



Letter to the Editor

Decay in mortality rates among landmark cardiovascular trials



Michael Winerger*

Cooperative Studies Program, Department of Veterans Affairs, West Haven, CT, USA
 Department of Biostatistics, Yale School of Public Health, New Haven, CT, USA

ARTICLE INFO

Article history:

Received 20 March 2019

Accepted 28 March 2019

Keywords:

Clinical trials

CRT

DANISH

Mortality

I read with great enthusiasm the editorial by Strik et al. [1], and its companion article by Döring et al. [2] Strik's Fig. 1 shows mortality trends in control groups from seven major clinical trials over time, as a bar plot, with fit-function overlaid. The function is not described numerically, but it would seem that the overlay is fitted to the studies congruously with their depiction, which gives the impression that they occur incrementally in time. Fitting a curve to these data, one gets an exponential decay function of $m(s) = e^{2.9 - 0.171s}$, i.e. mortality, m , as a function of study, s , where each study increments by one unit after MADIT. The decay constant is 0.171, which corresponds to a "half-life" of $\ln(2) \div 0.171 = 4$ studies, i.e. the

rate of death among patients on standard therapy for heart failure decreases by 50% in the timespan of four major clinical trials. This is not especially interpretable, especially given that the interval between studies varies.

Re-plotting the data by year would have been a more suited illustration. The fitted equation would then be $m(y) = e^{2.8 - 0.058y}$: mortality among these trials having a $\ln(2) \div 0.058 = 12$ years. Notwithstanding Strik's very worthy argument regarding CRT as standard therapy, there will be some who should like to know the decay rate among studies where CRT was not considered standard care; the curve fitted without DANISH is $m(y) = e^{2.7 - 0.044y}$, i.e. half-life of 16 years.

Strik et al. should be applauded for their righteous focus on the trends in mortality over time, and others planning clinical trials are smartly advised to consider the impact on mortality of advancements in standard therapy, and for that matter: what constitutes standard therapy.

References

- [1] M. Strik, K. Vernooy, F.W. Prinzen, Too old to shock? *Int. J. Cardiol.* 263 (2018) 65–66.
- [2] M. Döring, M. Ebert, N. Dages, A. Müssigbrodt, K. Bode, H. Knopp, M. Kühl, G. Hindricks, S. Richter, Cardiac resynchronization therapy in the ageing population – with or without an implantable defibrillator? *Int. J. Cardiol.* 263 (2018) 48–53.

* VA Connecticut Healthcare System, Cooperative Studies Program (151A), West Haven, CT 06516, USA.

E-mail address: michael.winerger@va.gov.