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Antibiotic prophylaxis of infective endocarditis in patients with predisposing cardiac conditions: French cardiologists' implementation of current guidelines

A. Cloitre [a], P. Lesclous [a,1], Q. Trochu [a], C. Selton-Suty [b], D. Boutoille [c], T. Le Tourneau [d], F. Delahaye [e], D. Thomas [f], B. Iung [g], A. Gaudin [a], X. Duval [h,2], J.N. Trochu [d,*]

[a] Inserm, UMR 1229, RMeS, Regenerative Medicine and Skeleton, Université de Nantes, UFR Odontologie, CHU de Nantes, Service Odontologie Restauratrice et Chirurgicale, PHU4 OTONN, ONIRIS, Nantes, F-44042, France
[b] Institut Lorrain du Cœur et des Vaisseaux, CHU Nancy Brabois, Nancy, F-54511, France
[c] CHU de Nantes, Service des Maladies Infectieuses, F-44042, France
[d] Institut du Thorax, Inserm, UMR 1087, CIC-1413, CHU de Nantes, Nantes F-44042, France
[e] Service de Cardiologie, Hôpital Louis Pradel, Lyon F-69677, France
[f] Institut de Cardiologie, Groupe Hospitalier Pitié Salpêtrière, AP-HP, Paris, F-75651, France
[g] Université Paris Diderot, Sorbonne Paris Cité, Service de Cardiologie, Hôpital Bichat Claude Bernard, AP-HP, Paris, France
[h] Inserm, UMR 1137, IAME, Université Paris Diderot, Sorbonne Paris Cité, Inserm CIC 1425, AP-HP, Hôpital Bichat Claude Bernard, Paris, France

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ABSTRACT

Background: To prevent infective endocarditis (IE), with the exception of the United Kingdom, antibiotic prophylaxis (AP) is recommended in patients with predisposing cardiac conditions (PCCs) worldwide. To conclude on the relevance of this strategy, how the current guidelines are applied is a crucial point to investigate. The first aim of this study was to assess cardiologists' implementation of the current guidelines. The secondary objective was to identify specific areas where the training and knowledge of French cardiologists could be improved.
Methods: A national online survey was carried out among the 2228 cardiologist members of the French Society of Cardiology.
Results: The high risk PCCs for which IE AP is recommended were correctly identified by the vast majority of the respondents so that IE AP is mostly prescribed correctly in such patients. But only 12% identified all the right indications for IE AP according to 13 predefined PCCs (3 at high-risk, 6 at moderate-risk and 4 at low-risk of IE) so that some IE AP misuses are recorded, overprescription in particular. Only 47% prescribed the proper amoxicillin schedule and only 15% prescribed the appropriate clindamycin schedule in cases with penicillin allergy.
Conclusion: This study evidenced relevant areas where the training of cardiologists could be improved such as knowledge of the risk of IE for certain PCCs and some common invasive dental procedures. Cardiologists' knowledge should be improved before any conclusion can be drawn on the relevance of this AP strategy and its influence on IE incidence.

1. Introduction

Infective endocarditis (IE) is a rare (<7 cases per 100,000 persons per year) and severe disease (20% early mortality, 40% at 5 years) [1]. A causal link between IE and the oral cavity has long been assumed, [2] stemming from bacteremia and particularly oral *Streptococcus* resulting from invasive dental procedures [3]. To prevent IE, antibiotic prophylaxis (AP) has been recommended in the United States since 1955 for patients with predisposing cardiac conditions (PCCs) undergoing invasive procedures [4]. The AP prescription strategy is based on the recognition of a PCC that carries a risk of developing IE and a procedure at risk of causing IE bacteremia. Whether AP is a crucial factor for the prevention of IE remains debatable since three case–control studies evidenced an association between dental procedures and streptococcal IE [5–7], whereas three others did not [8–10]. But before any conclusion may be drawn, the primary question, as suggested by several authors, is whether the current guidelines are correctly implemented by the main prescribers of IE AP, i.e., dentists and cardiologists [11,12].

* Corresponding author.
E-mail address: jeannoel.trochu@chu-nantes.fr (J.N. Trochu).
[1] Co-first author.
[2] Co-last author.

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A recent survey among French dentists illustrated their lack of knowledge and implementation of the current guidelines [13]. However, to date no data have been produced for a population of general cardiologists. Only very specific data on pediatric cardiologists or congenital heart disease (CHD) specialists regarding the compliance with the 2007 AHA guidelines [14] are available [15–17]. All of them highlighted the correct identification of PCCs at high risk of IE by the cardiologic populations surveyed but all of them underlined IE AP overprescription for PCCs at moderate risk of IE that no longer require IE AP or for some PCCs with a low risk for IE with no indication for IE AP.

The aim of this study was to assess cardiologists' knowledge regarding implementation of the current European Society of Cardiology (ESC) guidelines for IE AP in a wide practitioners' population and second, to identify specific areas where the training and knowledge of French cardiologists could be improved.

2. Methods

2.1. Study design

An online national survey was carried out among the 2228 cardiologist members of the French Society of Cardiology (FSC) in 2014. The survey was anonymous and was approved by the French data protection agency (agreement no. 169 83 56).

2.2. Data collection

A tailored anonymous questionnaire comprising 40 questions was constructed, mostly based on a previous survey managed by the Association for the Study and Prevention of Infective Endocarditis (AEPEI) in 2012 among French dentists [13].

This questionnaire was divided into four parts: 1/ demographic and practice-related characteristics: age, gender, type of practice; 2/ knowledge of patients at high risk of IE: knowledge of the definition of an invasive dental procedure, knowledge of the IE risk of 13 predefined IE PCCs (three PCCs with high risk for IE, six PCCs with moderate risk for IE and four with low risk for IE), knowledge of the indication for an AP according to the same 13 predefined PCCs; 3/ knowledge of IE AP: knowledge of the indication for IE AP according to 13 predefined PCCs for IE and for a patient with a valvular prosthesis according to seven dental procedures, knowledge of the antibiotics recommended for an IE AP, knowledge of the IE AP schedule (dosage, number and time of intake); 4/ applicability of the current guidelines: criteria of choice for an IE AP, changes in the prescription habits of an IE AP.

The questionnaire was formatted on the SurveyMonkey software (SurveyMonkey Europe Sarl, Luxembourg). Its validity had been previously ascertained among a limited cohort of 10 hospital physicians. Thereafter, a survey link was sent to all members of the FSC and was posted on its website for 2 months. No incentive was given to the responders and a recall was performed a couple of weeks before the closing date.

2.3. Data analysis

Descriptive statistics were performed using Microsoft Excel 2007. Then the data were compared using the chi-square test or the Fisher test. Differences were considered significant if $p < 0.05$.

3. Results

3.1. Demographic and practice-related characteristics of the respondents

Two hundred sixty-five cardiologists responded to the survey (crude response rate: 13.4%); nine were excluded because the questionnaire was not fully completed and 13 because the data were unusable. The 243 remaining were included (true response rate: 12.3%). The male/female ratio was 2.2 and practitioners were mainly 35–50 years (38%) and 51–60 years of age (32%) with a hospital-based practice (60%).

3.2. Knowledge of patients at high risk of IE and IE AP

For 61% of the respondents, an invasive dental procedure is defined as a procedure requiring manipulation of the gingival or perforation of the oral mucosa but for only 56% as a procedure inducing significant bacteremia, i.e., the right definition (multiple choice question).

Among the 13 different predefined PCCs, the three high-risk conditions for IE (prosthetic cardiac valve, previous IE, unrepaired cyanotic CHD) were correctly identified as PCCs at high risk for IE by at least 92% of the cardiologists (Fig. 1). Mitral valve prolapse was correctly identified by 70% of the cardiologists as a PCC at moderate risk for IE; 9% of the respondents considered this condition as a PCC with a high risk of IE. All other PCCs carrying a moderate risk were correctly identified by at least 68% of the cardiologists, except tricuspid valve and functional mitral valve failures by only 49% and 36%, respectively (Fig. 2). Regarding the PCCs with a low risk for IE, three of them, arterial hypertension, coronary artery disease and coronary bypass, were correctly identified by at least 94% of the respondents. Regarding most particularly pacemakers and implantable cardioverter defibrillators, only 23% of the cardiologists correctly identified them as PCCs with a low risk for IE, 60% of the respondents considering pacemakers and implantable cardioverter defibrillators as PCCs with a moderate risk for IE.

Taken together, only 18% of the cardiologists correctly identified the risk of developing IE for all the 13 predefined PCCs.

Of these 13 predefined PCCs, at least 93% of the cardiologists correctly identified the three high-risk conditions for IE requiring an IE AP before an invasive dental procedure (Fig. 2). Regarding PCCs with a moderate risk for IE, mitral valve prolapse was correctly identified as not requiring IE AP before an invasive dental procedure by 76% of the cardiologists but 21% of the respondents overprescribed IE AP for this condition. Cardiologists overprescribed IE AP by a large amount for two other PCCs at moderate risk of IE, i.e., 30% for functional mitral valve failure and 29% for bicuspid aortic valve. Arterial hypertension, coronary artery disease and coronary bypass were identified as not requiring IE AP before an invasive dental procedure by at least 95% of the cardiologists. Regarding pacemakers and implantable cardioverter defibrillators, although classified as a PCC with a low risk for IE, 18% of cardiologists overprescribed IE AP before invasive dental procedures.

Taken together, only 12% of the cardiologists identified all the right indications for IE AP according to the 13 predefined PCCs,

3.3. Knowledge of the IE AP indication in regard to dental procedures

Among seven different dental procedures, five required IE AP in high-risk patients. Three of them were correctly identified by at least 89% of the cardiologists (dental extraction, surgical management of soft tissue or bone tissue), but endodontic treatment of vital monoradicular tooth and scaling were less often recognized as warranting IE AP (73% and 65% of the respondents respectively) (Fig. 3). The two procedures that did not require IE AP (treatment of caries without pulp exposure and prosthetic preparation) were correctly identified by only 65% and 30% of the respondents respectively.

Taken together, only 25% of the cardiologists correctly identified all seven predefined dental procedures.

Regarding invasive dental procedures in a high-risk patient, cardiologists correctly prescribed more IE AP for tooth extraction than for endodontic treatment of a vital monoradicular tooth and scaling (89% vs 75% vs 58%, respectively; $p < 0.001$).

An appropriate amoxicillin first-line prescription for IE AP was given by 90% of the respondents but only 47% according to the right schedule: a 2-g single dose 1 h before the invasive dental procedure, the main misapplication being a 3-g dosage of amoxicillin. In case of allergy to penicillin, only 15% prescribed the appropriate second-line drug (clindamycin) at the right dosage (600 mg).

3.4. Applicability of the current guidelines

The IE AP prescription of the vast majority of the respondents (95%) was declared to be based on ESC current guidelines [11], whereas the remaining declared basing prescriptions on their own clinical experience. Regarding these guidelines, 16% of the cardiologists declared they had not changed their usual IE AP prescription from the previous 2002 guidelines of the French Society of Infectious Diseases (previously applicable guidelines by French cardiologists) [18].

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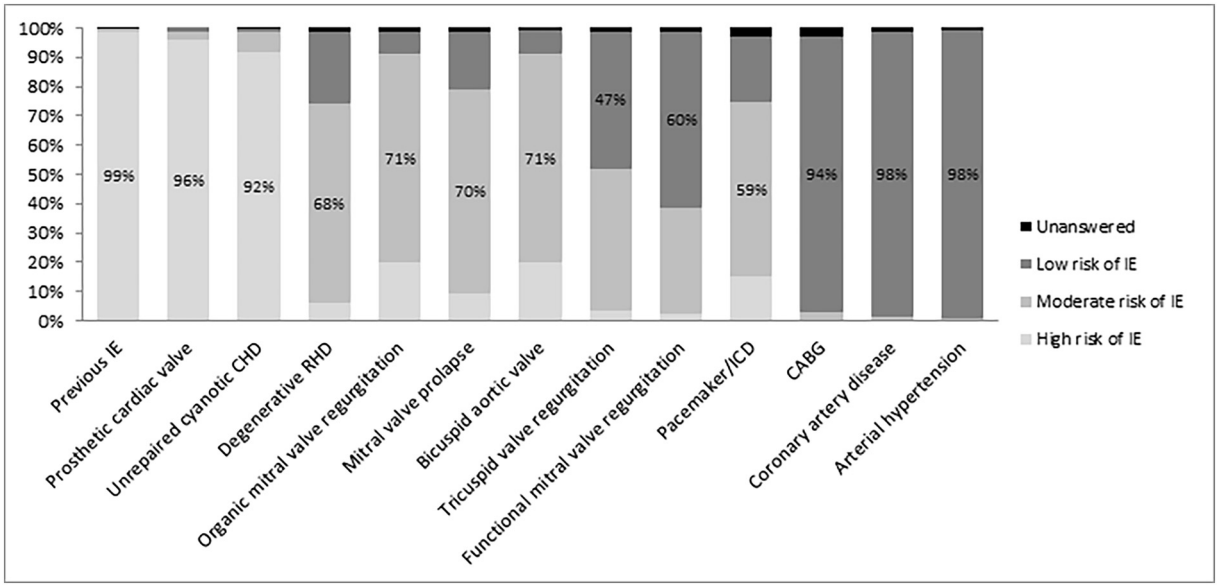

Fig. 1. Identification by cardiologists of infective endocarditis (IE) risk for patients with various cardiac conditions according to the current ESC guidelines. % Values in the histograms underlined the correct rate answer. CHD: cyanotic heart diseases; RHD: rheumatic heart disease; ICD: implantable cardioverter defibrillators; CABG: coronary artery bypass grafting.

4. Discussion

To our knowledge, this is the first study specifically devoted to evaluating the self-assessment of ESC guidelines for IE prevention in a general cardiologist population. The main results showed that cardiologists were overall well aware of these recommendations. Importantly, the high risk PCCs for which IE AP is recommended in case of invasive procedures, were correctly identified by the vast majority of the respondents except some seldom CHD mostly managed by cardiologists with a specialist interest. So, it is likely that cardiologists generally prescribed IE AP correctly in such patients. But significant misunderstandings were highlighted in this study. An IE AP overprescription was still recorded for some PCCs at moderate and low risk of IE, whereas some invasive dental procedures at risk of IE bacteremia were not accurately identified, inducing IE AP underprescription. Interestingly, this study provided specific areas where the training of cardiologists could be improved.

This survey demonstrated that cardiologists' knowledge of the different IE risk levels according to PCCs varied greatly. The main change introduced by the ESC guidelines (endorsing 2007 AHA guidelines [14]) was the limitation of AP to a population of patients with PCCs putting them at high risk for IE. In the present study, these three PCCs were clearly identified as an indication for IE AP by at least 92% of the respondents, in accordance with other studies [15,17]. But the good knowledge of PCCs at high risk of IE doesn't necessarily induce an appropriate management of patients at high risk of IE. In a crossover study about patients with prosthetic heart valves, Tubiana et al., highlighted that only approximately half received IE AP when undergoing an invasive dental

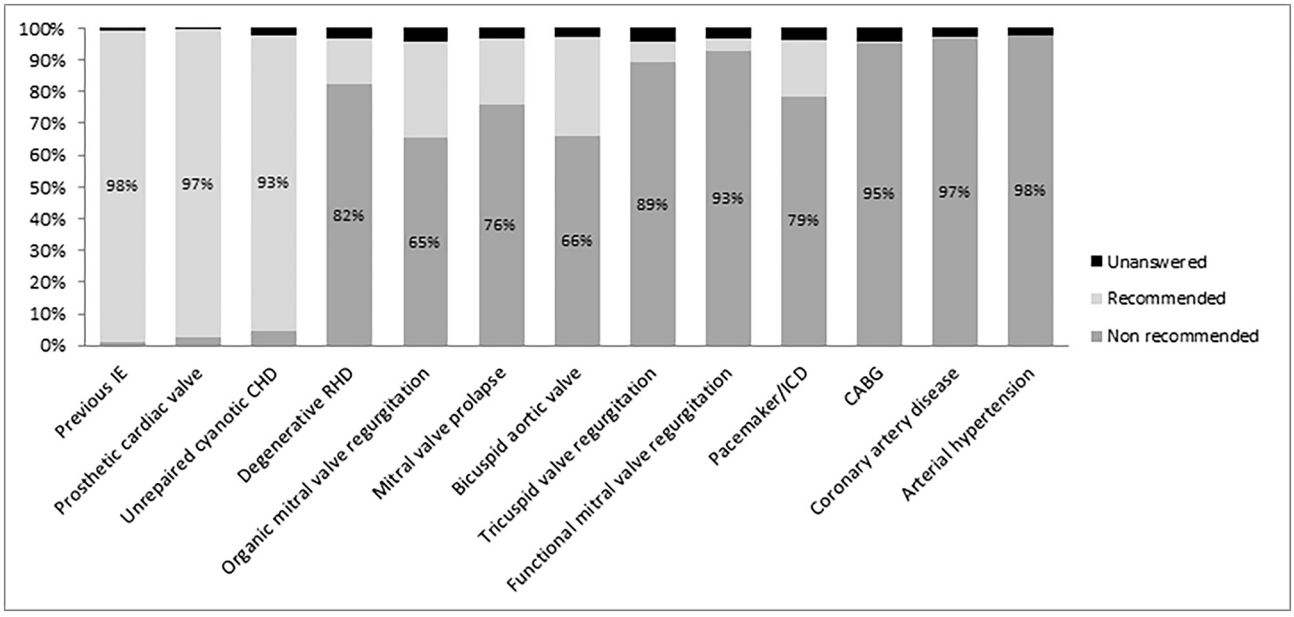

Fig. 2. Identification by cardiologists of indications for infective endocarditis (IE) antibiotic prophylaxis for various cardiac conditions according to the current ESC guidelines. % Values in the histograms underlined the correct rate answer. CHD: cyanotic heart diseases; RHD: rheumatic heart disease; ICD: implantable cardioverter defibrillators; CABG: coronary artery bypass grafting.

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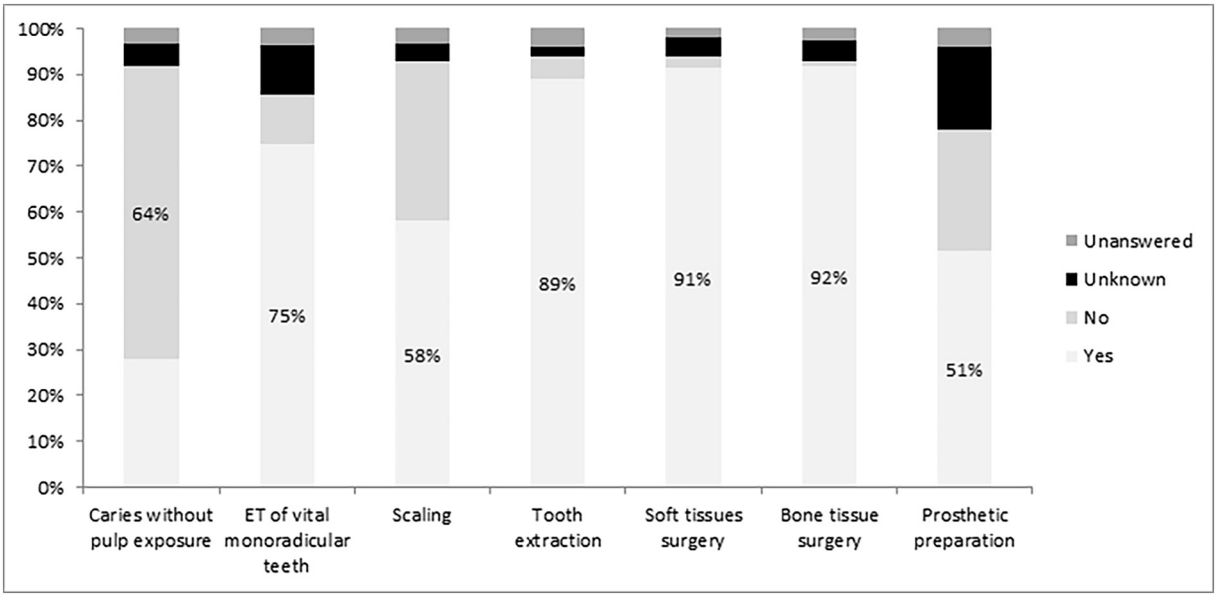

Fig. 3. Identification by cardiologists of dental procedures requiring or not antibiotic prophylaxis for a patient with a valvular prosthesis according to the current ESC guidelines. % Values in the histograms underlined the correct rate answer. CHD ET: endodontic treatment.

procedure [7]. Moreover, about 25% of such patients received an inappropriate IE AP prescription for a non-invasive dental procedure. But whether the IE AP prescription came from cardiologists or from dentists was not recorded in this study.

However, in some studies, the residual IE risk of some repaired CHDs appeared variously appreciated by specialized cardiologists such as perimembranous ventricular septal defect with no residual shunt or corrected tetralogy of Fallot with no residual shunt, inducing overprescription of IE AP [15–17]. Surprisingly, some cardiologists were less likely to recommend IE AP for patients at high risk for IE, mainly because some palliated cyanotic CHD cases are classified as being at high risk of IE by some authors [15] and at low risk for IE by others [16], such as Fontan palliation. However, our questionnaire was not intended to investigate such conditions. ESC guidelines appeared potentially ambiguous and need more specifications for certain cyanotic PCCs. Moreover, the responses also appeared ambiguous for PCCs with a moderate risk for IE, which no longer required IE AP for invasive dental procedures. This induced IE AP misuse, sometimes considerable, >30% overprescription for organic mitral valve failure or bicuspid aortic valve. Such tendencies were also recorded for rheumatic heart disease with aortic insufficiency or aortic stenosis in a limited cohort of cardiologists [11,18]. For such PCCs with a moderate risk for IE, highly experienced cardiologists were more likely not to prescribe IE AP than their less experienced counterparts [16]. We did not evidence this correlation in our study, possibly because the study reported by Patel et al. was conducted only in pediatric cardiologists less aware of some of these conditions that are more frequent in an adult population. We cannot exclude that some cardiologists had shown reluctance to discontinue IE AP in individuals who are accustomed to receiving IE AP. Recognition of the IE risk of these diseases and the fact that IE AP was unnecessary for invasive dental procedures clearly appear as specific points that could be improved in the cardiologists' training. The PCCs at low risk for IE were clearly identified and did not induced IE AP misuse except for one condition, pacemakers and implantable cardioverter defibrillators. This condition was inappropriately classified as a PCC with a moderate risk for IE by >70% of the respondents and was a source of IE AP overprescription by 20% of them. This is clearly another specific point to improve in the cardiologists' training. These misuses of IE AP was pointed out by the NICE (National Institute for health and Clinical Excellence - that recommended complete cessation of IE AP whatever the IE risk in UK in 2008), to lead to a greater number of deaths through fatal anaphylaxis than a strategy of no AP, to favor antibiotic resistance and not to be cost-effective [20]. But no fatal anaphylaxis after oral amoxicillin IE AP has been recorded in France and worldwide for decades whereas alternative clindamycin AP regimen for patients allergic to penicillin could be a greater source of adverse drug reactions including fatalities [14,21,22]. A strategy of directing AP at patients at high risk of IE is likely to be cost-effective even at low rates of AP clinical effectiveness [23]. The impact of antibiotic resistance associated with IE AP has not be formally assessed but antibiotic resistance is believed to be encouraged when repeated courses of antibiotics at inadequate doses are given and is minimized by infrequent doses of antibiotics at high doses as for IE AP [24].

As expected, cardiologists were less accurate in the identification of invasive dental procedures inducing bacteremia than in the identification of PCCs, except tooth extraction and surgical management of soft tissue or bone tissue. It is worrying that approximately 40% of the cardiologists do not prescribe IE AP for scaling in a high-risk patient since it is a very common invasive dental procedure. It is not surprising that more specific dental procedures such as invasive endodontic treatment of vital monoradicular tooth or noninvasive treatment of caries without pulp exposure were correctly identified by a small part of the cardiologists. These mistakes probably reflect the too general definition of an invasive dental procedure in the ESC guidelines: “procedures requiring manipulation of the gingival or the periapical region of the teeth or perforation of the oral mucosa” [11]. Of course cardiologists are not dentists but they are often the first line specialists to whom patients at high risk of IE ask for information about the risk associated with some dental (and not dental) invasive procedures. Thus, it could be important that cardiologists are aware of the most frequent risky dental procedures as those that are not risky. This is also a clear point revealed in this study to improve.

Regarding the IE AP prescription, although the vast majority of the cardiologists correctly identified the two recommended antibiotic drugs (amoxicillin and clindamycin in case of allergy to penicillins), only 47% prescribed the right regimen of 2 g of amoxicillin or 600 mg of clindamycin 1 h before the invasive dental procedure. The main misapplication was a 3-g dosage of amoxicillin (instead of 2 g in the current guidelines) accordingly to the 2002 guidelines of the French Society of Infectious Diseases [18].

The ESC guidelines were globally considered as applicable, clear, well presented and easily accessible by a majority of the respondents.

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This is of huge importance given that clinicians' compliance to guidelines firstly depends on factors related to their readability [19]. But these factors are not sufficient to induce a good implementation of guidelines. Assessment of the cardiologist compliance to the NICE guidelines in UK or in Ireland through questionnaire based surveys revealed that if the vast majority was aware, only a small part of them based their practice on these guidelines [25,26]. Most of these cardiologists clearly feel that AP still has a role in certain conditions (patients with prosthetic heart valve or patients with prior IE) and refer to alternative guidelines in case of invasive dental procedures.

This study has highlighted major differences regarding IE AP between dentists and cardiologists. As expected, PCCs and the related IE risk appear better identified by cardiologists. A nationwide survey of French dentists' knowledge and implementation of current guidelines for antibiotic prophylaxis of infective endocarditis in patients with predisposing cardiac conditions showed that high risk for IE are recognized by both specialties, but dentists clearly identify unrepaired cyanotic CHD less easily [13]. This difference is also recorded in the Anguita et al. study [27], probably due to dentists not having knowledge of this type of heart disease, whose incidence is increasing in the general population because of improved survival. PCCs with low and moderate risk for IE that no longer require IE AP also appear better identified by cardiologists except for pacemakers and implantable cardioverter defibrillators, better identified by dentists [13]. Interestingly, this specific finding is also recorded in the Anguita et al. study [27]. Targeted information on this specific point is needed in training for cardiologists.

As expected, dentists identify invasive dental procedures better, whether or not they require IE AP [13]. This could be explained by the exhaustiveness of the guidelines for dentists. The 2011 ANSM guidelines endorsed the ESC 2009 guidelines but added a large descriptive section regarding invasive dental procedures [12]. This study underscores that cardiologists have to be better informed about the most frequent invasive dental procedures such as scaling. The misunderstandings we observed led to more declarations of IE AP overprescription from cardiologists for noninvasive dental procedures and more underprescription for invasive dental procedures compared to dentists [13].

In this study, the cardiologists had a hospital-based practice more frequently than did the dentists, who worked more often in individual primary-care private practice [13]. This difference may in part explain the discrepancies in the knowledge of the current guidelines between both specialists, dentists knowing less well their dedicated guidelines [13]. Hospital practitioners are generally more aware of new developments, keep informed on a regular basis by attending conferences more frequently and become more involved in writing or disseminating recommendations to colleagues and students. Moreover, they are more often in charge of patients at risk for IE.

This study has a number of unavoidable methodological drawbacks, as do most survey studies examining self-assessment of guideline implementation. Only FSC members, accounting for approximately 32% of the French cardiologist population, were questioned [28]. Despite the low 12.3% true response rate to this online survey, the number of these responses made this study one of the most reliable. Even though only 243 responses were included in this survey, the profile of the respondents is roughly comparable to that of the French cardiologist population according to gender and age distributions [29]. It can also be questioned to what extent questionnaire respondents were those who knew the ESC guidelines best, which may have resulted in an overestimation of guideline implementation. Moreover, it should be underlined that both surveys were conducted at different times after guideline publications. The present cardiologists' survey was conducted 5 years after the 2009 ESC guidelines were published, whereas the dentists' survey was carried out only 1 year after the 2011 ANSM guidelines appeared. This was probably not long enough for a full completion of new guidelines because adoption of new habits always requires time [29].

Despite these limitations, this prospective study is the largest and the most detailed survey to date on IE AP in a general cardiologists' population.

In conclusion, although IE incidence has not increased in France since the restriction of IE AP [30], the interpretation of this result is confusing given the low level of complete implementation of ESC guidelines revealed by this survey. It is crucial to improve compliance with current guidelines by sustaining continuous medical education in the training of French cardiologists, particularly on specific areas revealed by this survey: regular dedicated sessions are organized during international, national and local meetings and guidelines and information are easily available on several websites (www.escardio.org, *www.endocardite.org*, *www.cardio-online.fr*, *www.fedecardio.org*). It also seems necessary to strengthen the dialogue between cardiologists and dentists and organize shared education sessions. Only then can the relevance of such guidelines be properly assessed.

Statement of authorship

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Authors' contribution

PL, JNT AC and XD contributed to the conception or design of the work. QT contributed to the acquisition, analysis and interpretation of data for the work. AC, PL and JNT drafted the manuscript. XD, CSS, DB, TLT, FD, DT, BI and AG critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Conflict of interest

The authors declare no conflict of interest. The survey was anonymous and was approved by the French data protection agency (agreement no. 169 83 56).

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