



Violations of protocols of non-inferiority trials occur frequently

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To the Editor:

I read with great interest the non-inferiority study comparing two different durations of fasting on gastric volume in children [1] and the Editorial accompanying it [2]. I greatly respect and agree with the Editorial and would like to add a few points.

The Editorial states “Misuse and misinterpretation of the study designs are frequently observed” [1]. This was stated based on a referenced article published in 2008. Unfortunately, the situation is no different or rather worse presently. The violations of protocols specified for a non-inferiority trial do happen very often nowadays right from the design to publication. As mentioned in the Editorial, “the power, significance level, and non-inferiority margin are important components for sample size calculation and should be determined during the trial’s design and planning phases” [2]. However, these details were not mentioned in the trial registry of the current study [1]. Indeed, it was not designed as a “non-inferiority study” at the point of trial registration.

Cho et al. [1] calculated the non-inferiority margin based on a study by Spencer et al. [3]. Ideally, it should be calculated based on a published superiority trial comparing the established (standard) intervention [4]. However, Spencer et al. only observed the relation between “the sonographic antral area and endoscopically suctioned gastric volumes” [3], and no comparison of different fasting state was done. Thus it is not an ideal study for calculating the non-inferiority margin. Instead, the study by Song et al. that compared the gastric volume in two different states of fasting

in children [5] could have been used for this purpose. Notably, that study [5] was cited by Cho et al. [1]. In addition, the mean difference and standard deviation were calculated in the current study [1] based on a previous study that included adult patients and not children.

Lastly, the title of a noninferiority trial should mention the two interventions (new/experimental versus the standard/reference/active control) followed by “non-inferiority trial/study” [4]. Although the term “active control” is an alternative for the standard or reference intervention, it is better to avoid the term “controlled” in the title as it can confuse a “placebo”.

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Declarations

Conflicts of interest RMS-has no conflict of interest.

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