

## Disparity Between Best Scientific Evidence and Cardiovascular Events

### To the Editor,

We read with great interest the article recently published in your journal about the impact of the type of hospital in the management of patients with non-ST segment elevation acute coronary syndrome (NSTEMI-ACS)<sup>1</sup> and your detailed discussion in an accompanying editorial.<sup>2</sup> The register is simple and elegant, well designed, and reports that NSTEMI-ACS patients admitted to hospitals with available hemodynamics are best served according to clinical practice guidelines, both in the use of diagnostic procedures (coronary angiography) as well as treatment (coronary revascularization and the use of drugs). However a reduction in cardiovascular mortality is not achieved.

We believe that it addresses one of the cornerstones of our health care system: equity in access to health care as defined in the General Health Law. It also analyzes a controversial issue in the literature, which is the barriers to translating efficiency into effectiveness.<sup>3</sup>

We agree with the reasons given in the editorial<sup>2</sup> that explain this, but we would like to emphasize two aspects that are not discussed: one of a methodological nature about the gold standard of clinical practice guidelines and a circumstantial aspect regarding available scientific evidence.

The gold standard of good clinical practice described in various studies such as this is defined as the percentage of use of the diagnostic procedures or therapies considered in the clinical practice guidelines as grade I recommendations or, at most, grade IIa. Perhaps the difficulty in translating the differences in management of patients with NSTEMI-ACS to cardiovascular events is that we use the *wrong gold standard*. Although the conduct of clinical practice guidelines follows strict methodological control, not all scientific questions of our daily practice are determined in clinical trials. In many cases the degree of recommendation is based on the opinions of experts on the guidelines and may not always correspond to the best available evidence, due to the difficulties found in the methodology of the clinical trials. The majority of these seek to demonstrate the benefit of drugs since a high percentage are sponsored by the industry that obviously hopes to achieve benefits from their own research. For example, the benefit of the use of IIb/IIIa receptor antagonists and of early coronary revascularisation overlap in many clinical trials (this is done on an average of 4 days in many of these) and it is not known if the benefit in high risk patients is due to

drug therapy or revascularisation, or how early it should be done – 24 hours? 48 hours? Or perhaps the use of glycoprotein IIb/IIIa inhibitors has no benefits if revascularization is performed in 24/48 hours. Another example would be the indications I/IIa for therapeutic approaches that do not translate into clinical events but mainly into angiographic events (permeability of the responsible artery). This is the case with clopidogrel as adjunct therapy to coronary syndrome with ST elevation. Obviously the analysis of this therapeutic approach does not necessarily result in clinical events although it is a class I indication.

Among the latter reasons that could explain this “alleged” disparity between the use of the best evidence and the translation of this knowledge into results for cardiovascular events is the apparent publication bias found in major biomedical journals, which are the knowledge base for subsequent implementation of guidelines. It is much easier to publish a substudy, even one not planned a priori, of a great clinical trial in a leading journal than studies analysing clinical practice or studies with negative results<sup>4,5</sup> that to try to explain this disparity.

In summary, translating our best scientific understanding to the patients should be the focus of our daily work under the premise of equity, and studies such as Ruiz Nodar<sup>1</sup>'s one help to do this.

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## Response

### To the Editor,

Dr Jiménez-Navarro et al propose additional reasons for why Dr Ruiz Nodar's study found that guideline adherence was not associated with improvement in clinical outcomes. The authors raise two interesting issues: *a)* the use of adherence to clinical practice guidelines as a “gold standard” for good practice; and *b)* publication bias in existing available evidence.

The authors correctly highlight that guidelines are based on varying levels of evidence. In fact, the majority of recommendations are not based on adequate randomized trial data.<sup>1</sup> Professional organizations such as the American College of Cardiology and the American Heart Association have recognized this inadequacy and have made great efforts to provide timely updates to practice guidelines as the evidence base changes<sup>2</sup>. Other alliances including the World Health Organization and the European Society of Thoracic Surgeons, have adopted a new grading system that more accurately reflects the evidence behind the guidelines (<http://gradeworkinggroup.org>). Concurrently, investigators globally are implementing clinical studies to address the void in existing knowledge ([clinicaltrials.gov](http://clinicaltrials.gov)).

As suggested, adherence to guidelines as a benchmark of good clinical care is an imperfect paradigm. Nevertheless, guideline-based therapy is in the best interest of our patients. In an analysis of acute coronary syndrome (ACS) patients, we found that the composite adherence guideline rate was significantly associated with lower in-hospital mortality.<sup>3</sup> Variation in practice existed even for therapies such as beta-blockers, whose role in ACS is generally well-established.<sup>3</sup> Therefore, we believe that the data support guideline-based process measures as a means of assessing quality of care. We agree that publication bias is a significant problem. We advocate holding ourselves to the highest ethical standards, allowing for dissemination of all scientifically sound evidence—whether positive or negative.

However imperfect, evidence-based therapy is still associated with improved clinical outcomes. Our obligation is to provide the highest standard of care possible. As the guideline evidence evolves, so should the standards that we hold ourselves to.

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