SEX CHROMOSOME TRISOMIES

Davis et al., in a paper which appeared in Am J Hum Genet (1), examined the phenotypic consequences of sex chromosome trisomies (47,XXY; 47,XYY; 47,XXX) in population-based cohorts rather than clinical samples. Data were drawn from three large biobanks — UK Biobank, the Million Veteran Program (MVP), and FinnGen — totaling about 1.5 million participants.

Although these cohorts include individuals from the general population, all participants underwent genome-wide genotyping with SNP microarrays at enrollment. These data, generated primarily for GWAS and genetic epidemiology, can also be used to detect copy number changes such as sex chromosome trisomies by analyzing SNP signal intensity and allelic ratios (high-level mosaicism can be detected, but low-level mosaic cases are likely missed).

A total of 2,769 individuals with sex chromosome trisomies were identified, most of whom had never received a clinical diagnosis. Phenome-wide association analyses revealed elevated risks of metabolic, cardiovascular, and neuropsychiatric conditions in carriers. Importantly, the spectrum of associated health outcomes was largely similar across the three types of trisomy, suggesting that the clinical burden depends more on the presence of an extra sex chromosome than on which specific chromosome it is.

1. https://www.cell.com/ajhg/abstract/S0002-9297(25)00287-3?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0002929725002873%3Fshowall%3Dtrue