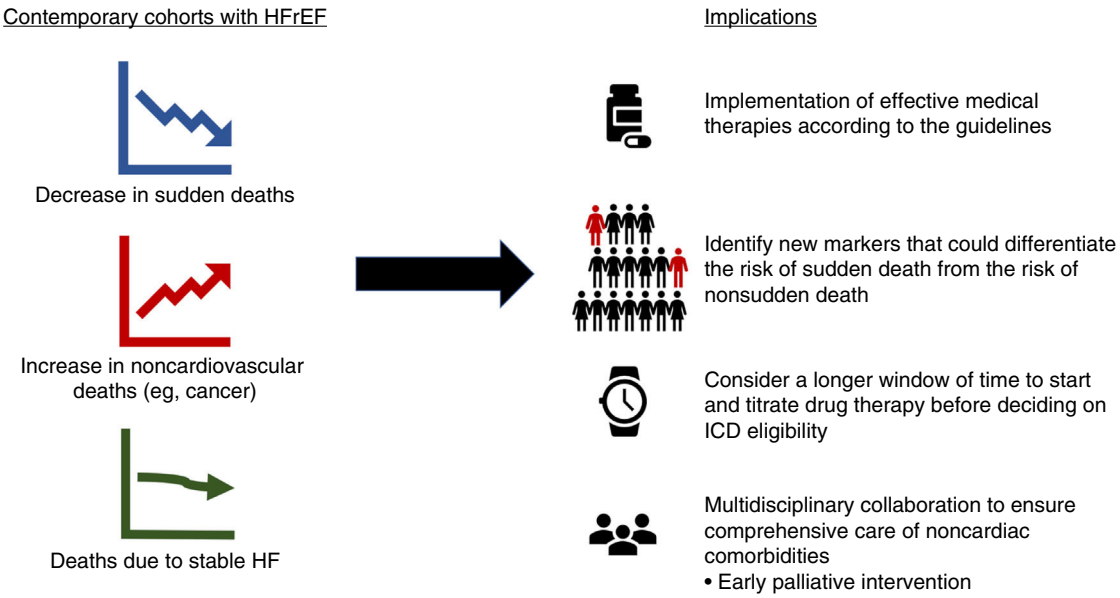

Figure 2. Implications of changes in the cause of death (reproduced and modified with permission from Patel et al.[4]). HF, heart failure; HFrEF, HF with reduced left ventricular ejection fraction; ICD, implantable cardioverter defibrillator.

valsartan (2016), which were only included in the European HF Guidelines after REDINSCOR-I was completed and which improve the prognosis of HFrEF.

Based on our experience, changes in the cause of death among contemporary patients with HFrEF could suggest the need for changes in the treatment of this condition (figure 2).[4]

Pedro Moliner[a,b] and Josep Lupón[c,d,e,*]

[a]*Unidad Multidisciplinaria de Insuficiencia Cardiaca Comunitaria, Servicio de Cardiología, Hospital Universitario de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain*
[b]*Programa de Enfermedades Cardiovasculares, Instituto de Investigación Biomédica de Bellvitge (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Spain*
[c]*Unidad de Insuficiencia Cardiaca, Servicio de Cardiología, Hospital Universitario Germans Trias i Pujol, Badalona, Barcelona, Spain*
[d]*Departament de Medicina, Universitat Autònoma de Barcelona, Barcelona, Spain*
[e]*Instituto de Salud Carlos III, CIBERCV, Madrid, Spain*

*Corresponding author:
E-mail address: jlupon.germanstrias@gencat.cat (J. Lupón).

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Tendencies in cause of death in patients with chronic heart failure and depressed systolic function. Response

Evolución de las causas de muerte de pacientes con insuficiencia cardiaca crónica y función sistólica reducida. Respuesta

To the Editor,

We congratulate and thank the authors for their letter, which reaffirms and complements our findings, highlighting the relevance of noncardiovascular mortality in the long-term in patients with heart failure (HF).[1] All the patients in our study[1] had a left ventricular ejection fraction < 40%; it has been demonstrated that, at this value, treatment affects disease prognosis, compared with 50% in the study by Moliner et al.[2] This feature, along with the more advanced functional class in our population, would have predisposed to a greater risk of death directly related to HF in the short- and mid-term. In our study, all patients were followed up for 4 years, allowing us to draw clear conclusions on mortality during this period. In the study by Moliner et al., the median follow-up was 4.2 years, which appeared similar but was actually highly variable, with quartiles of 1.9 years and 7.8 years, because the authors included patients throughout the study period (2002-2018), the same period in which the causes of death were studied. Therefore, the patients included in the earlier years and with a

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longer follow-up time (> 4 years) can be considered HF survivors, who are more vulnerable to death from other causes in the long-term. This would explain the sharp increase in noncardiovascular mortality observed in the last 3 years: up to two thirds of deaths in 2018.[2] Therefore, there is a bias due to the longer follow-up of HF survivors. However, both studies concur in finding a lower sudden death rate attributable to improvements in treatment, which reaffirms the importance of treatment adherence. They are also complementary, as the study by Moliner et al.[2] allows us to see what would happen to patients in our study who survived beyond this 4-year period. Current treatments have mainly reduced the risk of sudden death and delayed death due to HF, which, if avoided, means that other forms of noncardiovascular death predominate at long-term follow-up. Whether it is simply a question of time or whether there is a correlation between diseases such as HF and cancer remains an open question.

Domingo A. Pascual Figal[a,b,c,*] and David Fernández-Vázquez[a]

[a]*Servicio de Cardiología, Hospital Clínico Universitario Virgen de la Arrixaca, Universidad de Murcia, IMIB-Arrixaca, El Palmar, Murcia, Spain*

[b]*Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain*

[c]*Centro Nacional de Investigaciones Cardiovasculares, Madrid, Spain*

[*] Corresponding author:
E-mail address: dpascual@um.es (D.A. Pascual Figal).

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The sample size myth

El mito del tamaño de la muestra

To the Editor,

Quite often, a researcher will send a project to a committee to apply for funding or an article to a journal for review and will receive as a response the objection that the sample size is not scientifically justified and that it may not be sufficient for the study objective. After correcting this point in their proposal or manuscript, adding one or two sentences, the funding or publication is approved.

In some cases, this is a logical and necessary process, in which the judges detect that something is missing and the author rectifies it appropriately. But in many cases, it is a completely illogical process,[1,2] in which both parties do not know the subject they are discussing but rather feign knowledge and accept the use of sentences that do not make sense.

Indeed, few subjects in the field of research methodology are so poorly understood as the minimum sample size needed for a study.[3] Many authors and reviewers assume that statistics can provide formulas that give the "right" sample size for each investigation and the reviewers ask the authors to "rigorously" justify the sample size used.

Many authors do not understand the use of formulas related to this question and, feeling obliged to say that they have used them to determine the sample size, resort to copying sentences from other projects. Since they do not understand what these sentences are saying, they often make transcription errors that make them unintelligible. Then, later on, other authors may use these as models to copy, each adding more errors that end up turning the sentence into a jumble of words that makes absolutely no sense. This comes full circle when these paragraphs are read by certain reviewers who also do not understand the subject, but who, seeing these technical terms related to it, assume that they provide a "rigorous" justification of the sample size and accept them.

This widespread attitude is a frontal attack on logic (it violates the most basic principles of common sense), on ethics (everyone is "faking it") and on style. The worst (and most striking) part of this ritual of confusion is that it does not benefit anyone and harms everyone. Nobody wins with this chain of absurd nonsense and everybody loses time, energy and dignity. Unfortunately, many biostatistics professors contribute, in their classes and books, to these continued misunderstandings.

Not all reviewers and evaluators take part in this nonsense, but many do. Experts in biostatistics should not look the other way and let this unfortunate situation be perpetuated indefinitely. Solutions are needed. We must support initiatives to make things easier and accurate, working together to put an end to this wrongdoing, which is, incidentally, endemic in all countries that conduct medical research.

Breaking this chain of nonsense does not require researchers to have a master's in biostatistics. An unrushed read of an article that explains the subject clearly[4,5] would be enough for a doctor to get out of this circuitous, fruitless maze, showing them the limitations inherent to applying these formulas and enabling them to understand in which situations they should use them and how.

We hope that sooner rather than later, scientific journals, universities and medical societies will decide to join forces for the benefit of everyone. Many thousands of doctors doing research would appreciate it enormously.

CONFLICTS OF INTEREST

The authors of this Letter to the Editor have no conflicts of interest to declare.

José Abellán-Huerta[a,*] and Luis Prieto-Valiente[b]

[a]*Servicio de Cardiología, Hospital General Universitario de Ciudad Real, Ciudad Real, Spain*

[b]*Bioestadística Médica y Metodología de la Investigación, Análisis Estadístico y Big Data, Universidad Católica de Murcia, Murcia, Spain*