

# Prophylaxis of Infective Endocarditis: A Cross Sectional Survey among Physician Members of the Portuguese Society of Cardiology



## Estudo Transversal sobre Profilaxia da Endocardite Infeciosa: Inquérito a Médicos da Sociedade Portuguesa de Cardiologia

Catarina de SOUSA<sup>1,2</sup>, Ana G. ALMEIDA<sup>1,3</sup>, Fausto J. PINTO<sup>1,3</sup>  
 Acta Med Port 2022 Dec;35(12):874-880 • <https://doi.org/10.20344/amp.17379>

### ABSTRACT

**Introduction:** In the last decade, the downgrading of indications for antibiotic prophylaxis for infective endocarditis caused an uncertain impact on the incidence of this condition. Since no data is available on the practice of infective endocarditis prophylaxis in Portugal, we aimed to characterize the pattern of antibiotic use for infective endocarditis prophylaxis and the compliance/awareness of scientific guidelines among physician members of the Portuguese Society of Cardiology.

**Material and Methods:** A cross sectional observational study was conducted. An online self-completed questionnaire with 12 items on infective endocarditis prophylaxis was sent to 1330 physicians, specialists and residents, members of the Portuguese Society of Cardiology. In addition, descriptive statistical analysis was performed.

**Results:** Two hundred and fifty-three valid questionnaires were responded. Eighty-seven per cent of respondents were cardiologists (specialists or residents), mostly between 30 and 40 years old (26.7%) and 50 to 80 years old (44.3%). The majority (83.0%) follow the European scientific guidelines. Still, 61.0% had or may have had doubts regarding prophylaxis of infective endocarditis in certain patients. Variable adherence to scientific guidelines was noted. Further scientific evidence was required by 60.6% of respondents.

**Conclusion:** Infective endocarditis prophylaxis was generally guided by European scientific guidelines among physicians of the Portuguese Society of Cardiology. There was, however, an evident discrepancy between the guidelines and real-world perception of the risk of infective endocarditis. This highlights the sensed gap in accessing more robust scientific evidence.

**Keywords:** Antibiotic Prophylaxis; Endocarditis; Portugal; Surveys and Questionnaires

### RESUMO

**Introdução:** Na última década, a restrição das indicações para a profilaxia antibiótica na endocardite infecciosa teve um impacto incerto na incidência desta condição. Uma vez que não existem dados sobre a prática da profilaxia da endocardite infecciosa em Portugal, procurámos caracterizar o padrão de utilização antibiótica para a profilaxia da endocardite infecciosa e a conformidade/sensibilização das orientações científicas entre médicos, membros da Sociedade Portuguesa de Cardiologia.

**Material e Métodos:** Foi realizado um estudo observacional transversal. Um questionário online de autopreenchimento com 12 itens sobre profilaxia da endocardite infecciosa foi enviado a 1330 médicos, especialistas e internos, sócios da Sociedade Portuguesa de Cardiologia. Foi realizada uma análise estatística descritiva.

**Resultados:** Foram validados 253 questionários respondidos. Oitenta e sete por cento dos inquiridos eram cardiologistas (especialistas ou internos), a maioria entre os 30 e os 40 anos (26,7%) e os 50 e 80 anos (44,3%). A maior parte (83,0%) segue as orientações científicas europeias. Ainda assim, 61,0% admitiu ter ou poder ter dúvidas sobre a profilaxia da endocardite infecciosa em determinados doentes. Verificou-se uma adesão variável às orientações científicas. A necessidade de mais evidência científica foi defendida por 60,6% dos respondedores.

**Conclusão:** Entre médicos da Sociedade Portuguesa de Cardiologia, a profilaxia da endocardite infecciosa foi geralmente orientada pelas orientações científicas europeias. Existiu, no entanto, uma evidente discrepância entre as orientações e a perceção do risco de endocardite infecciosa na prática clínica. Isto reforça a necessidade de acesso a dados científicos mais robustos.

**Palavras-chave:** Endocardite; Inquéritos e Questionários; Portugal; Profilaxia Antibiótica

### INTRODUCTION

Despite tremendous medical advances, the management of infective endocarditis (IE) is clinically challenging and carries a substantial rate of morbidity and mortality worldwide.<sup>1</sup> Its crude incidence ranges from 1.5 to 11.6 cases per 100 000 people.<sup>2</sup> Moreover, in-hospital mortality rate affects nearly one-fifth of patients as documented in international registries such as the International Collaboration Endocarditis Cohort<sup>3</sup> or the recently published EURO-endo<sup>4</sup> (18% and 17%, respectively).

Approximately a century ago, the role of bacteremia leading to IE in patients with preexistent valve disease was demonstrated.<sup>5</sup> In addition, SD Elliot<sup>6</sup> demonstrated that transient bacteremia occurring following a dental infection or trauma could lead to subacute IE. Moreover, the concept of prevention through oral treatment emerged. In 1970, Hilson<sup>7</sup> defended the use of chemoprophylaxis for patients with increased susceptibility to endocarditis, citing Kelson and White who, in 1945, estimated a risk of endocarditis of

1. Centro Cardiovascular da Universidade de Lisboa. Faculdade de Medicina. Universidade de Lisboa. Lisboa. Portugal.

2. Lusíadas Knowledge Center – Lusíadas Saúde. Lisboa. Portugal.

3. Departamento de Coração e Vasos. Hospital de Santa Maria. Centro Hospitalar Universitário Lisboa Norte. Lisboa. Portugal.

✉ **Autor correspondente:** Catarina de Sousa. [catarinasousacardio@gmail.com](mailto:catarinasousacardio@gmail.com)

**Recebido/Received:** 25/10/2021 - **Aceite/Accepted:** 19/05/2022 - **Publicado Online/Published Online:** 09/06/2022 - **Publicado/Published:** 02/12/2022

Copyright © Ordem dos Médicos 2022



1 in 500 after dental extraction.

Since then, several regimens have been proposed for the prevention of IE in susceptible patients. Scientific guidelines<sup>8</sup> include previous history of IE, prosthetic or repaired cardiac valves, cyanotic congenital heart disease and any repaired congenital heart disease for up to six months after repair or lifelong prophylaxis in residual shunt or regurgitation as high-risk cardiac conditions. The downgrading of antibiotic indications for endocarditis prevention in 2007 in the USA<sup>9</sup> and in 2009 in Europe<sup>8</sup> has, nonetheless, led to heterogeneous compliance by physicians, as shown by Chambers *et al.*<sup>10</sup> And this downgrading has not been adopted by several scientific societies, such as in Brazil or in Latin America. These still consider that native valve disease (such as aortic bicuspid valve or mitral valve prolapse) is a high risk situation and maintain antibiotic use before genitourinary or gastrointestinal procedures involving mucosa in high risk patients.<sup>11</sup>

Several electronic surveys conducted in Spain<sup>12</sup> or France<sup>13</sup> with dentists revealed that their knowledge of cardiac conditions and antibiotic side effects was inadequate.

The impact of this downgrading in antibiotic prophylaxis on the incidence of IE is still inconsistent<sup>14</sup> even though it has been shown in Germany<sup>15</sup> or in England.<sup>16</sup> In Portugal, no study has analyzed this impact on local or national incidence.<sup>17,18</sup> Nevertheless, an increasing trend was noted in the incidence of IE in Portugal in the last decade and the in hospital all-cause mortality rate affects one fifth of patients hospitalized with infective endocarditis.<sup>17</sup> The compliance of physicians with guidelines needs to be considered for quality and standard of care and assessment. No study has evaluated the pattern of antibiotic prophylaxis for IE among Portuguese physicians. Surveys are an essential tool to gather information on the attitudes and practice of care delivery among physicians.<sup>19</sup>

Therefore, we aimed to assess acceptance and compliance with scientific guidelines regarding IE prophylaxis among physician members of the Portuguese Society of Cardiology.

## MATERIAL AND METHODS

### Study design

A cross sectional descriptive study was carried out between the 8<sup>th</sup> February and the 28<sup>th</sup> February 2021, in a partnership between the Valvular Heart Diseases Working Group (Portuguese Society of Cardiology) and the Faculty of Medicine of the University of Lisbon.

After reviewing the most recent scientific guidelines<sup>8,20</sup> regarding antibiotic use in IE prevention, a 12 item questionnaire in Portuguese was developed (Appendix 1: [https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/17379/Appendix\\_01.pdf](https://www.actamedicaportuguesa.com/revista/index.php/amp/article/view/17379/Appendix_01.pdf)). All 12 questions were closed questions with an area in the end of the questionnaire for personal comments.

The questions regarding antibiotic prophylaxis in IE included data on 1) personal/professional background (age, specialty, year of medical degree), 2) international scientific

guidelines and national/institutional guideline recommendations, 3) identification of high-risk conditions, 4) identification of high-risk procedures and 5) risk assessment and choice of antibiotics during dental procedures.

The questionnaire was planned to take less than five minutes to answer. All answers were anonymous. We gathered all quantitative and qualitative data for analysis. The questionnaire was active for three weeks and a reminder email was sent one week before the final date.

### Sample

All physician members of the Portuguese Society of Cardiology (a total of 1330) were invited to participate in this online questionnaire, sent via email.

### Statistical analysis

We performed a standard descriptive analysis of the results obtained from a convenience sample.

Continuous variables were presented as mean  $\pm$  standard deviation and categorical variables were expressed as frequencies and percentages. Missing values were excluded from analyses (we performed an available data analysis).

The data were analyzed using Excel 365 for Windows software.

**Table 1** – Characteristics of physicians that participated in the questionnaire

Medical Specialty		
Cardiology	190	74.5%
Resident - Cardiology	30	11.8%
Internal Medicine	4	1.6%
Resident - Internal Medicine	0	0.00%
Cardiothoracic surgery	9	3.5%
Resident - Cardiothoracic Surgery	1	0.4%
Paediatric Cardiology	16	6.3%
Family physician	1	0.4%
Not mentioned	4	1.6%
Age (year-old)		
20 to 30	26	10.2%
30 to 40	68	26.7%
40 to 50	41	16.1%
50 to 80	113	44.3%
> 80	5	2.0%
Year of Medical graduation		
1960 - 1989	99	39.3%
1990 - 1999	31	12.3%
2000 - 2009	61	24.2%
2010 - 2019	61	24.2%
Frequent evaluation of valve disease patients		
Yes	238	93.3%
No	16	6.3%

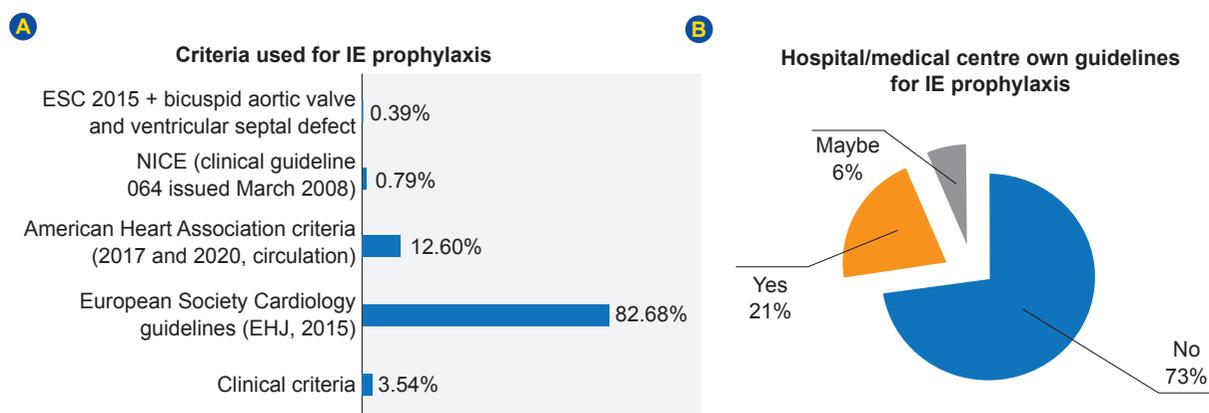


Figure 1 – (A) Usual criteria used by physicians for IE prophylaxis; (B) Institutional guidelines issued by medical institutions for antibiotic use in IE prevention.

### Ethics

The Ethics Committee of the University of Lisbon Academic Centre study approved the study (reference number 349/19). All respondents gave their informed consent.

### RESULTS

Of the 1330 invitations to physicians to participate in this survey, 255 questionnaires were returned, corresponding to a 19% response rate. However, two questionnaires contained no answers and were excluded. Most physicians were cardiologists and 60% of the participants were between 40 and 80 years old (Table 1); 93.3% reported regularly following patients with heart valve disease.

### Compliance with scientific guidelines in IE prophylaxis

Nearly 83% of the respondents regularly followed the European Society of Cardiology scientific guidelines for IE prophylaxis (Fig. 1A). One quarter of physicians had institutional guidelines for IE prophylaxis (Fig. 1B).

Thirty nine percent of the respondents had no doubts regarding IE prevention (Fig. 2).

### Cardiac conditions and procedures considered for IE prophylaxis

Patients with cardiac valve prosthesis, prosthetic material used in valvuloplasty, cyanotic congenital cardiac disease and previous IE were among the most frequently conditions identified by responders as high-risk conditions for IE (Table 2). The previous history of rheumatic valve disease was identified in 29.4% of the answers.

Most physicians identified dental procedures as a condition that increased the risk of IE, followed by implantation of intracardiac devices. Permanent tattooing and body piercing raised more doubts than any other procedure regarding the recommendation for IE prophylaxis (Fig. 3).

### Dental procedures and IE

From the total number of respondents, 60.6% defended that further scientific evidence was needed to demonstrate the benefit of antibiotic use in invasive dental procedures.

Dental invasive procedures were identified as being

high risk for the risk of IE whereas brushing teeth or eating was perceived as low risk activities (Fig. 4A). Nearly 93% of physicians used amoxicillin for IE prevention during dental procedures (Fig. 4B).

### DISCUSSION

To the best of our knowledge, this is the first study to evaluate the current practice among physicians regarding IE prophylaxis in Portugal. In our study, applied to physicians who were members of the Portuguese Society of Cardiology, the European guidelines<sup>8</sup> were the most followed and the identification of high-risk cardiac conditions and procedures was mostly in accordance with them. Nonetheless, previous rheumatic fever, the presence of native valve disease or intracardiac devices were substantially identified as being high-risk cardiac conditions for IE, thus conflicting with current indications. Also, 61% of responders had doubts regarding IE prophylaxis in certain patients. Lastly, further evidence regarding dental procedures and IE prophylaxis was warranted by a substantial proportion of physicians.

The accepted standard of care relies more and more often on scientific expert guidelines. Ethically, though, deviation from these recommendations may be feasible if they are fully discussed with patients to ensure informed consent<sup>21</sup> and supported on scientific evidence.

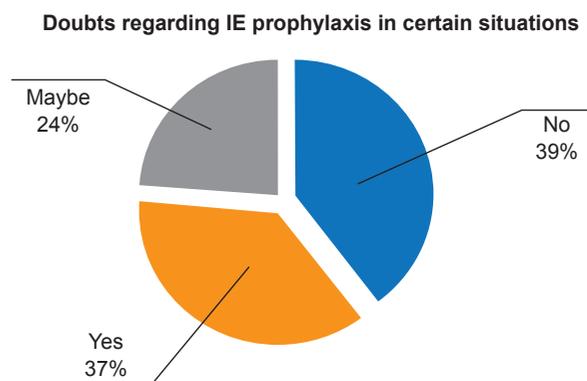


Figure 2 – Doubts regarding IE prophylaxis in clinical practice

Table 2 – Clinical conditions in which IE prophylaxis should be applied

Patients with cardiac valve prosthesis	241	94.5%
Patients with prosthetic material used in cardiac valvuloplasty	174	68.2%
Patients with history of rheumatic fever	75	29.4%
Patients with cyanotic congenital cardiac disease	228	89.4%
Patients with cardiac murmur or other evidence of native valve disease	32	12.6%
Patients with intracoronary stent intracoronary or coronary-aortic bypass graft surgery	6	2.4%
Patients with previous IE	230	90.2%
Patients with intracardiac device (pacemaker/implantable cardioverter defibrillator)	46	18.0%
All the options	6	2.4%
None of the options	4	1.6%
Other:		
Bicuspid aortic valve	3	1.2%
Recently implanted cardiac devices	1	0.4%
Patients with residual lesions after congenital defect repair	2	0.8%
Ventricular septal defect	1	0.4%
Percutaneous or surgically repaired congenital cardiac condition within 6 months of procedure	1	0.4%

From 2007 to 2009, several scientific societies<sup>9,22,23</sup> limited the use of antibiotic indication in the prophylaxis of IE. The United Kingdom's (UK) National Institute for Health and Care Excellence (NICE) guidelines<sup>22</sup> were the most restrictive, advising against all forms of antibiotic use for IE prophylaxis. These overall measures were justified by the lack of scientific evidence of the benefit associated with the risk of inefficient use of antibiotics concerning side effects and increased risk of resistance.<sup>8</sup> Nevertheless, its impact has been controversial. A significant increase in the incidence of IE in England was noted by Dayer *et al.*,<sup>24</sup> followed by

similar findings in the Netherlands<sup>25</sup> and Germany.<sup>25</sup> Still, uncertainty persists<sup>26</sup> as significant heterogeneity between different studies and the follow-up period is still too short to allow drawing more permanent conclusions. Additionally, compliance can be challenging. Dayer *et al.*<sup>10</sup> concluded that 39% of cardiologists/cardiac surgeons did not adopt the most recent NICE guidelines.

Most physician members of the Portuguese Society of Cardiology accepted the 2015 European guidelines.<sup>8</sup> Still, substantial conflict persists as many respondents expand IE prophylaxis use in cardiac conditions no longer

Procedures in which IE prophylaxis is recommended

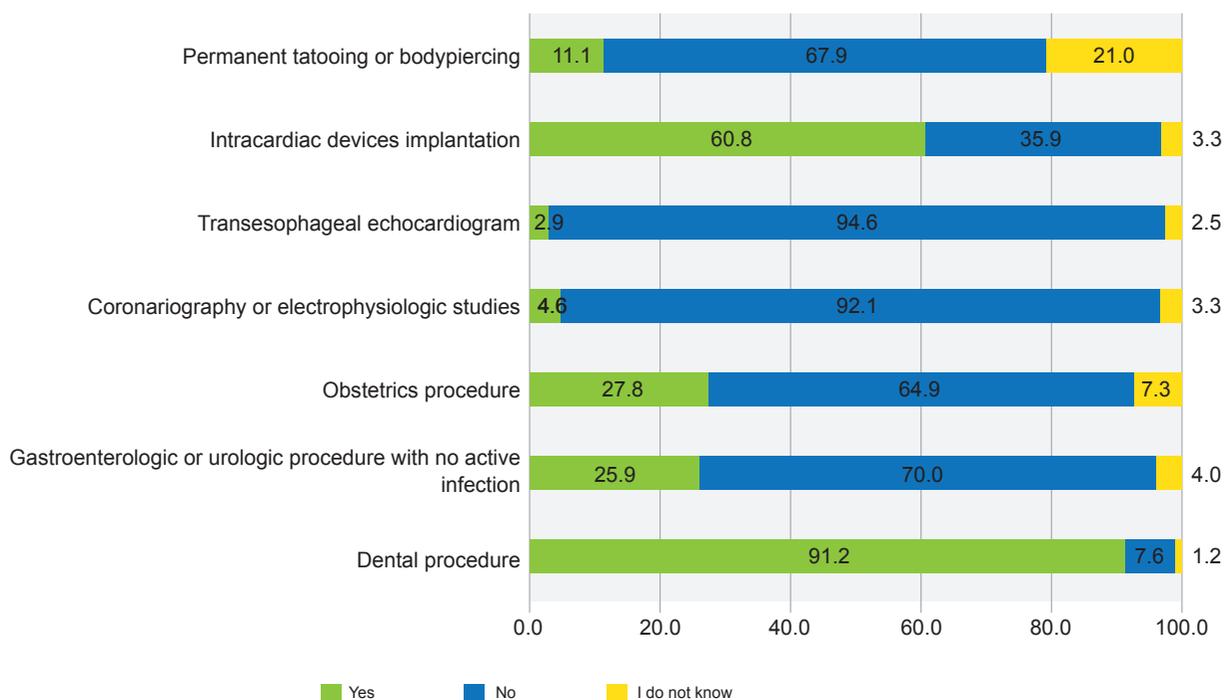


Figure 3 – IE prophylaxis recommendation in specific settings (%)

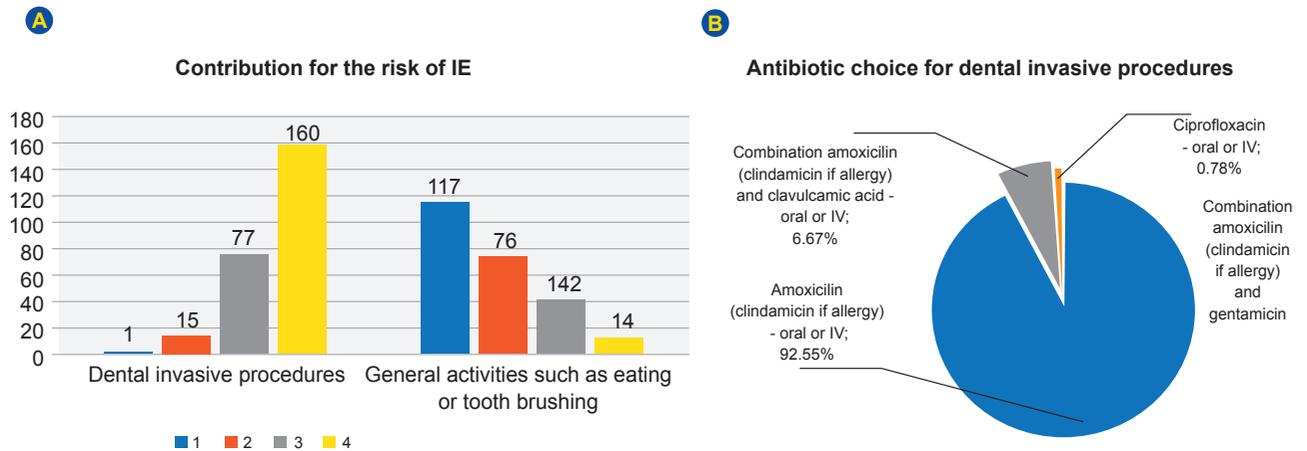


Figure 4 – (A) Perceived contribution that each of the following factors plays in the risk of developing infectious endocarditis (value of 1 to 4, being 1- no contribution and 4 - major contribution); (B) Antibiotic regimen (%) usually used in antibiotic prophylaxis in dental procedure.

considered high risk by the more recent guidelines, such as previous rheumatic fever, intracardiac devices or native valve disease carriers. Other studies have shown this heterogeneity. Grattan *et al*<sup>27</sup> concluded that among pediatric cardiologists, the 2007 American Heart Association guidelines<sup>9</sup> led to a reduction of IE prophylaxis recommendations among low risk patients by 44.9% but unexpectedly a reduction of 9.3% among high risk patients as well. This was also shown by Pharis *et al*<sup>28</sup> in a study carried out among New Zealand, Canada, Australia and American pediatric and adult congenital cardiologists in 2008.

The same is true for high-risk procedures. Dental procedures were almost always considered a high-risk situation by this group of 253 physicians. Nevertheless, other procedures currently removed from scientific guidelines such as obstetric procedures, urologic and gastroenterological procedures in the absence of active infection were also identified as procedures where IE prophylaxis was recommended. Remarkably, body piercing and permanent tattooing were the procedures that raised a significant proportion of doubt among respondents. In 2008, Armstrong *et al*<sup>29</sup> collated all cases of IE related to body art and concluded that transient bacteraemia can arise. Despite the fact that no antibiotic use is currently recommended by European guidelines,<sup>8</sup> education is crucial and in patients with high risk cardiac conditions and native valve disease these procedure should be discouraged.

Still, the epidemiology of infective endocarditis is changing worldwide.<sup>4</sup> Portugal is no exception. Patients hospitalized with IE in the last decade are older, have a higher burden of comorbidities such as arterial hypertension or diabetes *mellitus*, or cancer. There is an increasing proportion of patients with cardiac implantable electronic devices (CIED) or cardiac valve prosthesis.<sup>17</sup> Non-rheumatic valve disease is proportionally two-fold more frequent compared to rheumatic valve disease. Thornhill *et al*<sup>30</sup> also evaluated the impact of previous cardiac conditions on the risk of developing IE. Ultimately, in addition to the already known 'high risk' situations, other 'moderate risk' conditions such as congenital valve anomaly, hypertrophic cardiomyopathy, heart trans-

plant, or left ventricle assist devices had a similar risk as some 'high risk' conditions. Contemporary risk stratification algorithms need to be revisited,<sup>30,31</sup> allowing for a better definition of prevention strategies. This is probably why in our study and in Pharis *et al*<sup>28</sup> a significant proportion of physicians expressed doubts regarding antibiotic use in IE prophylaxis in certain patients, probably for fear of leaving some at risk by not prescribing.

Regarding dental procedures, most respondents in our study considered invasive dental procedures to represent a higher risk of IE when compared with typical daily activities such as eating or brushing teeth. In 1977, Everett *et al*<sup>32</sup> reviewed bacteraemia occurring after several medical procedures and classified them almost always as short lived. However, the rate of post dental extraction bacteraemia was considered high (60% - 90%), which is substantially higher than with brushing teeth or dental flossing. Lockhart *et al*<sup>33</sup> 2008 study and a more recent meta-analysis by Cahill *et al*<sup>26</sup> concluded on the significant incidence of transient bacteraemia after tooth brushing. Still, transient bacteraemia is probably not the suitable surrogate for IE as it is more likely that low levels of bacteraemia occurring in most daily activities and medical procedures are insufficient to cause IE.<sup>34</sup> More robust and high-quality research is required, according to nearly two thirds of our responders.

### Limitations

Firstly, a 19% response rate is considered low, which could partially implicate the impact of the presented results on the overall population of physicians dealing with valvular or congenital patients in Portugal. In fact, according to Abdulaziz K *et al*, physician surveys are characterized by a low response rate which can increase the presence of a nonresponse bias.<sup>19</sup> Nevertheless, higher response rates do not seem to impact the nonresponse bias in physician surveys.<sup>35</sup> The input of other specialities would be valuable to ascertain, namely dentists, family physicians or gastroenterologists and should deserve further analysis. Secondly, no further characterization of the location of the leading clinical activity was requested due to the compelling

requirement to maintain anonymity. This variable may, however, influence individual practice. Still, our study was not aimed at identifying why physicians have different practice patterns.

## CONCLUSION

This survey is an initial effort to understand the practice of IE prophylaxis in Portugal. In this sample, IE prophylaxis is mostly guided by international scientific guidelines, mainly European. Nonetheless, there is some discrepancy regarding identifying high-risk cardiac conditions and procedures among professionals. Therefore, a substantial rate of uncertainty is assumed by most when deciding for certain patients and more scientific evidence is warranted. Interventions to promote continuous physician education should be considered, promoting a practice based on the best available evidence. Further studies should be conducted among other specialties outside of the scope of the Portuguese Society of Cardiology to take the complete national picture of IE prophylaxis practice.

## ACKNOWLEDGEMENTS

The authors thank the Portuguese Society of Cardiology members for having completed the questionnaire. Additionally, the authors thank Nuno Moura, from the Portuguese Society of Cardiology, for all logistic support regarding questionnaire management.

## REFERENCES

- Cahill TJ, Baddour LM, Habib G, Hoen B, Salaun E, Pettersson GB, et al. Challenges in infective endocarditis. *J Am Coll Cardiol*. 2017;69:325–44.
- Bin Abdulhak AA, Baddour LM, Erwin PJ, Hoen B, Chu VH, Mensah GA, et al. Global and regional burden of infective endocarditis, 1990-2010: a systematic review of the literature. *Glob Heart* 2014;9:131–43.
- Murdoch DR, Corey GR, Hoen B, Miro J, Fowler V, Bayer A, et al. Clinical presentation, etiology and outcome of infective endocarditis in the 21st century: the international collaboration on endocarditis-prospective cohort study. *Ann Intern Med*. 2009;169:463–73.
- Habib G, Erba PA, Lung B, Donal E, Cosyns B, Laroche C, et al. Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study. *Eur Heart J*. 2019;40:3222–32.
- Lewis T, Grant R. Observations relating to subacute infective endocarditis. *Heart*. 1923;10:21–77.
- Elliott SD. Bacteriæmia and oral sepsis. *Proc R Soc Med*. 1939;32:747–54.
- Hilson GR. Is chemoprophylaxis necessary? *Proc Roy Soc Med*. 1970;63:267–71.
- Habib G, Lancellotti P, Antunes MJ, Bongiorno MG, Casalta JP, Del Zotti F, et al. 2015 ESC guidelines for the management of infective endocarditis. *Eur Heart J*. 2015;36:3075–128.
- Wilson W, Taubert KA, Gewitz M, Lockhart PB, Baddour LM, Levison M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association. *Circulation*. 2007;116:1736–54.
- Dayer MJ, Chambers JB, Prendergast B, Sandoe JA, Thornhill MH. NICE guidance on antibiotic prophylaxis to prevent infective endocarditis: a survey of clinicians' attitudes. *QJM*. 2013;106:237–43.
- Tarasoutchi F, Montero M, Grinberg M, Barbosa M, Piñeiro D, Sánchez C, et al. Diretriz brasileira de valvopatias - SBC 2011/ I Diretriz interamericana de valvopatias - SIAC 2011. *Arq Bras Cardiol*. 2011;97:1–67.
- Torres F, Renilla A, Florez J, Secades S, Benito E, de la Hera J. Knowledge of infective endocarditis and prophylaxis among Spanish dentists. *Rev Esp Cardiol*. 2012;65:1134–5.
- Cloitre A, Duval X, Hoen B, Alla F. A nationwide survey of French dentists' knowledge and implementation of current guidelines for antibiotic prophylaxis of infective endocarditis in patients with. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2018;125:295–303.
- Khan O, Shafi AM, Timmis A. International guideline changes and the incidence of infective endocarditis: a systematic review. *Open Heart*. 2016;3:e000498.
- Keller K, Bardeleben RS Von, Ostad MA, Hobohm L, Munzel T, Konstantinides S, et al. Temporal trends in the prevalence of infective endocarditis in Germany between 2005 and 2014. *Am J Cardiol*. 2017;119:317–22.
- Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB, Thornhill MH. Incidence of infective endocarditis in England, 2000-13: a secular trend, interrupted time-series analysis. *Lancet*. 2015;385:1219–28.
- Sousa C, Nogueira P, Pinto FJ. Insight into the epidemiology of infective endocarditis in Portugal: a contemporary nationwide study from 2010 to 2018. *BMC Cardiovasc Disord*. 2021;21:138.
- de Sousa C, Ribeiro RM, Pinto FJ. The burden of infective endocarditis in Portugal in the last 30 years – a systematic review of observational studies. *Rev Port Cardiol*. 2021;40:205–17.
- Abdulaziz K, Brehaut J, Taljaard M, Émond M, Sirois MJ, Lee JS, et al. National survey of physicians to determine the effect of unconditional incentives on response rates of physician postal surveys. *BMJ Open*. 2015;5:1–6.
- Baddour LM, Wilson WR, Bayer AS, Fowler VG, Tleyjeh IM, Rybak MJ, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. *Circulation*. 2015;132:1435–86.
- Metcalfe D, Pitkeathley C, Herring J. 'Advice, not orders'? The evolving legal status of clinical guidelines. *J Med Ethics*. 2020;medethics-2020-106592. doi: 10.1136/medethics-2020-106592.
- National Institute for Health and Care Excellence. Prophylaxis against infective endocarditis: antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures. 2008. [cited 2019 May 16]. Available from: <https://www.nice.org.uk/guidance/cg64>.
- Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, et

## AUTHOR CONTRIBUTIONS

CSS: Data analysis, draft and critical review of the manuscript.

AGA, FJP: Data analysis, critical review and approval of the manuscript.

## PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

## DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

## COMPETING INTERESTS

The authors have declared that no competing interests exist.

## FUNDING SOURCES

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

- al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). *Eur Heart J*. 2009;30:2369–413.
24. Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB, Thornhill MH. An increase in the incidence of infective endocarditis in England since 2008: a secular trend interrupted time series analysis. *Lancet*. 2015;385:1219–28.
  25. Van Den Brink FS, Swaans MJ, Hoogendijk MG, Alipour A, Kelder JC, Jaarsma W, et al. Increased incidence of infective endocarditis after the 2009 European Society of Cardiology guideline update: a nationwide study in the Netherlands. *Eur Hear J Qual Care Clin Outcomes*. 2017;3:141–7.
  26. Cahill TJ, Harrison JL, Jewell P, Onakpoya I, Chambers JB, Dayer M, et al. Antibiotic prophylaxis for infective endocarditis: a systematic review and meta-analysis. *Heart*. 2017;103:937–44.
  27. Grattan MJ, Power A, Fruitman DS, Islam S, Mackie AS. The impact of infective endocarditis prophylaxis recommendations on the practices of pediatric and adult congenital cardiologists. *J Cardiol*. 2015;31:1497. e23-8.
  28. Pharis CS, Conway J, Warren AE, Bullock A, MacKie AS. The impact of 2007 infective endocarditis prophylaxis guidelines on the practice of congenital heart disease specialists. *Am Heart J*. 2011;161:123–9.
  29. Armstrong ML, DeBoer S, Cetta F. Infective endocarditis after body art: a review of the literature and concerns. *J Adolesc Health*. 2008;43:217–25.
  30. Thornhill MH, Jones S, Prendergast B, Baddour LM, Chambers JB, Lockhart PB, et al. Quantifying infective endocarditis risk in patients with predisposing cardiac conditions. *Eur Heart J*. 2018;39:586–95.
  31. Sun YP, O'Gara PT. Cardiovascular conditions predisposing to infective endocarditis: time to reconsider the current risk classification system? *Eur Heart J*. 2018;39:596–8.
  32. Everett E, Hirschmann J. Transient bacteremia and endocarditis prophylaxis. a review. *Medicine*. 1977;56:61–77.
  33. Lockhart PB, Brennan MT, Sasser HC, Fox PC, Paster BJ, Bahrani-Mougeot FK. Bacteremia associated with toothbrushing and dental extraction. *Circulation*. 2008;117:3118–25.
  34. Holland TL, Baddour LM, Bayer AS, Hoen B, Miro JM, Fowler VG. Infective endocarditis. *Nat Rev Dis Prim*. 2017;2:1–49.
  35. McFarlane E, Olmsted MG, Murphy J, Hill CA. Nonresponse bias in a mail survey of physicians. *Eval Heal Prof*. 2007;30:170–85.