Up-to-date International Guidance on antibiotic prophylaxis and prevention of infective endocarditis

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Introduction

Infective endocarditis (IE) is a severe bacterial infection, characterized by the development of infected vegetations on the heart valves or inner lining of the heart chamber (endocardium),[1] that often occurs on congenitally malformed or degenerated cardiac valves.[2]

IE is a serious life-threatening infection,[3,4] affecting around 5-10 people per 100,000 every year.[5] Despite improvements in is diagnosis and management, IE remains associated with high morbidity, with severe adverse outcomes including: (i) valve dysfunction, heart block, arrhythmia; (ii) uncontrolled infection, abscesses, fistula around the valve due to ineffective antibiotics, resistant organisms; and (iii) vegetation embolism risk; resulting in heart failure, sepsis and death.[1,6]

Prognosis is poor with an in-hospital mortality rate of 15-20%, rising to approximately 30% at 1 year.[7-9] Factors such as older age, obesity, diabetes, cardiopulmonary disease, vascular disease, haemodialysis, lack of access to tertiary care, and immunosuppression affect morbidity and mortality in patients with IE.[3]

Prevention is a high priority for the entire medical community including physicians, surgeons, and dentists.[10] Antibiotic prophylaxis (AP) against IE has become routine in most developed countries, even though no study has proved that it is effective. There are contradictory views and a lack of agreement in medical and dental practice and teaching on guidelines for IE prophylaxis.[11])

The purpose of this review is to enhance dental practitioners' understanding of current scientific evidence, developing trends, expert opinion, clinical guidelines, and the ethical basis for decision-making on AP for the prevention of IE in the dental practice setting, with the aim of increasing awareness, compliance and patient safety.

Global epidemiological characteristics and temporal trends of infective endocarditis

The epidemiological characteristics and temporal trends of IE summarized in this review are based on the Global Burden of Disease Study from 204 countries and regions for the period 1990 to 2019.[12]

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• *Age standardized incidence rate (ASIR)*

The incidence of IE continues to increase in many countries.[13-,15] The ASIR increased from 9,91% to 13.8% per 100,000 person years over the past 30 years12 According to Yang and co-workers,[12] "the estimated number of incident cases has increased by 128% from 1990 to 2019, with an increased ASIR for the population over 60 years old, with an overall five-fold increased risk of IE compared with the general population of adults." In contrast, the incidence of IE in the population under 25 years of age in the middle to high sociodemographic regions have gradually decreased, whilst in the low sociodemographic regions it has remained unchanged.[12]

It is suggested that the increase in IE incidence in the past 30 years, especially in higher sociodemographic regions,[12] could probably be related to population aging and the rapid increase in prosthetic valve replacement, CIED, haemodialysis, intravenous catheters, immunosuppression, cancer, diabetes, use of intravenous drugs and changes in IE prevention guidelines.[13,16,17-24]

• *Age standardized mortality rate (ASMR)*

The highest growth in ASMR was seen in the higher sociodemographic regions, because IE patients are often older and weaker, with more comorbidities.[25] Although the incidence of IE is low in lower sociodemographic regions, its ASMR level is higher due to delayed diagnosis and inaccessible medical care.[12]

• *Risk factors*

The patient population with highest risk of IE has gradually shifted from the young to elderly.[12] Elderly patients are most affected by IE, as older age is a significant risk factor that contribute to negative outcomes, among other comorbidities.[25] Other predisposing risk factors associated with increased incidence of IE include, intravascular prostheses, nosocomial infections, haemodialysis and age-related valvular sclerosis, especially in developed countries.[26]

Rheumatic heart disease (RHD) and congenital heart disease have been recognised as the main risk factors for IE in young people.[27] The development and availability of antibiotics, prenatal screening for congenital heart disease, and advances

in medicine have reduced the incidence of IE in young people in middle to high sociodemographic regions.[12]

Globally, the improvement of living standards, availability of streptococcal antibiotics, have reduced the prevalence of RHD.[28,29] Degenerative valvular diseases, CIEDs, intravenous medication, congenital heart disease (CHD), diabetes, and cancer have replaced RHD as the main risk factors for IE.[12]

- ***Microbiological factors and antimicrobial resistance***

Studies show that the causative flora implicated in IE have also evolved, with *Staphylococcus aureus* emerging as the predominant pathogen.[30] IE (with underlying cardiac disease) caused by *S aureus*, enteric Gram-negative bacilli, or *enterococci* is associated with higher morbidity and mortality, compared to IE caused by *Viridans Group Streptococci* (VGS), including in those with RHD and congenital valve disease.[3]

Observational studies have shown that patients undergoing transcatheter implantation for prosthetic aortic valves (TAVI) or transcatheter placement of other cardiac valves were associated with IE caused by *staphylococci* or *enterococci* and are associated with a high risk of morbidity and mortality.[31,32,33,34]

Hypervirulent *Staphylococcus*, resistant to many antibiotics, has gradually replaced penicillin-sensitive *Streptococcus* as the most common cause of IE.[19,35] Currently, *S. aureus* is the most frequently isolated IE-related microorganism which tends to acquire antibiotic resistance.[36]

What do we learn from current scientific data?

Clinical guidelines and good practice in clinical decision-making on AP for prevention of IE is based on the assumption that evidence-based information is available to support clinical guidelines, competency in diagnostics and treatment skills, and that effective and safe medications are available. Evidence-based data, although of a low level,[37] have been taken into account in most guidelines.

- ***Conceptions of bacteraemia***

Low-grade but repeated bacteraemia occurs frequently during daily routine activities such as toothbrushing, flossing or chewing, and more in patients with poor dental health,[38] In an earlier study it was suggested that the cumulative exposure to bacteraemia from routine daily activities in 1 year may be as high as 5.6×10^6 times greater than that resulting from a single tooth extraction.[39]

- ***Efficacy of antibiotic prophylaxis***

The efficacy of AP on bacteraemia and the prevention of IE has only been proven in animal models whilst the effect on bacteraemia in humans remain conflicting and controversial.[38,40-43] A recent Cochrane Systematic Review[44] concluded the following: (i) "There remains no clear evidence about whether AP is effective or ineffective against bacterial endocarditis in at-risk people who are about to undergo an invasive dental procedure." (ii) "There are no studies that assessed the number of deaths, serious adverse events requiring hospital admission, other adverse effects, or cost implications of treatment." (iii) "It is unclear whether potential harms and costs of prophylactic antibiotic administration outweigh any beneficial effects."

- ***Cost effectiveness***

Evidence on the cost effectiveness of AP for at-risk patients undergoing interventional procedures is contradictory as well.[45-49] It remains unclear whether AP is effective or not against IE.

- ***Risk/Benefit analysis***

The estimated risk of IE following dental procedures is very low. Antibiotic prophylaxis may therefore avoid only a small number of IE cases, as shown by estimations of 1 case of IE per 150 000 dental procedures with antibiotics and 1 per 46 000 for procedures unprotected by antibiotics.[50]

Antibiotic administration carries a small risk of anaphylaxis, which may become significant in the event of widespread use. The lethal risk of anaphylaxis is low when using oral amoxicillin.[51] The risk of death from penicillin anaphylaxis is 20 per million.[52] A cost-effectiveness analysis showed that in a cohort of 10 million moderate – or high-risk people penicillin would prevent 19 cases of IE, but cause 181 deaths due to anaphylaxis.[47]

Widespread use of antibiotics may result in the emergence of resistant microorganisms.[54] Emergence of antibiotic resistance as a significant public health concern combined with the risk of antibiotic-related adverse effects, albeit infrequent, such as anaphylaxis or *Clostridium difficile* colitis is reflected in the recommendations of different professional societies in the last decade.[55-60]

- ***Limitations of scientific data presented***

AP guidelines for prevention of IE are mostly based on animal experiments, observational studies and expert opinion because of the low incidence of IE.[55,58,61] No published prospective randomized controlled trials have investigated the efficacy of AP for a dental procedure on the occurrence of IE, and it is unlikely that such a trial will be conducted given the number of subjects needed.[2,3]

Who and What are the primary drivers of AP guidelines for prevention of IE?

The emergence of AMR in bloodborne bacteria is a major health problem globally.[62,63] Furthermore, the misuse and the overuse of antibiotics are among the main drivers of AMR.[64]

Recent concerns about adverse drug reactions and antibiotic resistance led to important modifications of the guidelines.[55] Guidelines for AP for preventing IE related to dental procedures have been developed by professional societies like the American Heart Association (AHA), [55] the European Society of Cardiology (ESC),[65] and the UK National Institute for Health and Care Excellence (NICE)[66].

In 2006 the British Society for Antimicrobial Chemotherapy (BSAC) published new AP recommendations for the UK,[59]

Table 1: Current guidelines on antibiotic prophylaxis (AP) to prevent infective endocarditis (IE)*

American Heart Association (AHA) (2021 Guidelines /Amendments) [3]	European Society of Cardiology (ESC) (2015 Guidelines / Amendments) [6]	National Institute for Health and Clinical Excellence (NICE) (2015 / 2016 Guidelines / Amendments) [72]
Patients Recommended for Antibiotic Prophylaxis Cover		
Those at highest risk of an adverse outcome from IE	Those at highest risk if IE undergoing a high risk procedure	AP against IE is not recommended routinely for patients undergoing dental or other procedures
Patients at Highest Risk of Adverse Outcome from IE	**Patients at Highest Risk of IE**	**Those at Risk of Developing IE**
• Previous IE • Prosthetic cardiac valve or prosthetic material used for valve repair • CHD – Unrepaired cyanotic CHD including palliative shunts and conduits • Completely repaired congenital heart defect with prosthetic material or device, whether placed by surgery or catheter intervention during first 6 months after the procedure • Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch • Cardiac transplantation recipients who develop valvulopathy	• Patients with previous episode of IE • Patients with a prosthetic valve, including transcatheter valve, or in those in whom any prosthetic material was used for cardiac valve repair • Any type of cyanotic CHD • Any type of CHD repaired with a prosthetic material, whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if residual shunt or valvular regurgitation remains after the procedure	• Previous IE • Acquired valvular heart disease with stenosis or regurgitation • Structural CHD, including surgically corrected or palliated structural conditions, but excluding isolated atrial septal defect, fully repaired ventricular septal defect, or fully patent ductus arteriosus, and closure devices that are judged to be endothelialised • Hypertrophic cardiomyopathy
Moderate / Intermediate Risk		
	• Patients with previous history of rheumatic fever • Patients with any other form of native valve disease including: bicuspid aortic valve, mitral valve prolapse, and calcific aortic stenosis • Patients with unrepaired congenital anomalies of the heart valves	
High-Risk procedures for which Antibiotic Prophylaxis should be considered		
• All dental procedures that involve the gingival tissue or the periapical region of teeth or perforation of the oral mucosa excluding local anaesthesia injections • Procedures on respiratory tract • Procedures on infected skin, skin structures or muscu-loskeletal tissue	• Only for dental procedures involving the gingival or periapical region of teeth or perforation of the mucosa, excluding local anaesthesia injections	• Advice / Recommendations not given
Recommended Antibiotic Prophylaxis Regimen (for those Not Allergic to Penicillin or Ampicillin)		
• Amoxicillin 2g orally 30-60 minutes before the procedure (Adult) / 50mg/kg (Child)	• Amoxicillin or ampicillin 2g orally 30-60 minutes before procedure	• Advice not given
Recommended Antibiotic Prophylaxis Regimen for those Allergic to Penicillin or Ampicillin (30-60 minutes before procedure)		
• Cephalexin§ 2g (Adult) / 50mg/kg (Child) OR • Azithromycin 500mg (Adult) / 15mg/kg (Child) • Clarithromycin 500mg (Adult)/ 15mg/kg (Child) • Doxycycline 100mg (Adult) / 2.2mg/kg (Child <45kg)	• Clindamycin 600mg orally (Adult) / 20mg/kg orally (Child)	• Advice not given

*(*Adapted from Thornhill, Dayer, Lockhart, et al 2017[10])*

and supported by a Cochrane review[2] argued that "there was no evidence to support the use of AP during invasive dental procedures." The BSAC recommendation that "AP for invasive dental procedures should be restricted to those at highest risk" caused outrage amongst UK cardiologists,[67,68] and the topic was referred to the newly formed NICE for review.

Subsequently, in their 2007 guidelines, the AHA recommended that "AP be restricted to patients at high risk of IE who undergo invasive dental procedures".[55] In 2009, a very similar guideline was published by the ESC.[65]

In March 2008, the NICE revealed the outcome of its review, and to the disbelief and shock of many cardiologists and cardiothoracic surgeons, recommended "the complete cessation of AP for all procedures and all patients to prevent IE."[66,69] The main reason given by the NICE for this recommendation was "the lack of evidence to support effectiveness of AP"[69] "and the results of their health economic analysis that concluded that AP was not cost-effective."[70]

In 2008 the NICE guidelines went a step further and advised against any antibiotic prophylaxis for dental and non-dental procedures whatever the patients risk.[60] Their conclusions have been challenged since estimations of the risks of IE are based on low levels of evidence. In 2012, The Swedish Medical Products Agency published its national guidelines, promoting the cessation of AP in dentistry for the prevention of IE.

The AHA or ESC guidelines for "AP for high-risk groups" have been widely adopted internationally, except Sweden and the UK, who have adopted the UK NICE guidelines on "complete cessation of AP".

The AHA[3] and ESC[6] concluded in their updated guidelines that "the weight of evidence and opinion is in favour of the efficacy and usefulness of AP in preventing IE in those at high risk, and that AP should be given before invasive dental procedures in patients at high-risk of IE." (Table 1) On the other hand the NICE deemed that there was insufficient evidence to warrant any change to their existing guidance and continued to recommend "complete cessation of AP".[71] Following their decision, the NICE came under considerable pressure from academics, health care practitioners, politicians and patients to reconsider. As a consequence their guidance was subtly changed in July 2016 to state that "AP against IE is not recommended routinely for people undergoing dental procedures". The inclusion of the word "routinely" indicates that AP may therefore be appropriate in individual cases.[72]

Revised clinical guidelines for AP for prevention of IE

The classification of high-risk patients recommended for AP, procedures for which AP should be considered, and recommended AP regimens are summarized in Table 1.

The AHA has made no changes to its 2007 VGS IE prevention guidelines.[55] The AHA continues to recommend "VGS IE prophylaxis only for categories of patients at highest risk for adverse outcome while emphasizing the critical role of good oral health and regular access to dental care for all".[3] The AHA developed its classification system based on greatest risk of adverse outcomes from VGS IE rather than risk of acquisition of VGS IE. (Table 1) Adverse outcomes from complications of VGS IE include, heart failure, need for cardiothoracic surgery, development of heart block requiring placement of a pacemaker, perivalvular extension and abscess, and other complications, including death.[3]

The revised recommendations for AP against IE of the ESC also remain the same, recommending that the weight of evidence/opinion is in favour of AP for prevention of IE for patients at highest risk of IE for dental procedures involving the gingiva, or periapical region of teeth or perforation of the oral mucosa.[6] Dental procedures for which AP for patients at high risk of IE is reasonable are defined in Table 1.

Parental antibiotic regimens are generally recommended for those patients undergoing a general anaesthetic.[3,6]

Cephalosporins§ should not be used in an individual with a history of anaphylaxis, angioedema, or urticarial with penicillin or ampicillin.[3] If an AP is inadvertently not administered before a dental procedure, then it may be administered up to 2 hours after the procedure.[3] In patients who are receiving a short course (7-10 days) oral antibiotic therapy before a dental procedure, it is preferable to select a different class of antibiotic listed in Table 1. Alternatively, if possible, it is preferable to delay an elective dental procedure for at least 10 days after completion of a short course of antibiotic therapy.[3]

What impact has the change in AP guidelines made?

- ***Acceptance and compliance of clinical guidelines***

Based on the results from clinical studies and surveys, there is good general awareness of clinical guidelines but variable compliance was demonstrated in the US and UK".[3]

Studies show that antibiotic prescribing by dentists is generally far from optimal.[73] A recently conducted cohort study in the Veterans' Health Administration (USA), concluded that of every 6 AP prescriptions, 5 were inconsistent with clinical guidelines.[74] In a survey of a random sample of 5500 dentists in the US, 70% of dentists reported "that they had patients who continued to take AP although the guidelines no longer recommend it, primarily because of physician recommendation (57%), or patient preference (33%)."[75] A survey of dentists in Canada demonstrated a general lack of compliance and that dentists recommended prophylaxis for moderate AHA risk groups, whilst some dentists did not prescribe for patients in AHA high-risk group.[76]

Dayer and co-workers analysed the impact of the NICE Guidelines and demonstrated that there was a 79% decrease in prescriptions for AP, which confirmed high compliance with the NICE recommendations in the UK.[5]

- ***Incidence of IE?***

Observational studies have found no significant change in the incidence of IE, despite the changes made in AP guidelines.[77-81]

However, according to Dayer and co-workers,[80] "most of these studies have several methodological limitations making it difficult to draw firm conclusions from these studies."

The AHA has also concluded that "there is no convincing evidence of an increase in cases of VGS IE among patients with high, moderate or low risk of IE, or adverse outcome from VGS IE since publication of its 2007 guidelines".

Following the 2008 NICE guidelines that recommended the complete cessation of AP in the UK, a follow-up study of National data in the UK was conducted demonstrating an 88% decrease in AP prescribing and a significant increase in the incidence of IE in both the high-risk and low-risk groups during the period following introduction of the NICE guidelines[5] The study by Quan and co-workers[82] suggests that there is a trend towards an increase in the overall incidence of microorganism specific IE in the UK from 1998 to 2017. This increase was not related to oral streptococci (VGS IE).[82] The latter finding was confirmed in a recent national cohort study in Sweden reporting that "cessation of AP has not led to an increased incidence of oral streptococci IE among high-risk individuals".[83] "Because no data were available on the microbiological cause of IE in these patients, it is suggested that no valid conclusion could be drawn about the impact of the NICE guidelines on the incidence of VGS IE, or AP for a dental procedure."[5]

Ethical analysis as basis for AP decision-making

Due to the high morbidity and mortality rate, IE has become a major threat of modern medicine[7,84] Thus, as a measure of prevention, the administration of AP prior to dental procedures is recommended. However, it remains unclear whether AP is effective or not against IE.[37] Evidence to support or discourage the use of AP prior to dental procedures as a prevention for IE is also very low and controversial.[37,38,85,86] Although AP is the primary choice for preventing IE, overuse of antibiotics has resulted in AMR to common antibiotics, and also the occasional adverse effects of antibiotics (e.g., anaphylaxis)[44] The emergence of superbugs or multi-resistant bacteria and millions of deaths due to AMR, has subsequently become one of the most recognized and greatest emerging threats to public and animal health.[63,87-89]

Dentists face an ethical conundrum of prescribing AP to prevent IE, or not to prescribe AP to prevent antibacterial resistance. This decision is further amplified by the following questions: (i) who is making the decision, (ii) what is the basis for the decision, and (iii) who takes the responsibility to prescribe AP? Furthermore, it is not possible to make suggestions for AP that deal with every possible circumstance of every possible hypothetical situation.[3] Therefore, clinical guidelines that fall outside the specific parameters and suggestions require ethical analysis, clinical judgment and shared decision making with the patient. The person who is making the decision to prescribe or not, irrespective of whether it is the dentist or cardiologist, is ultimately responsible and should be done on the basis of scientific evidence and ethical analysis.[90]

AP continues to be provided to some patients for whom it is no longer recommended, and withheld from others for whom it is advised.[3] There are instances when providers disagree with recommendations, or when patients request treatment that falls outside the guidelines.

Despite the widespread antibiotic use in dentistry, little formal ethical analysis exists regarding antibiotic stewardship in dentistry. Ethical analysis is based on the fundamental ethical principles of beneficence, non-maleficence, autonomy, and justice.[91]

• *Beneficence*

Dental practitioners have an ethical and medico-legal responsibility to protect their patients from IE. The ethical rationale for AP is individual patient beneficence by reducing the risk of IE, even if an exceedingly small number of IE cases could be prevented by AP for a dental procedure.[3] In the absence of RCT data, the benefits of AP are hard to quantify.[10] The NICE guidelines in 2008 suggests that 277 AP prescriptions are needed to prevent one case of IE and provides a reasonable estimate of AP effectiveness.[92] Thus, the cost of AP is modest whereas the cost of treating IE is very high.[93]

Treatment planning discussions between dental practitioner and patients at risk of IE should include an increased focus on dental/oral health, risk stratification, avoidance of co-morbidities and contributary risks, and vigilance for infection.[3]

In general, maintenance of good oral health and regular access to dental care are considered more important to prevent IE than AP for a dental procedure.[3,38]

• *Non-maleficence*

Patients' place their trust in their dentist to protect them from harm and to minimize the risk of developing a life-threatening illness such as that associated with IE. The administration of AP to prevent IE is not risk free, even in those who receive only a single dose. According to the AHA: "It should be emphasized to the patient that there is no proven benefit from AP to prevent IE from a dental procedure, however, there are risks from administration of AP".[3]

The main potential problems with AP are risk of adverse drug reactions, cost, and risk of promoting antibiotic resistance.[10] The AHA has recommended that "antibiotic stewardship is now a major component of combatting the development of adverse events, resistance, and cost control."[3]

Dentists have a duty to cover risks that are recognizable and potentially treatable. Patients receiving AP are at increased risk of adverse effects. A recent study found no recorded cases of death associated with a single dose (3g oral dose) of Amoxicillin AP and a very low rate of non-fatal adverse reactions following 22.6 million AP prescriptions.[92] The incidence of adverse reactions with Clindamycin was higher than anticipated with 13 fatal and 149 non-fatal adverse reactions/million prescriptions, nearly all of which related to Clostridium difficile infections.[92] Clindamycin causes more adverse reactions than other antibiotics used for AP, and its use is no longer recommended in the AHA guidelines.[3]

Fatal reactions to a single dose of a macrolide (azithromycin, clarithromycin), are extremely rare.[94,95] However, use of

azithromycin may increase the risk of serious cardiovascular events in certain patients.[3] Doxycycline is an alternative in patients who are unable to tolerate penicillin, cephalosporin or macrolide. An adverse reaction from a single dose of doxycycline is extremely rare.[3]

- ***Autonomy***

Guidelines and recommendations use all available evidence with the aim to assist health care professionals in making clinical decisions in selecting the best management strategies.[6] However, the final decision to use antibiotics before a dental procedure with the intention of avoiding IE rests with both provider and patient. Informing patients of their choices together with shared clinical decision-making improves outcomes, patient experience, and compliance.[3]

Dental practitioners have a legal and ethical obligation to discuss and document potential benefits and risks of AP with their patients. Despite the low infection risk, patients may request AP and dentists may prescribe AP in the context to uphold or respect patient autonomy.

Dentists should offer patients at risk of IE, clear and consistent information about prevention. [3]

- ***Justice***

The extensive and overuse of antibiotics is an issue of major global concern, because it may result in the development of antibiotic resistance.[3,89] The Centers for Disease Control and Prevention (CDC) estimate that "antibiotic resistant infections cause 23000 deaths, 2 million infections, and as much as $20 billion in direct health care costs annually in the US." [96]

According to an AHA Statement[3]: "Antibiotic stewardship is therefore considered essential to maintain our ability to manage life-threatening infections such as IE, by ensuring that antibiotics are used only in situations in which they are necessary and cost-effective, that the most appropriate antibiotic choice is made, and that the dosage regimen used will be effective while avoiding the development of antibiotic resistance."

AMR from inappropriate or overuse of antibiotics compromise justice by way of disparate allocation. That is, "AMR may detract from the rights of patients, including future patients to access adequate therapy. Thus AMR may be unjust for future generations who will be denied the benefits of an autonomous choice about antibiotics."[89]

To prevent development of resistant Streptococci against amoxicillin, Khalil and colleagues[97] suggest that for at-risk patients requiring repeated dental procedures likely to result in bacteraemia, either an alternative antibiotic regimen should be used each time, or there should be intervals of at least 4 weeks between treatment sessions.

Good oral health and regular access to dental care for all is emphasized in all clinical guidelines as a critical element of a IE prevention strategy.

Conclusion

IE is a severe life threatening infection with significant morbidity and mortality, which despite best efforts and AP continues to present in practice. Evidence to support or discourage the use of AP prior to dental procedures as a prevention for IE is very low. Variable compliance with AP continues to be provided to some patients for whom it is no longer recommended, and withheld from others for whom it is advised.

Clinical guidelines for AP to prevent IE provide a compilation of quality-assessed evidence with critical evaluation by leading experts in the field of cardiology, with resultant recommendations that are highly desired by health care providers to guide complicated clinical decision making. Patients deserve clear and consistent advice from their clinicians to facilitate shared decision making.

Dentists will be held liable for omissions in AP cover and are unlikely to be supported if AP is withheld and runs contrary to the recommendations of the patients' physician. Patients should be educated on benefits and risks of AP, recommendations against AP, importance of a high standard of oral hygiene, symptoms of infective endocarditis and risks of invasive procedures including non-medical procedures like body piercing and tattooing.

There is currently a paucity in scientific evidence-based data to support or contradict clinical efficacy of AP for prevention of IE. New well-designed studies are needed for clarity.

References

The full list of References 1-97 is available from:
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