Delivery route for gender affirmation treatment may affect heart health

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A comprehensive review of research into the delivery method of estrogen treatment (e.g., oral, intramuscular injection, transdermal patch, etc.) and cardiovascular risk in transgender women and gender-diverse

people found that treatment route may affect heart health, but there is not enough available data for metanalysis. The study is published ahead of print in the *American Journal of Physiology-Heart and Circulatory Physiology*.

Gender-affirming hormone therapy has been an established medical intervention since the World Professional Association for Transgender Health began publishing Standards of Care for the Health of Transgender and Gender Diverse People in 1979. Transgender and gender-diverse (TGD) people who have access to gender-affirming therapies, including hormone therapy, have markedly reduced cases of depression and anxiety.

TGD people assigned male at birth who identify as women are known to have increased cardiovascular health risks—such as blood clots, stroke and heart attacks—compared to people assigned female at birth who identify as women (i.e., cisgender women). This increased risk may be linked to use of gender-affirming estrogen therapy (GAET). In cisgender women, taking estrogen-based medications (e.g., birth control pills) orally is associated with greater cardiovascular risk than estrogen administered via other routes, such as injections.

A research team from the University of Calgary in Canada analyzed current literature to learn more about estrogen administration route and cardiovascular events in the TGD population. They searched the major bibliographic databases MEDLINE, Embase and PsycINFO for clinical studies that included TGD people on GAET and looked at cardiovascular outcomes.

The search uncovered 3,113 unique studies, but after thorough vetting, only five met all necessary criteria—reporting cardiovascular outcomes by route of estrogen administration. The remaining five studies lacked the standardization necessary to allow for metanalyses. For example,

only two studies reported systolic and diastolic blood pressure, one combined reporting for transdermal and intramuscular administration routes, and none of the studies reported possible confounding factors such as such as diabetes, ethnicity, race or socioeconomic status.

The researchers noted that in the absence of appropriate cohort studies, "treatment protocols are therefore often extrapolated from the cisgender population." This extrapolation will offer imperfect guidance at best, as it cannot account for population-specific confounding variables, such as the use of antiandrogen medications. The current study "highlights the need for large prospective cohort studies with appropriate stratification of gender-affirming estrogen therapy" to best provide cardiovascular care for TGD people using GAET.

"Gender-affirming estrogen therapy route of administration and cardiovascular risk: a systematic review and narrative synthesis" is published ahead of print in the *American Journal of Physiology-Heart and Circulatory Physiology*.

More information: Keila Turino Miranda et al, Gender-affirming estrogen therapy route of administration and cardiovascular risk: a systematic review and narrative synthesis, *American Journal of Physiology-Heart and Circulatory Physiology* (2022). DOI: 10.1152/ajpheart.00299.2022