LETTER TO THE EDITOR

Response to Letter to the Editor: Deep waters of science

Dear Editor,

We read with great delight the letter of Prof. Malik on our work on Total-cosine-R-to-T (TCRT) as a predictor of mortality; published last year in the Journal (Tse, Gong, Wong, Chan et al., 2017). There are several important aspects of his letter that we would like to highlight and offer our perspectives.

First of all, some of his comments have surprised us as they reflect a poor understanding of the principles and procedures of conducting a systematic review and meta-analysis, which involves search of the literature, qualitative synthesis, and interpretation with appropriate statistical analysis (Egger & Smith, 1997; Naylor, 1997). The first paragraph of Prof. Malik's letter concerns his own significant contributions to this field that are extensively acknowledged by our group, through citation of most of his relevant papers. Even more, we sent Prof. Malik an email dated 21th November 2016, kindly asking him to provide us the risk ratio for $T_{peak} - T_{end}$ (Smetana et al., 2011). In the same email, we invited Prof. Malik to join our article. However, we did not receive a response from him.

Regarding the inclusion of the three papers from St George's Hospital (Batchvarov et al., 2003; Hnatkova et al., 2001; Malik, Hnatkova, & Batchvarov, 2004), our original manuscript included only one of these articles (Batchvarov et al., 2003). This was changed due to a specific request of a reviewer for a different journal, who explicitly asked for the three papers to be meta-analyzed. The reviewer seemed to be extremely well-familiarized with Prof. Malik's work. Nevertheless, at Prof. Malik's request, we have re-run our meta-analysis including only Batchvarov et al. (2003), which has the highest study population size out of the three studies (Figure 1). This

demonstrated a mean difference of -0.33 ± 0.20 , which is comparable to the value of -0.34 ± 0.14 obtained previously.

To address Prof. Malik's point that "If Tse et al. have read our articles", we give an example that we had studied his articles very carefully. A reviewer for this Journal asserted that "Careful reading the full texts of the articles by Batchvarov et al. shows that these two articles described results in partially (if not completely) overlapping populations. It is very wrong to treat these studies as independent contributions to the meta-analysis". Yet, this reviewer appears to have been mistaken because Batchvarov et al. (2003) included patients ≥ 75 years of age, whereas Malik et al. (2004) included patients ≤ 75 years of age. This is why we had initially included both studies, but later removed one of them at the request of this reviewer.

Regarding the omission of the Okin et al. (2005) article, which Prof. Malik co-authored, there is no mention to TCRT at all in their Abstract. Description on TCRT only comes from the Results section of the study. In our meta-analysis, abstracts, but not full texts, were screened. Thus, the two reviewers responsible for screening independent excluded this entry because of a lack of information provided in the Abstract. This was the reason for the involuntary omission. Nevertheless, the omission of this article is a good observation and we thank Prof. Malik to notice it. We decided to re-run the meta-analysis by including Okin et al. (2005) using their data comparing survivors and noncardiovascular deaths with cardiovascular deaths (Figure 2). This yields a mean difference in TCRT of -0.34 ± 0.13 , which is not significantly different from the value of -0.34 ± 0.14 obtained previously. Furthermore, if the re-analyses described in Figure 1 (by including only Batchvarov et al., 2003) and

FIGURE 1 Forest plot demonstrating the mean differences of TCRT between event-positive and event-negative patients by including one of the three studies from St. George's Hospital

FIGURE 2 Forest plot demonstrating the mean differences of TCRT between event-positive and event-negative patients, including Okin et al., (2005)

FIGURE 3 Combining the re-analyses described in Figure 1 (by including only Batchvarov et al., 2003) and in Figure 2 (by including Okin et al., 2005)

in Figure 2 (by including Okin et al., 2005) were combined, a mean difference of -0.32 ± 0.18 is observed (Figure 3). Again, this is similar to the value of -0.34 ± 0.14 obtained previously.

The last sentence of Prof Malik's letter was debated extensively within the IHIS Network (International Health Informatics Study Network). The IHIS Network is a nonprofit group composed by 41 individuals from 11 countries, with a disparity of scientific backgrounds, expertise, interests, and publication portfolios. The vast majority of the group is composed by young, energetic, and highly motivated individuals at different stages of training, ranging from first year medical students to junior faculty supported by senior academics. The more senior participants act as supervisors of a given project and provide guidance to the new generation of researchers. IHIS has developed a deep and systematic approach to data analysis through systematic review and meta-analyses. This is reflected in its multiple publications, whether by IHIS authors independently or through IHIS itself, in many leading journals such as Heart Rhythm (Tse, Gong, Wong, Georgopoulos et al., 2017), Heart Asia (Cheung et al., 2018; Tse, Ip et al., 2018),

International Journal of Cardiology (Tse, Wong et al., 2018), Journal of Electrocardiology (Tse, Gong, Meng et al., 2018), Journal of Geriatric Cardiology (Luk et al., 2017; Tse, Wong et al., 2017), Pacing and Clinical Electrophysiology (Zhang et al., 2018), Journal of the American Medical Directors Association (Tse, Gong, Nunez et al., 2017; Tse, Gong, Wong et al., 2018), Stroke (He et al., 2017), Metabolism (Lakhani et al., 2018), Journal of Infection (Lee et al., 2018) etc.

We do believe that the new generation of researchers should be welcomed by the scientific community, and the more senior "experts" should not feel intimidated by the presence of new colleagues, with new ideas and maybe, different approaches to science. This, we believe, will represent major advances in our understanding on how to produce and communicate science.

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