



Temporal changes in the number of European and American guideline recommendations and underlying evidence base for the management of infective: An update of previous published data

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Abstract This report aimed to examine temporal changes in the number of recommendations on management of infective endocarditis in the European and American guidelines. The number of recommendations has increased since 2004 without an increment in evidence base in the European iteration. American guidelines have reduced the number of recommendations with a main evidence base of level B. (*Am Heart J* 2024;274:115–118.)

Infective endocarditis (IE) is a complex disease with a high morbidity and mortality.¹ European and American guidelines on IE aim to assist clinicians in the management of this complex disease.^{1,2} The European Society of Cardiology (ESC), the American Heart Association (AHA), and the American College of Cardiology (ACC) have since 2004 published four iterations of guidelines for prevention, diagnostic work-up, and treatment of IE.^{2–8} Before the most recent guideline iterations from the ESC and AHA/ACC, our research group reported, in 2017, a substantial increase in the number of guideline recommendations over calendar time. This increment in recommendation was mainly based on level of evidence (LOE) B or C (primarily data from observational studies) with a stable, low number of recommendations based on LOE A.⁹ Identifying the overall evidence base of guidelines is an area of interest in the incorporation phase of guidelines. In 2020 and 2023, new iterations of the European and American guidelines on IE were published and it is of importance for clinicians, guideline committees, and researchers to identify whether this number of recommendations keep rising and if the evidence base has grown stronger.^{1,2}

Methods

As previously published, the number of guideline recommendations for the 2004, 2009, and 2015 ESC and the 2005, 2007, and 2015 AHA/ACC guidelines on the management of IE were computed with the accompanying LOE.⁹ For the purpose of this updated analysis, guidelines from the ESC 2023 and the AHA/ACC 2020 were added to the previous published data and reported separately. Further, the AHA published a scientific statement on IE prevention in 2021¹⁰ and a scientific statement on the prevention, diagnosis, and management of cardiac implantable electronic device (CIED) infections in 2023.¹¹ These scientific statements provide clinical suggested strategies without an accompanying LOE, hence suggestions for these scientific statements were computed and reported but not included in the primary analysis.

In a supplementary analysis, recommendations were stratified according to clinical care (“Treatment and follow-up,” “Diagnosis,” and “Prevention”).

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Results

Class of recommendation

For the ESC guidelines, an increase in total recommendations was observed from 100 in 2015 to 120 recommendations in 2023, **Figure 1**. Further, the figure depicts the increasing number of recommendations since

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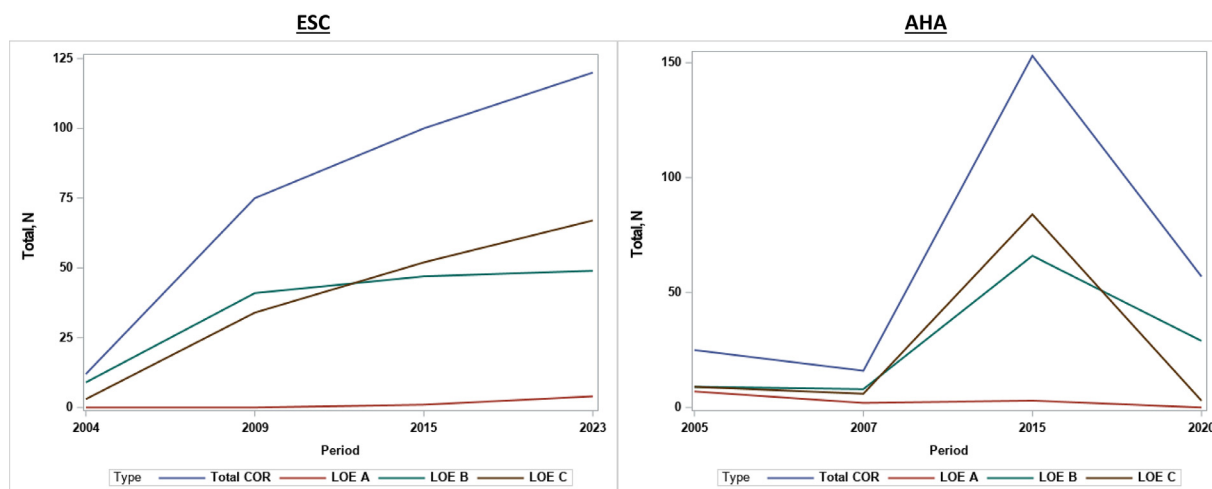
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Figure 1. The figure shows the total number of recommendations (blue curve), recommendations with LOE A (red curve), recommendations with LOE B (green curve), and recommendations with LOE C (brown curve). The left panel shows for the ESC guidelines and the right panel shows for the AHA/ACC guidelines. ESC: European Society of Cardiology, AHA: American Heart Association, IE: infective endocarditis, COR: class of recommendation, LOE: level of evidence.

Temporal changes in the number of guideline recommendations and underlying level of evidence for the ESC and AHA guidelines for the management of IE



2004. A reduction in the American guidelines was identified with 153 recommendations in the 2015 guidelines while 32 recommendations were found in the AHA/ACC 2020 guideline iteration, Figure 1. For the ESC 2023 iteration, 51.7% of recommendations were class I, 43.3% were class II recommendations, and 5.0% were class III recommendations compared with 59.4%, 37.5%, and 3.1% for the AHA/ACC 2020 guidelines, Table. Of the total 120 ESC recommendations, 82 (68.3%) were categorized in “Treatment and follow-up,” 18 (15.0%) within “Diagnosis,” and 20 (16.7%) within “Prevention,” Table. For the 32 recommendations in the AHA/ACC guidelines, 18 (56.3%) were categorized in “Treatment and follow-up,” 14 (43.7%) within “Diagnosis,” and 0 recommendations within “Prevention,” Table. For the suggestive strategies from AHA/ACC on IE prevention and CIED infection, two scientific statements were published without underlying LOE. A total of 25 suggestions were included in these scientific statements stratified by 10 suggestions on “Treatment and follow-up,” 5 suggestions on “Diagnosis,” and 10 suggestions on “Prevention.”

Level of evidence

In the ESC 2023 iteration, 3.3% of recommendations had LOE A, 40.8% had LOE B, and 55.8% had LOE C, Table. The figure shows how the increasing number of recommendations have mainly been carried by LOE C and since 2015 most of the recommendations have been underlined with LOE C. For the AHA/ACC 2020 iteration, 0.0% had a LOE A, 90.6% had LOE B, and 9.4% had LOE

C, Table. The figure illustrates that the AHA/ACC recommendations in 2005 and 2007 were equally supported by LOE B and C. However, leading up to 2015, a significant increase in guideline recommendations occurred, with the majority being underlined with LOE C.

Discussion

This study is a follow-up of previously published data on temporal changes in the number of guideline recommendations from the ESC and AHA/ACC on IE. The current analysis add data from the new guideline iterations on IE from ESC 2023 and AHA/ACC 2020. This study had two main findings, (1) the total number of recommendations have been steadily increasing for the ESC guidelines from 2004-2023. For the AHA/ACC 2020 guidelines, total number of recommendations decreased from 153 in 2015 to 32 in 2020; (2) the recommendations were primarily underscored by LOE B or C with <5% of recommendations carrying LOE A in the ESC and AHA/ACC guidelines.

The purpose of clinical guidelines is to secure optimal, uniform, and safe patient care. For rare, and heterogeneous diseases, such as IE, the LOE is sparse as reported in the previous study from our research group and from updated data presented in this study.⁹ The low evidence base must be considered when guidelines are implemented into clinical practice. One may argue that implementation should be more cautious when the evidence base is low. On the other hand, recommendations are built on the best available evidence including expert con-

sensus, which could be a guidance to secure standardized care. A report by Beval et al. reviewed the 28 guideline documents from the AHA/ACC in 2018 and found that among 3509 recommendations, 47.3% were COR I, 41.8% were COR II, and 10.8% were COR III.¹² The proportion of recommendation underlined by LOE A was 8.9%, while 46.7% was underlined by LOE B, and 44.5% with LOE C.¹² Our report supplements previous findings with a detailed description within the area of IE and in the context of our findings, the area of IE must, in general terms, be considered as an area with low-level evidence.

In our previous report on the evolution of guideline recommendations and the corresponding LOE, we identified similar patterns for the European and American guidelines. However, in the newest iterations we observed notable differences.⁹ While the number of European recommendations continued to rise, there was a substantial decrease in American recommendations. Fewer recommendations could lead to areas within management of IE that become less uniform. Nonetheless, at times “less is more” and fewer recommendations might convey a clearer message, potentially enhancing guideline implementation.

A substantial decrease was identified from 2015 to 2020 for the American guideline recommendations. As the American recommendations on IE were published as part of guidelines for the management of patients with valvular heart disease, detailed IE recommendations may have been reduced in order to ensure a balanced number of recommendations within the subcategories of valvular heart disease. Further, word restrictions within the American guidelines of valvular heart disease could have resulted in a more restricted version of the American IE guidelines, hence European and American guidelines are in this recent iteration dissimilar and comparisons are difficult. However, it must be noted that recommendations on prevention in the American guidelines were reported in separate scientific statements. The scientific statements provide suggestions and not recommendations where the suggestions are neither provided with a categorized strength nor underlying evidence base.

Conclusion

This report adds to previously published data on temporal changes in the number of recommendations and supporting evidence base for the European and American guidelines on the management of IE. The number of recommendations in the European iteration increased from 2015 to 2023 and has been increasing since 2004. Recommendations with LOE C constitutes the main proportion in the European iteration. For American guidelines, the number of recommendations decreased substantially compared with the 2015 guidelines, and the underlying evidence base is mainly based on LOE B. This study adds awareness to the low LOE in the management

of IE which should be kept in mind for the implementation of guideline recommendations.

Conflict of interest

Lauge Østergaard: Independent research grant from the Novo Nordisk Foundation for the research of mitral valve regurgitation. Lars Køber: Speakers honorarium from Novo, Novartis, AstraZeneca, Boehringer and Bayer. Emil Loldrup Fosbøl: Novo Nordisk Foundation and the Danish Heart Association: Independent research grant related to valvular heart disease and endocarditis. Sofie Truong, Eva Havers-Borgersen and Jeppe Petersen: None.

CRedit authorship contribution statement

Lauge Østergaard: Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Sofie Truong:** Writing – review & editing, Validation, Project administration, Methodology, Data curation. **Jeppe Petersen:** Writing – review & editing, Methodology, Investigation. **Eva Havers-Borgersen:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Lars Køber:** Writing – review & editing, Supervision, Methodology, Investigation, Conceptualization. **Emil Loldrup Fosbøl:** Writing – original draft, Supervision, Methodology, Investigation, Conceptualization.

References

1. Delgado V, Ajmone Marsan N, de Waha S, et al. 2023 ESC guidelines for the management of endocarditis. *Eur Heart J* 2023;44:3948–4042.
2. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. *Circulation* 2021;143:e35–71. doi:10.1161/CIR.0000000000000923.
3. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America. *Circulation* 2005;111:e394–434. doi:10.1161/CIRCULATIONAHA.105.165564.
4. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2007;116:1736–54.

5. Baddour LM, Wilson WR, Bayer AS, 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.
6. Habib G, Lancellotti P, Antunes MJ, et al. 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;36:3075–128.
7. Horstkotte D. Guidelines on prevention, diagnosis and treatment of infective endocarditis executive summary the task force on infective endocarditis of the European Society of Cardiology. *Eur Heart J* 2004;25:267–76.
8. Habib G, Hoen B, et al. Endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and by the International Society of Chemotherapy (ISC) for Infection and Cancer, Authors/Task Force Members. 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.
9. Østergaard L, Valeur N, Bundgaard H, et al. Temporal changes in infective endocarditis guidelines during the last 12 years: high-level evidence needed. *Am Heart J* 2017;193:70–5.
10. Wilson WR, Gewitz M, Lockhart PB, et al. Prevention of viridans group streptococcal infective endocarditis: a scientific statement from the American Heart Association. *Circulation* 2021;143:e963–78. doi:10.1161/CIR.0000000000000969.
11. Baddour LM, Esquer Garrigos Z, Rizwan Sohail M, et al. Update on cardiovascular implantable electronic device infections and their prevention, diagnosis, and management: a scientific statement from the American Heart Association: Endorsed by the International Society for Cardiovascular Infectious Diseases. *Circulation* 2024;149:e201–16. doi:10.1161/CIR.0000000000001187.
12. Bevan GH, Kalra A, Josephson RA, Al-Kindi SG. Level of scientific evidence underlying the current American College of Cardiology/American Heart Association clinical practice guidelines. *Circ Cardiovasc Qual Outcomes* 2019;12:e005293.