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Quick Response Code:

Authors' response

We read the correspondence by Habibzadeh *et al*[1] on our article[2] with great interest. They stated that Perkins and Schisterman[3], in their article clearly recommended the use of the Youden's index (Se + Sp – 1) and warned about using the minimum distance criterion. We feel that the authors are overenthusiastic about the advantages of Youden's Index[1]. Perkins and Schisterman[3] have presented the following: "Since the (0,1) criterion is visually intutive, we have provided an amended (0,1) criterion in Appendix 2 that is likewise geometrically saitisfying while consistently dentifying the same "optimal" cutpoint as J". They have also mentioned that the added advantage in using the Youden's Index is the benefit of providing confidence interval and measurement of error. However, we would like to reiterate that Perkins and Schisterman[3] have not categorically provided any kind of warning about using one statistic over another as stated by Habibzadeh *et al*[1].

It is a known fact that the best cut-off is decided based on the scenario in which the proposed diagnostic test is going to be used, such as, whether the diagnostic test will be used as a "screening test" or as a "confirmatory test". Researchers would like to have higher sensitivity if the diagnostic test is to be used as a screening test and choose a higher specificity if the diagnostic test is used as a confirmatory test. The researcher will have the flexibity to choose the cut-off based on the desired requirement. Thus, in a given clinical scenario, the cut-off values need not be decided only by (0,1) and Youden's Index. The reliabity of Youden's Index has also been commented upon as well[4].

The Youden's index is optimal when the working procedure becomes the function of prevalence and the costs associated with false-positive and false-negative results. Thus, the cut-off decided using prevalence and cost is subject to further scrutiny at the place where it is being employed. As the prevalence and cost are likely to vary from place to place, many researchers repeat the study to validate the cut-off values.

Our aim was to generate and validate the cut-off that was reported by various studies[5-7] and, therefore, we preferred to use the same method that was used in the previously published studies. Habibzadeh *et al*[1] have presented two prevalence scenarios for diabetes mellitus, namely, 0.09 (in the community) and 0.41 (in referral hospital setting). They have stated "Suppose we want to use HbA_{1c} as a screening test in general population in the studied region. Under such circumstance, the pr is no longer 0.41; it is 0.09 - the prevalence of type 2 diabetes in the studied region, Rayalaseema area in Andhra Pradesh, southern India." and have quoted a study by Reddy *et al*[8] as a reference for this figure of 0.09. Reddy *et al*[8] did not conduct their study in a general population, but in "party workers belonging to a political party, drawn from each district of the then undivided Andhra Pradesh State who underwent an intensive training program". These party workers were prospectively screened for the prevalence of coronary risk factors. As depicted in Table 3 of this article[8], 153 of the 616 persons (25%) studied from Rayalseema area were found to have diabetes mellitus. It is not clear as to how the authors[1] have derived the figure of 0.09 as the prevalence of diabetes mellitus in Rayalaseema area from this study[8].

However, in order to do use glycosylated haemoglobin (HbA_{1c}) as a diagnostic test for type 2 diabetes, the HbA_{1c} estimation must be carried out on an instrument functioning on high-performance liquid chromatography (HPLC)-based ion exchange chromatography that conforms to the National Glycohemoglobin Standardization Program (NGSP) standardized to the Diabetes Control and Complications Trial (DCCT)[9] as was used in our study[2]. In India, this facility is usually available in referral hospitals and large laboratories in big cities only. In many smaller cities, towns, and rural areas, practitioners use point-of-care (POC) diagnostic tests for HbA_{1c} estimation instead of the above described standard method. The HbA_{1c} estimation done anywhere and everywhere with non-standard POC machines cannot be used as a diagnostic test for diabetes mellitus. In the scenario in which HbA_{1c} (estimated by the standard method as described above) is used as a diagnostic test for type 2 diabetes, the prevalence will be high. Moreover the prevalence of type 2 diabetes is high in the State of Andhra Pradesh[10]. Thus, the exercise using prevalence of 0.09 as proposed by the authors[1] has little clinical relevance and constitutes a mere academic exercise.

Further, contrary to the argument raised by the Habibzadeh *et al*[1] of using HbA_{1c} as a screening test in general population in the studied region, we wish to state that we have derived and validated a HbA_{1c} cut-off for use as a confirmatory diagnostic test (rather than a screening test) in a hospital-based scenario (rather than in a general population). We have also stated in the last sentence in the Discussion section[2] that "...it would not be advisable to replace the oral glucose tolerance test (OGTT) by HbA1c as a diagnostic test for type 2 diabetes in the prevalence surveys in the general population." We have also cautioned about the false-positive test results and stated that "However, the specificity was about 85 per cent which indicated that about 15-20 per cent of patients without type 2 diabetes would be wrongly labelled as having type 2 diabetes and would probably be started on unnecessary medication. While this may be resolved in a hospital-based situation on follow up of the patients, if HbA_{1c} is used as the diagnostic test in prevalence surveys of type 2 diabetes in the general population, the actual number of such misclassifications could be large[2]."

In our study[2] the Youden's Index was 0.75; the HbA_{1c} cut-off that provided such index was >6.3; both (0,1) approach and the Youden's Index provided the same cut-off. As a note of caution we feel that any recommendations that arise from simulated data with various prevalence and cost assumptions should also be given consideration in addition to data (study) driven recommendations alone.

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