Additional commentary on deception in statin research

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We thank Dr. Ferenci for having an interest in our work, but he appears to have misunderstood our primary point. According to Dr. Ferenci, we were "methodologically wrong" when we stated that absolute risk reduction (ARR) should be used "instead of" relative risk reduction (RRR). However, we did not make that statement in our paper. We called for a balanced presentation of ARR with RRR, which is more appropriate than presenting the RRR alone. The reason why we accused the authors of statin trials and their sponsors of statistical deception is because they present their findings in publication abstracts, to the media, in advertisements and in reviews exclusively with the RRR format. The basis for this statistical ploy is that it is far more impressive to present a 36% RRR, as in the Lipitor trial, rather than a 1% ARR, which is the arithmetic difference in the rate of coronary events between the statin-treated and placebo groups.

We are not alone in our critique as numerous experts in the field of epidemiology and statistics have deplored this form of data presentation.[1–7] For example, Vine and Hastings [5] asserted that the routine presentation of RRR, without ARR, "exaggerates the apparent clinical importance of the data." As pointed out by Smith,[2] the relative risk concept "is meaningless because it has no mathematical connection to reality. The only conceivable reason for using it is to exaggerate trivial relationships." Perhaps the strongest condemnation of the reporting of RRR without ARR was by Gigerenzer et al.,[7] who stated that investigators that presented only RRR in their clinical data presentations committed the "first 'sin' against transparent reporting." The deception in presenting only the RRR in statin trials led Thompson and Temple [6] to conclude that "The small differences favouring the drug have been magnified … by the use of relative differences between statins and placebo groups, rather than absolute differences. … We argue that the latter is a much more honest version of the clinical reality."

Despite the widespread criticism of the strategy to present only the RRR, trial directors and their sponsors have continued to mislead the public and the scientific community with the exclusive use of the RRR in reporting statin trial findings. A representative example of a publication committing Gigerenzer's "first sin" is the assessment of the JUPITER trial effects by W.C. Roberts, Editor in Chief of *The American Journal of Cardiology* and Baylor University Medical Center Proceedings.[8] In discussing the JUPITER outcomes, Dr. Roberts used the RRR data format exclusively in stating: "The combined primary endpoint of myocardial infarction, stroke, arterial revascularization, hospitalization for unstable angina pectoris, or death from cardiovascular causes was reduced by 41%, including a 48% reduction in stroke and a 20% reduction in death from any cause. These are spectacular results … ". The fact is however, that the ARR effects in JUPITER were only about a 1 percentage point difference between the placebo and treated groups.

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Table 1. Comparison of the incidence of coronary heart disease mortality, fatal myocardial infarction (MI) and breast cancer in the CARE study expressed as the raw data (%), ARR and RRR.

		Treatment group	Placebo group
Coronary heart disease mortality	n	96/2081	119/2078
	%	4.6	5.7
	ARR; %	−1.1	
	RRR; %	−19	
Fatal MI	n	24/2081	38/2078
	%	1.2	1.8
	ARR; %	−0.6	
	RRR; %	−33	
Breast cancer	n	12/291	1/291
	%	4.1	0.3
	ARR; %	+3.8	
	RRR; %	+1267	

The flaw in data presentation associated with the exclusive use of RRR is illustrated with outcomes of the 5-year long secondary-preventive pravastatin-trial CARE.[9] In this study the ARR for coronary heart disease deaths and fatal myocardial infarction was 1.1% and 0.6%, respectively. These data expressed as the RRR were transformed into a more impressive reduction in death rate to 19% and 33%, respectively. It is also notable that there was a statistically significant difference in the incidence of cancer reported in the study ($p = 0.002$); 12 women in the statin-treated group and only one woman in the control group developed breast cancer. The authors of the study did not present the ARR or RRR for cancer incidence, but it is notable that the difference in breast cancer rate between the two groups resulted in an absolute risk *increase* in cancer with statin treatment of 3.8%, which corresponds to a *relative risk increase* of +1267% (Table 1). This vast amplification in the appearance of a great risk of cancer with statin treatment with relative risk analysis illustrates the flaw in presenting the RRR alone. But just as we consider it inappropriate to use beneficial RRR data to claim that "statins are the best life insurance against atherosclerotic events",[8] we also consider it inappropriate to claim that statins cause a 1267% increase in cancer, despite the fact that the statement is statistically valid.

Finally, Dr. Ferenci is correct that RRR is constant if the benefit is the same after many years of treatment, but we have no evidence that this is the case with statins. Moreover, Dr. Ferenci chose to ignore the issue of side effects in his calculations. We advocate that the appropriate way to present clinical trial results is to give the ARR, RRR and the length of the trial together, with benefits and side effect data handled in the same manner. In the case of statins, readers will have a better perspective on how their adverse effects offset their benefits.

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