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Claims of sex-related differences in genetic association studies often not properly validated

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A review of previous research suggests that prominent claims of sex differences of gene-disease associations are often insufficiently documented and validated, according to an article in the August 22/29 issue of JAMA.

In the human genome era, for many common diseases, published research has often considered that some common gene variants may have different effects in men vs. women. Many diseases or traits with strong genetic backgrounds have different prevalence in the two sexes and many studies try to determine differences in risks between men and women, according to background information in the article.

Nikolaos A. Patsopoulos, M.D., of the University of Ioannina School of Medicine, Ioannina, Greece and colleagues evaluated a large sample of prominently claimed sex differences for genetic effects and whether these claims were methodologically strong or were made based on selected and/or suboptimal analyses and with insufficient or questionable documentation. From a database search the authors identified 77 articles with 432 sex-difference claims.

Of these claims, 286 (66.2 percent) sex comparisons were reported as being decided a priori (in advance of the study) and 68 (15.7 percent) were acknowledged to be post hoc (after the study) analyses; in the other 78 (18.1 percent), the analysis plan was unclear. Appropriate

documentation of gene-sex interaction was recorded in 55 claims (12.7 percent); documentation was insufficient for 303 claims and spurious (not valid) for the other 74. Data for reanalysis of claims were available for 188 comparisons. Of these, 83 (44.1 percent) were nominally statistically significant, and more than half of them (n = 44) failed to reach nominal statistical significance of a certain level. Of 60 claims with seemingly the best internal validity, only one was consistently replicated in at least two other studies.

"… the majority of these claims were insufficiently documented or spurious, and reporting of statistical interaction tests was rare," the authors write.

Source: JAMA and Archives Journals