Evidence on higher rates of diabetes unclear in trans people, but data on higher rates of heart disease are clear

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The latest data on the metabolic problems faced by trans people are presented at a session at this year's Annual Meeting of the European Association for the Study of Diabetes (Hamburg 2–6 October). While evidence on increased or decreased rates of diabetes among trans men and women remains unclear, the evidence that they face higher rates of cardiovascular disease continues to mount. The talk is by Dr. Dorte Glintborg, Department of Endocrinology, Odense University Hospital,

Denmark.

"While increased rates of cardiovascular disease might normally go hand-in-hand with increased rates of diabetes, for trans men (assigned female at birth AFAB), use of testosterone usually increases lean body mass and this could be protecting against an increased risk of diabetes," explains Dr. Glintborg.

"For trans women (assigned male at birth, AMAB), hormone treatments such as estrogen will increase fat mass and lower lean body mass, and increased estrogen is usually associated with increased risk of autoimmune disease and inflammation. Some studies found a higher risk of type 2 diabetes in transgender women, but this could not be confirmed by others," continues Dr. Glintborg.

She adds, "Several other factors apart from body fat/leanness and muscle mass could affect risk of vascular and metabolic diseases in transgender populations and we still need more long-term data. Indeed, it has been discussed that mental support as part of transgender care could relieve minority stress and could be protective against development of cardiovascular disease. Lifestyle changes during hormone treatment and especially higher physical activity in transgender men could protect against T2D."

However, Dr. Glintborg explains the field is still rapidly evolving and "we lack large study cohorts."

Dr. Glintborg will discuss various studies on the elevated cardiovascular risk faced by the transgender population, including one by herself and colleagues, published in *The European Journal of Endocrinology*, which showed that compared with cis-gender individuals, transgender men and women were at increased risk of cardiovascular disease. The main outcome measure was cardiovascular diagnosis (any CVD) including

medicine prescriptions for CVD during 2000–2018.

The authors used Danish health registers to determine cardiovascular outcomes (ICD-10 codes) and medicine prescriptions regarding CVD medicine. The Danish transgender cohort (n=2,671) included persons with International Classification of Diseases-10 diagnosis code of "gender identity disorder" (1,583), which implied contact with a Danish center of gender identity and persons who had had a legal sex change (n =1,088), which implied that they had contacted the legal system and changed their gender. In total, the transgender study cohort included 1,270 persons who were assigned female at birth (AFAB, transgender men) and 1,401 were assigned male at birth (AMAB, transgender women).

The control population (n=26,710) were matched to the transgender population by age (n= 5 controls of same and n= 5 controls of other birth sex) of the respective transgender case. The cohort was young—median age at study inclusion was 22 years for AFAB and 26 years for AMAB. By definition, younger people generally have much lower rates of CV disease, but in this study hypertension (high blood pressure) and dyslipidaemia (abnormal blood fats) were the most common problems and could usually be treated a visit to the person's general practitioner and receiving a prescription.

The mean follow-up time was 4.5 years for AFAB and 5.7 years for AMAB. The increased risk of any CVD was significantly higher in both transgender men and women as compared with control men or women. Transgender males (AFAB) had a 2.2 times increased risk of CVD compared with control men and a 63% increased risk compared with control women. Transgender females (AMAB) had a 93% increased risk of any CVD versus control men, and a 73% increased risk compared with control women.

Analysis of the use of gender-affirming hormone treatment (GAHT) suggested around a third of the increased risk for CVD outcomes in transgender males could be attributed to GAHT—previous research has also associated the use of hormones such as testosterone with increased cardiovascular risk. Yet in transgender females, use of GAHT (estrogen in combination with testosterone blocker), could not explain increased CVD risk.

The authors highlight that this register-based data study did not allow them to investigate the influence of BMI, family history of CVD, minority stress and lifestyle factors (diet, smoking, exercise) on study outcomes. From this study, they concluded, "Cardiovascular and metabolic outcomes were more prevalent in transgender persons compared to controls. Gender-affirming hormone therapy exposure could contribute to the elevated cardiovascular risk in transgender men, assigned female at birth. Future studies will be able to bring further knowledge regarding mechanisms for higher cardiovascular risk in transgender men and women."

Dr. Glintborg adds, "We need to determine more about the mechanisms for adverse metabolic outcomes—are they mediated by changes in body composition or other mechanisms such as stress and lifestyle changes? For example, in many countries you need to lose weight (in Denmark to a body mass index of below 27) to become eligible for gender-affirming surgery and you have to stop smoking. This could be protective against adverse outcomes.

"A more detailed evaluation of fat, muscle, and liver function and could all be very valuable regarding mechanisms for changes in metabolic function. And randomized controlled trials regarding different treatment regiments would help massively in increasing our understanding of metabolic changes."

Another important element affecting transgender care is the huge increase in demand for services in most European / Western countries. The resulting delay in patients receiving their first and subsequent appointments is leading to more trans women self-medicating with cyproterone acetate to supress the side effects of hormone (testosterone) therapy. Cyproterone acetate is a synthetic progestin and some studies have found higher risk of hypertension in trans women using the drug.

"We need to investigate if use of cyproterone acetate in Europe is a risk factor for CVD in transgender women," explains Dr. Glintborg.

In fact, many different medication regimens are used throughout the transition journeys of trans men and trans women, and Dr. Glintborg would like to see as many combinations as possible investigated for their effects on the health of transgender people.

Dr. Glintborg will also discuss the idea that "the benefits of GAHT on mental health could outbalance negative effects on cardiovascular markers caused by being part of this minority group—or so-called 'minority stress.' Like all patients with metabolic issues, doctors should discuss with their transgender patients the important of physical activity, avoiding weight gain, and stopping or avoiding starting smoking."

Provided by Diabetologia

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