

Levels of evidence in the European Society of Cardiology Guidelines: Gaps in knowledge?

Massimo F Piepoli^{1,2} and Claudio Ceconi³

European Journal of Preventive Cardiology
2019, Vol. 26(18) 1941–1943
© The European Society of Cardiology 2019
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2047487319869414
journals.sagepub.com/home/cpr



In the present issue, the paper from van Dijk and colleagues is published without changes after the usual peer reviewing process and it truly reflects the opinions of the authors as they were independently expressed. This editorial choice is not due only to the indisputable interest of the concepts expressed,¹ but also to the decision to publish ideas originated in the Cardiologists Community that we hope will generate further contributions, responses and letters. The paper is contributing to the important debate on the recommendations and their levels of evidences reported by the European Guidelines, developed under the umbrella of the European Society of Cardiology (ESC).

There is no doubt that Guidelines preparation and update constitutes one of the pillars of the ESC, and groups of experts in the field from across Europe are commissioned to write and review documents according to a structured process that extends over a two-year period. This process finally involves around 100 experts and influences the care provided to millions of people worldwide.²

In recent years guidelines from both sides of the Atlantic^{3,4} have increasingly been criticized for the limited amount of evidence underlying many of their recommendations. Multiple systematic analyses have shown that a limited number (<15%) of the recommendations in European and American cardiovascular guidelines are supported by evidence from multiple randomized controlled trials (RCTs) and meta-analyses.

Although very relevant, the meaning of these findings can remain largely unclear as they lacked a detailed breakdown to where (e.g. therapeutic versus diagnostic recommendations) the suggested lack of evidence is most problematic, unexpected, or potentially solvable.

To know which paucities in the evidence base are problematic and where to focus improvement efforts to them, it is necessary to identify areas of recommendations not supported by high-quality evidence and identify the underlying reasons. To reveal where gaps exist in the current cardiovascular evidence base, and allow better interpretation of the evidence underlying recommendations, van Dijk and colleagues performed a really

valuable work trying to identify which types of recommendations (e.g. therapeutic or diagnostic) and which recommended actions (e.g. pharmaceutical intervention or non-invasive imaging) are supported by which level of evidence (LoE) in the Guidelines of the ESC.

They observed that with a median of 128 recommendations per guideline, most recommendations were of class I (47.7%), followed by class II (44.7%) and only 7.6% class III. However, only 14.1% of the recommendations are supported by multiple RCTs or meta-analysis (LoE A). Moreover the evidence levels supporting recommendations vary widely per:

1. *Type*. Recommendations on diagnostic topics were supported by lower levels than recommendations on therapeutic topics.
2. *Recommended action*. Recommendations on open surgical interventions were less supported by RCTs than were pharmaceutical and minimal-invasive interventions.
3. *Sub-specialty*. Recommendations on the sub-specialty of General Cardiology showed substantially lower levels of evidence than, for instance, the sub-specialty of Coronary Artery Disease.

Ten years ago, Tricoci et al.³ already reported similar findings for the American College of Cardiology/American Heart Association guidelines, confirmed more recently by Fonaroff et al.⁴ They identified several shortcomings in the organization of clinical research and guideline development process as possible explanations for this shortage in recommendations supported

¹Heart Failure Unit, Cardiology, Guglielmo da Saliceto Hospital, Piacenza, Italy

²Institute of Life Sciences, Sant'Anna School of Advanced Studies, Pisa, Italy

³U.O. Cardiologia, ASST Garda, Desenzano del Garda, Italy

Corresponding author:

Massimo F Piepoli, Heart Failure Unit, G da Saliceto Polichirurgico Hospital, Cantone del Cristo Piacenza, Emilia Romagna 29100, Italy.
Email: m.piepoli@gmail.com

by high-quality evidence. These shortcomings included fragmentation of the research enterprise (a lack in common goals, vision and collaboration), missing incentives to fill evidence gaps and potential conflicts of interests.

On the other side, RCTs are usually confined to patients of specific ages with single conditions. There will never be enough time, effort or funding to implement RCTs to address all clinical scenarios that confront physicians. Individual patients are unique and many differ from those enrolled in the RCTs on which the guidelines are based, but consistent deviation should be explained. Elderly individuals with multiple comorbid conditions, who constitute an increasing number of patients seen in clinical practice, are excluded from most RCTs.⁵ This results in the common need to extrapolate guideline recommendations built on ideal patients to the real patients seen in practice, which has elevated cardiovascular registries to a higher level of prominence. Despite the imperfections of registry data, which are often derived from administrative information embedded in electronic health records and have the potential for confounding inherent in non-randomized databases, registries have the potential to confirm results of RCTs or to extend them to individuals with more complex, comorbid conditions.

It is unlikely that there will ever be RCTs confirming that a routine blood sample should be performed as soon as possible in the suspicion of acute coronary syndrome (LoE C), or that a haemoglobin and white blood cell blood test and electrocardiogram should be performed in patients with symptoms of heart failure (LoE C), or that a multidisciplinary team is beneficial when making management decisions for patients with complex coronary artery disease or valvular heart disease (LoE C), or that *parachutes can reduce the risk of injury* (Figure 1). The primacy of these recommendations ensures that guidelines remain patient-centric and do not evolve to a just-the-facts recitation of data distilled from RCTs of tests, treatments and devices.

It should be understood that guidelines are not rules but are what the word implies – guides. Guidelines provide advice to practising physicians, clarify contemporary areas of consensus, but also of disagreement, improve standards and guide clinical decision-making for routine clinical practice. In all the preambles of ESC Guidelines it is pointed out that they have been developed to support healthcare professionals and cannot substitute for individual care and expertise. Health professionals are encouraged to take the Guidelines fully into account when exercising their clinical judgement, as well as in the determination and the implementation of preventive, diagnostic or therapeutic medical strategies. However, the Guidelines do not override in any way whatsoever the individual responsibility of health

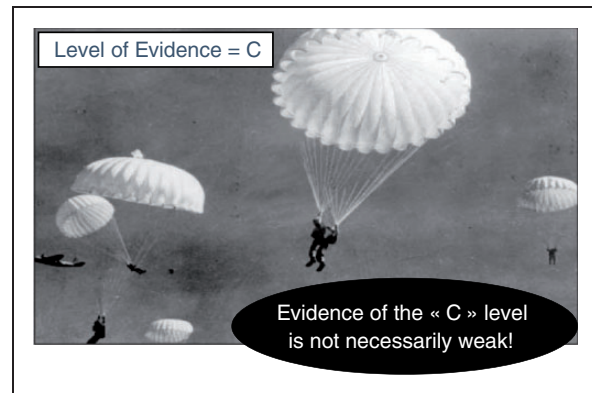


Figure 1. Example of Level of C recommendation. Parachutes appear to reduce the risk of injury but their effectiveness has not been proved with randomised controlled trials.

professionals to make appropriate and accurate decisions in consideration of each patient's health condition and in consultation with that patient and the patient's caregiver where appropriate and/or necessary.

So the paper from van Dijk and colleagues is very much appreciated and provides crucial points of discussion to a very important topic.

A final point: the authors criticize the current Preventive Guidelines⁶ on the included topics on population-based intervention because the related recommendations do not provide therapeutic procedures, in their opinion. But these guidelines for the first time provide tools for healthcare professionals to promote population-based strategies in all settings, with the aim to integrate these into national or regional prevention frameworks and to translate these in locally delivered healthcare services, in line with the recommendations of the World Health Organization global status report on non-communicable diseases.

All these aspects are indeed open for a discussion that will certainly contribute to awareness in cardiologists on the basis of their best clinical practice.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. van Dijk VB, Grobbee DE, de Vries MC, Groenwold RHH, van der Graaf R, Schuit, E. A Systematic Breakdown of the Levels of Evidence 1 Supporting the European Society of Cardiology Guidelines. *Eur J Prev Cardiol* 2019; 26: 1944–1952.

2. Vaucher J, Marques-Vidal P, Waeber G, et al. Population impact of the 2017 ACC/AHA guidelines compared with the 2013 ESH/ESC guidelines for hypertension management. *Eur J Prev Cardiol* 2018; 25: 1111–1113.
3. Tricoci P, Allen JM, Kramer JM, et al. Scientific evidence underlying the ACC/AHA clinical practice guidelines. *JAMA* 2009; 301: 831–841.
4. Fanaroff AC, Califf RM, Windecker S, et al. Levels of evidence supporting American College of Cardiology/American Heart Association and European Society of Cardiology Guidelines, 2008–2018. *JAMA* 2019; 321: 1069–1080.
5. Vigorito C, Abreu A, Ambrosetti M, et al. Frailty and cardiac rehabilitation: A call to action from the EAPC cardiac rehabilitation section. *Eur J Prev Cardiol* 2017; 24: 577–590.
6. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts): Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur J Prev Cardiol* 2016; 23: NP1–NP96.