance on the Use of Systemic Antibiotics in Endodontics. *J. Endod.* **2017**, *43*, 1409–1413. [[CrossRef](#)]
23. Savarrio, L.; Mackenzie, D.; Riggio, M.; Saunders, W.P.; Bagg, J. Detection of bacteraemias during non-surgical root canal treatment. *J. Dent.* **2005**, *33*, 293–303. [[CrossRef](#)]
24. Baumgartner, J.C.; Heggers, J.P.; Harrison, J.W. Incidence of bacteremias related to endodontic procedures. II. Surgical endodontics. *J. Endod.* **1977**, *3*, 399–402. [[CrossRef](#)]
25. Segura-Egea, J.J.; Gould, K.; Sen, B.H.; Jonasson, P.; Cotti, E.; Mazzoni, A.; Sunay, H.; Tjaderhane, L.; Dummer, P.M.H. European Society of Endodontology position statement: The use of antibiotics in endodontics. *Int. Endod. J.* **2018**, *51*, 20–25. [[CrossRef](#)]

26. Lockhart, P.B.; Tampi, M.P.; Abt, E.; Aminoshariae, A.; Durkin, M.J.; Fouad, A.F.; Gopal, P.; Hatten, B.W.; Kennedy, E.; Lang, M.S.; et al. Evidence-based clinical practice guideline on antibiotic use for the urgent management of pulpal- and periapical-related dental pain and intraoral swelling: A report from the American Dental Association. *J. Am. Dent. Assoc.* **2019**, *150*, 906–921. [\[CrossRef\]](#)
27. Medicines Complete. In *British National Formulary*, 78th ed.; BMJ Group: London, UK; Pharmaceutical Press: London, UK, 2019.
28. Gould, F.K.; Elliott, T.S.; Foweraker, J.; Fulford, M.; Perry, J.D.; Roberts, G.J.; Sandoe, J.A.; Watkin, R.W.; Working Party of the British Society for Antimicrobial C. Guidelines for the prevention of endocarditis: Report of the Working Party of the British Society for Antimicrobial Chemotherapy. *J. Antimicrob. Chemother.* **2006**, *57*, 1035–1042. [\[CrossRef\]](#) [\[PubMed\]](#)
29. Aminoshariae, A.; Kulild, J.C.; Fouad, A.F. The Impact of Endodontic Infections on the Pathogenesis of Cardiovascular Disease(s): A Systematic Review with Meta-analysis Using GRADE. *J. Endod.* **2018**, *44*, 1361–1366.e3. [\[CrossRef\]](#) [\[PubMed\]](#)
30. Cotti, E.; Cairo, F.; Bassareo, P.P.; Fonzar, F.; Venturi, M.; Landi, L.; Parolari, A.; Franco, V.; Fabiani, C.; Barili, F.; et al. Perioperative dental screening and treatment in patients undergoing cardio-thoracic surgery and interventional cardiovascular procedures. A consensus report based on RAND/UCLA methodology. *Int. J. Cardiol.* **2019**, *292*, 78–86. [\[CrossRef\]](#)
31. European Society of Endodontology. Quality guidelines for endodontic treatment: Consensus report of the European Society of Endodontology. *Int. Endod. J.* **2006**, *39*, 921–930. [\[CrossRef\]](#) [\[PubMed\]](#)
32. Alim, B.A.; Guneser, M.B.; Dincer, A.N. Cardiologists' and cardiovascular surgeons' attitudes toward managing endodontic infections and oral health in patients with cardiovascular diseases. *Postgrad. Med.* **2020**, *132*, 156–161. [\[CrossRef\]](#) [\[PubMed\]](#)
33. Keller, K.; Hobohm, L.; Munzel, T.; Ostad, M.A. Incidence of infective endocarditis before and after the guideline modification regarding a more restrictive use of prophylactic antibiotics therapy in the USA and Europe. *Minerva Cardioangiol.* **2019**, *67*, 200–206. [\[CrossRef\]](#) [\[PubMed\]](#)
34. Farook, S.A.; Davis, A.K.; Khawaja, N.; Sheikh, A.M. NICE guideline and current practice of antibiotic prophylaxis for high risk cardiac patients (HRCP) among dental trainers and trainees in the United Kingdom (UK). *Br. Dent. J.* **2012**, *213*, E6. [\[CrossRef\]](#) [\[PubMed\]](#)
35. Thornhill, M.H.; Dayer, M.J.; Forde, J.M.; Corey, G.R.; Chu, V.H.; Couper, D.J.; Lockhart, P.B. Impact of the NICE guideline recommending cessation of antibiotic prophylaxis for prevention of infective endocarditis: Before and after study. *BMJ* **2011**, *342*, d2392. [\[CrossRef\]](#)