
What's New?
HIVC
HIV BY ORGAN SYSTEM

Cardiovascular Risk in Women with HIV

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1) CV System Overview

2) Selected studies including data regarding CVD risk in WWH

3) What's new?
   -New PLWH Statin Guidelines
   -"Immune-plaque Paradox" Hypothesis

OBJECTIVES

1. Review REPRIEVE results for women
2. Immune complex paradox
3. Cardiovascular disease conditions and risk factors which are more common and/or unique to women.
4. Review that women have atypical presentation of heart disease and arrhythmia
5. There is underutilization of guideline-recommended medical and device therapies in women compared to men.
6. There arecardiovascular risk reduction benefits of newer lipid lowering agents and obesity medications, but more data is needed in women.
7. Menopause increases cardiovascular risk, but the role of hormone replacement therapy is controversial.
8. Microvascular disease and endothelial dysfunction as a cause of heart disease and angina in women.

Cardiovascular System

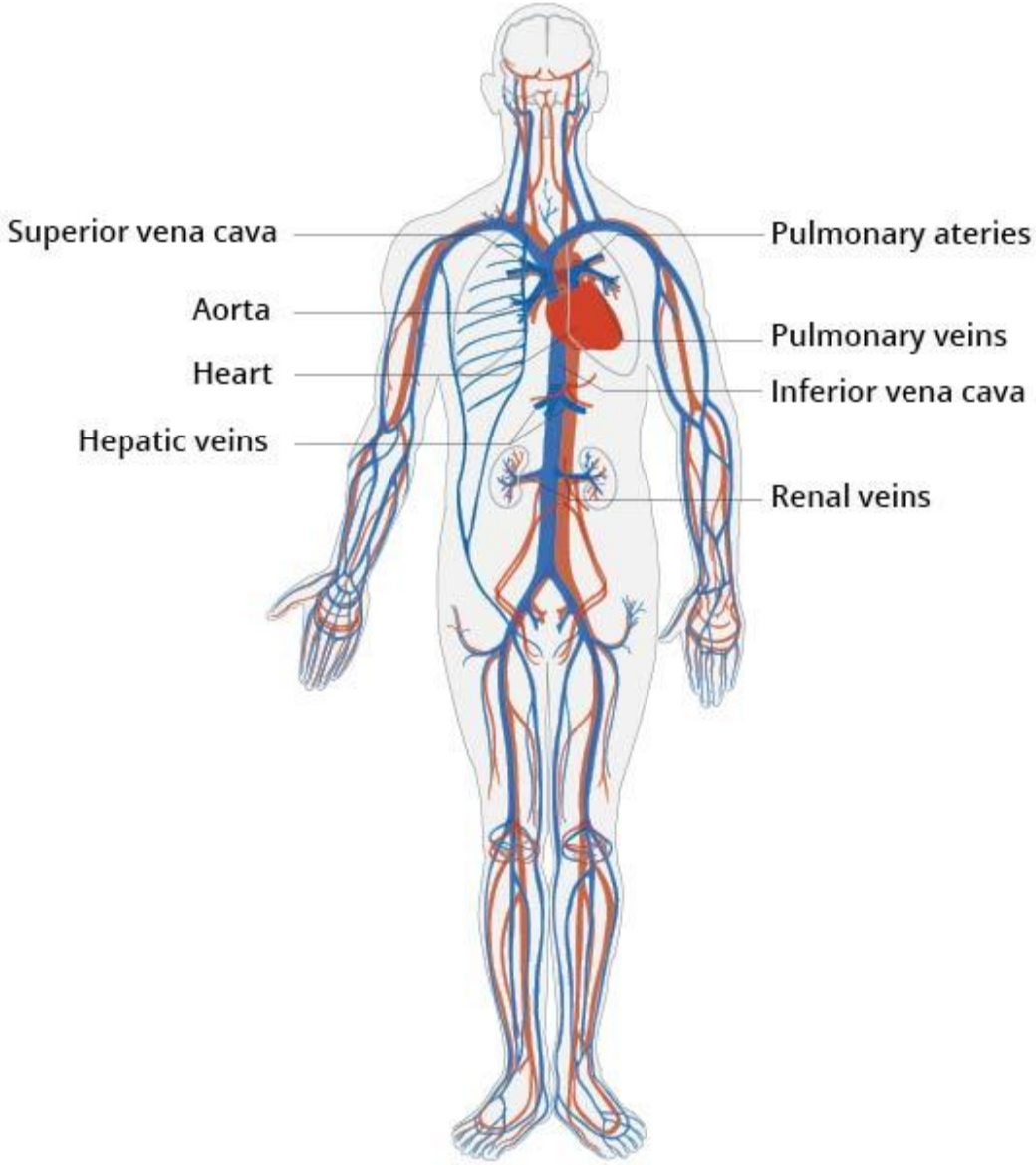
The cardiovascular system is a transport system composed of the heart, blood vessels, and blood.

The heart is the pump that sends the oxygen and nutrient-rich blood out to the body via the arteries and arterioles.

The oxygen and nutrients in the blood leave the capillaries and enter the tissues. Carbon dioxide and metabolic wastes leave the tissues, re-enter the capillaries, and pass through the venules and veins on their way to the lungs, liver, and kidneys.

The lungs eliminate carbon dioxide, and the liver and kidneys alter or eliminate other waste products.

Most commonly discussed “heart” or “cardiovascular” disease is heart attack from clogged arteries, but there are other conditions that need attention like heart failure, or unique to women hormones, or what we don’t know until we have studies with women.


Superior vena cava
Aorta
Heart
Hepatic veins
Pulmonary ateries
Pulmonary veins
Inferior vena cava
Renal veins

The heart disease risk in the general population may state that women have a lower risk of heart disease than men,

…but this does not appear to be the case for women with HIV.

Per evaluation of data from Triant JCEM, 2007 (Increased Acute Myocardial Infarction Rates and Cardiovascular Risk Factors among Patients with Human Immunodeficiency Virus Disease),

the adjusted relative risk of MI and stoke incidence was approximately *two-fold higher in women with HIV.*

Additional studies demonstrate a relative risk of HIV and CVD in high income regions ranging from 1.5-2 times higher.

Increased Acute Myocardial Infarction Rates and Cardiovascular Risk Factors among Patients with Human Immunodeficiency Virus Disease (Triant, 2007)

In gender-stratified models, the unadjusted AMI rates per 1000 person-years were higher for HIV patients among women (12.71 vs. 4.88 for HIV compared with non-HIV women). The RRs (for HIV vs. non-HIV) were 2.98 (95% CI 2.33–3.75; P < 0.0001) for women. A limitation of this database is that it contains incomplete data on smoking. Smoking could not be included in the overall regression model, and some of the increased risk may be accounted for by differences in smoking rates.

Conclusions: AMI rates and cardiovascular risk factors were increased in HIV compared with non-HIV patients, particularly among women.

REPRIEVE Study

- The REPRIEVE study of pitavastatin for prevention of cardiovascular disease showed that statins **reduced the risk of major cardiovascular events such as heart attack and stroke by a similar extent in men and women (approximately 35%).**

- The study recruited people with HIV who had a low-to-moderate risk of cardiovascular disease based on their age, cholesterol levels and other major risk factors.(Zanni, 2024)

- **But the study uncovered an unanticipated level of cardiovascular risk in women with HIV, especially in high-income countries**.(Zanni, 2024)

REPRIEVE

- Randomized Trial to Prevent Vascular Events in HIV

REPRIEVE Study

- In the general population, women have a lower estimated cardiovascular risk than men.
- Yet when the incidence of major cardiovascular events was compared in four strata of baseline cardiovascular risk, from less than 2.5% to above 10% risk,
- women had the same rate of events as men.
- In the highest risk strata, there was a strong trend towards a higher incidence of major events in women.
- Female sex-at-birth was not protective against major cardiovascular events in the study population after controlling for other risk factors.(Zanni, 2024)

REPRIEVE Study

- The cardiovascular risk score under-predicted the rate of cardiovascular events in women and in trial participants in high-income countries.
- In women, the rate of events exceeded the predicted number by 42%.
- In high-income country participants, the rate of events exceeded the predicted number by 30%.
- The mismatch between predicted and actual events was most pronounced in women in **high-income countries,** where the **cardiovascular event rate was two-and-a-half times higher** than would have been predicted from the scores.(Zanni, 2024)

Pooled Cohorts Equations for 10-year ASCVD Risk Score

- Age
- Race
- HTN Rx
- SBP
- DM
- Smoking
- TC
- HDL-C
- Sex

Female sex lowers calculated risk score!

REPRIEVE Study

- The REPRIEVE study enrolled 31% women with a mean ASCVD risk score of 1.9% compared to men with a mean score of 5.4%, despite similar median ages.
- Women were less likely to smoke but had higher instances of high blood pressure.

- Additionally, a larger percentage of women were Black or African American.
- As above, REPRIEVE demonstrated a significant mismatch between predicted and actual events in the female study population at higher risk strata and in higher-income countries.(Zanni, 2024)

Predictors of Female CV Risk

- Women have a more robust innate immune response to HIV than men, leading to greater immune activation.
- Inflammation and immune activation promote the development of plaques, accumulations of fats that block arteries.
- The reproductive hormone estrogen affects several of the pathways through which heart disease develops and **when estrogen production declines at the menopause, cardiovascular risk increases**.
- A baseline analysis of REPRIEVE participants found that greater reproductive ageing was associated with greater immune activation and greater waist circumference.
- As weight rises, so does blood pressure, a critical risk factor for heart disease.

“Immune-Plaque Paradox”

- Analysis of the REPRIEVE study data demonstrated the **prevalence of coronary artery plaque was lower among women with HIV vs. men** with HIV overall and controlling for PCE 10y ASCVD risk score + BMI.

- Yet, in women with HIV there is evidence of accelerated reproductive ageing with associated increased immune markers and waist circumference.

- To date, there exists in the data a “immune-plaque paradox”.(Zanni, 2024)
- AKA, we don’t’ know.

- significantly faster decline in their fertility

“Immune-Plaque Paradox”

- Possible explanatory hypotheses include:
- Among women with HIV, **subclinical coronary atherosclerotic** plaque has higher prognostic value for atherothrombosis.
- Among women with HIV, MI risk may also be mediated through **pathways not directly involving epicardial artery plaque** (e.g. coronary microvascular dysfunction).(Zanni, 2024)

“Immune-Plaque Paradox”

- Therefore, caution could be warranted in discussing statin therapy with women with HIV and a clinical history of unremarkable cardiac cath or low CT calcium score.
- As above**, women with HIV should be alerted to our current data suggesting that the 10y ASCVD risk score underestimates MI/stroke risk in this population, especially in cases of advanced ASCVD risk strata and high-income countries**.

Symptoms of CVD in Women

- Symptoms of heart disease and pending heart attack may differ in women.

- Shortness of breath, nausea, vomiting and back or jaw pain are more common symptoms in women but are often missed, according to the American Heart Association.

Women and HIV/CVD Research "Follow YOUR Heart" Campaign

- **Background:** Women are underrepresented in HIV and cardiovascular disease (CVD) research, highlighting the need for strategies to enhance their participation.

- **Objective:** This study aims to gather insights from women with or at risk for HIV regarding their involvement in CVD research, informing an evidence-based campaign to empower older women with HIV to join a large-scale CVD prevention trial.

Women and HIV/CVD Research "Follow YOUR Heart" Campaign

- **Methods:** In a community-based setting, **40 women with or at risk for HIV surveyed** about factors which might facilitate or impede engagement in CVD research.
- **Applied insights derived from these surveys developed into the Follow YOUR Heart** campaign, educating women about HIV-associated CVD and **empowering them to learn more about a multi-site HIV-associated CVD prevention trial: REPRIEVE.**

- **Results:** Endorsed best methods for learning about a CVD research study included peer-to-peer communication (54%), provider communication (46%) and video-based communication (39%).
- Top endorsed non-monetary reasons for participating in research related to gaining information (63%) and helping others (47%).
- Top endorsed reasons for not participating related to lack of knowledge about studies (29%) and lack of request to participate (29%).

Women and HIV/CVD Research "Follow YOUR Heart" Campaign

- **Conclusions:** Understanding the factors affecting women's participation in HIV-associated
- CVD research can help develop strategies to improve their enrollment in large-scale trials, potentially enhancing research across various fields.

- Our goals today are to inform PLH in San Diego specifically abou
- this new recommendation for statins in HIV, and
- to remember that the usual ways to predict heart disease in women is based on men, and underestimates the woman's risk.