Response:

It is unfortunate that the author (M. Ortiz) misunderstood and misapplied the numbers reported in the 2008 paper. The numbers presented were raw percentages and as such should not be used in the calculation of the sensitivity and specificity of the AUC (area under the curve) and ROC (Receiver Operating Characteristic). The MMAS scale ranges from 1 to 8, and for descriptive purposes, we presented the percentages in a 2 x 3 table. Ortiz made false assumption that this 2 x 3 table was the actual scale and erroneously dichotomized this into a 2 x 2 contingency table. The MMAS scale should not be degraded into a yes/no scale, but rather the original scale should be appropriately used in a multiple logistic regression model. From this multiple logistic regression analysis, the predicted values were generated and the AUC ROC estimated. These analyses can be performed using standard statistical packages such as SAS and R. The sensitivity and specificity were calculated based on the predicted values of the ROC – this cannot be hand calculated from the erroneously collapsed raw percentages. This study was not based on a 2 x 2 model design but considers many sociodemographic factors in the analysis. Not only would the 2 x 2 Chi-Square yield the wrong sensitivity and specificity since the model was misspecified, it also lacked context – both methodologically and conceptually. Methodologically, the logistic regression needs to control for sociodemographic factors such as age and income, education, etc. Conceptually, the MMAS scale does not exist in a vacuum but should be analyzed in the clinical context which include patient characteristics, clinical setting and patient chronic conditions.

The original study was mainly on patients with hypertension. The 2017 meta-analysis paper includes patients with other medical conditions aside from hypertension, such as diabetes, osteoporosis, myocardial infarction, seizure, etc. Translated versions were also sometimes used. As such, the meta-analysis results show an expected heterogeneity. The sensitivity and specificity measures are diagnostic assessment tools meant to help clinicians. In general, the higher the sensitivity, the lower the specificity and vice versa. There is a tradeoff between achieving high sensitivity vs high specificity. Depending on the context, higher sensitivity may be preferred over specificity in some cases, and in other cases, higher specificity would be preferred over sensitivity.

This issue had been brought up more than 40 years ago (see Cohen, 1983), which discussed the huge cost of dichotomization (i.e., loss of statistical power, loss of precision of scale, etc.) and there is rarely any justification for dichotomizing when the true scale is available (MacCallum et al, 2002.) Based on the flawed hand calculated unadjusted sensitivity and specificity, the author makes a totally faulty conclusion saying that the “measure may be no more accurate in detecting patients with uncontrolled BP, than tossing a coin to decide.” This is totally false due to his faulty simple analysis and assumptions, plus the fact that he completely misunderstood what the function of sensitivity and specificity were. In order to make that conclusion, one should examine the entire ROC curve at various cutoff points. The cutoff point of 6 is just one suggested cutoff point. Various cutoff points of the ROC should be examined and possibly perform some likelihood ratio tests in order to assess the viability of the scale. In the meta-analysis, the AUC ranges roughly from 0.6 to 0.7 on average in most of the studies. This is greater than 0.50, which means the measure may be useful in predicting adherence. The meta-analysis implied possibly using higher cut off points to increase either sensitivity or specificity. There are also other factors to consider when assessing the scale - the reliability, validity, factor loadings and variance explained by the scale which the critique failed to mention. The sensitivity and specificity of the measure can vary among different studies depending on the study population and patient characteristics, and is just a diagnostic tool and should not be miscalculated or misused to invalidate measures as suggested by the author.

Table 1: Illustration of how Data can be Degraded by Dichotomizing the Original Scale

|  |  |  |  |
| --- | --- | --- | --- |
| **Measurement Scale used** | **Analytical procedure** | **Analysis** | **Results** |
| Original MMAS scale ranges from 1 to 8 | Run logistic regression with BP in control (yes/no) and original MMAS scale to get predicted probabilities | Plot ROC curve, compute AUC. Determine ideal cut off point | Sensitivity & Specificity computed from original scale with no loss of information. |
| Collapse MMAS measure to a binary scale (i.e., not adherent vs. adherent) | Create a 2 x 2 contingency table with BP in control(yes/no) and adherent (yes/no) | Use equation to compute sensitivity and specificity | Sensitivity and specificity are underestimated due to dichotomization & loss of information |

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