

Review of: "Risk of death derived from Hazard Ratio should not be communicated as Relative Risk reductions for death in cancer clinical trials. Intentional or inadvertent?"

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Potential competing interests: No potential competing interests to declare.

I read with interest and really appreciated this review.

The text is quite clear and exhaustive, the results are critically discussed, the Tables properly show the data and the Figures explain graphically the concepts.

I would suggest only some adjustments:

- The Author could focus only on the 4 trials (GOG179, GOG240, Keynote-826 and EMPOWER) he analysed in detail, and summarize the other ones.
- Pag. 10 It is quite complex to read the results of Keynote-826. Maybe a Table can summarize the data.
- Pag. 17 line 12 Results from the above randomized trials are shown in...It is not specified where one can read the results.
- Figure 4 (pag.21) could be explained in more detail.

The first message of the Author is to shed light on potential statistical mistakes in interpreting the results of clinical studies. The difference among HR, RR and AR is explained very accurately and in detail.

The misinterpretation and misreporting of hazard ratios as relative risks is an important problem. This mistake is frequent in oncology, and other areas of medicine and can lead to wrong conclusions on the effectiveness of certain drugs.

As a consequence of these false conclusions the scientific community could be induced to choose low-effective but very expensive therapies even when they are marginally superior than the standard treatments. The picture could be quite different if new therapies were compared with low-cost alternatives. We could have a value-oriented system for pricing medicines both in oncology and in other areas of clinical medicine. This is the second message of the Author.

He highlights that the high prices of novel cancer drugs could result in a big economic problem for the Health System in many Countries.

"The prices of new oncology drugs, determined by the pharmaceutical industries, are growing much faster than the benefits they offer. Prices even rise when competitors appear, when the size of the market expands, when drugs work less than hoped. Many new oncology medicines do not reflect the value they have for doctors and patients", affirmed Prof. Peter B. Bach, Director of the Center of Health Policy and Outcomes at Memorial Sloan Kettering Cancer Center, New

York, USA.

The real problem, according to the Author, is to communicate to the medical community, to the patients and to the public the results of the clinical trials, not confusing RRR with HRR. The title of the manuscript is paradigmatic: the wrong communication is intentional or inadvertent?

In conclusion, I would definitely recommend this paper to any medical oncologist interested in clinical trial appraisal.