

## **Multicenter Analysis of Cardiometabolic-Related Diagnoses in Transgender Adolescents**

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**Background:** Studies of transgender adults on gender affirming hormone therapy have shown increased rates of cardiovascular events (myocardial infarction and stroke) and features of metabolic syndrome including increased body mass index (BMI, transgender males) and dyslipidemia (transgender males and females). Studies in youth are limited by mostly small, single-center studies. With 1.8% of adolescents identifying as transgender, and increasing referral rates to gender clinics for care, more information is needed to better inform clinicians, patients and families about potential health risks in this cohort. PEDSnet, a pediatric Learning Health System, captures data from some of the largest pediatric care institutions in the U.S. We aimed to evaluate differences in diagnoses related to metabolic syndrome or cardiometabolic risk among youth with a diagnosis of gender dysphoria compared to matched cisgender controls.

**Methods:** All youth with a diagnosis of gender dysphoria (n=4,177) and at least one outpatient encounter were extracted from the PEDSnet database (6 sites, years 2009-2019) and propensity-score matched on 7 variables (year of birth, age at last visit, site, race, ethnicity, insurance status, duration in database) to 4 controls without gender dysphoria (n=16,664). The odds of having a diagnosis of overweight/obesity, hypertension, dyslipidemia, dysglycemia, liver dysfunction, polycystic ovary syndrome (PCOS) or metabolic syndrome, was examined using generalized estimating equations with an interaction term for sex (as listed in the chart).

**Results:** Of the transgender youth, 66% were female sex, 73% were white race, 9% were of Hispanic ethnicity, and 61% had private insurance. The control group was similar: 67% female sex, 72% white, 9% Hispanic, and 61% had private insurance. Transgender youth and controls both had on average 7 years duration in the database and were 16.2 years old at last visit. Transgender youth had higher odds of dyslipidemia (OR: 1.6 [95% CI: 1.3, 1.8],  $p < 0.0001$ ) and metabolic syndrome diagnoses (1.9 [95% CI: 1.2, 3.0],  $p = 0.0086$ ), with no significant difference based on sex, as compared to controls. Transgender youth with a female sex (though not male sex) had higher odds of overweight/obesity (1.7 [95% CI: 1.5, 1.9],  $p < 0.0001$ ) and PCOS diagnoses (1.9 [95% CI: 1.3, 2.8],  $p = 0.0006$ ), as compared to controls. There was no significant difference in the odds of having a diagnosis of hypertension, dysglycemia or liver dysfunction in transgender youth compared to controls.

**Conclusions:** This large, geographically diverse cohort of transgender youth had a higher odds of being diagnosed with dyslipidemia and metabolic syndrome (both sexes), as well as elevated BMI or PCOS among those with a female sex listed. Future investigations will include analyses based on GAHT prescriptions and will further inform risk analysis and monitoring guidelines in this population.