

D:A:D

Gender Differences in the Use of Cardiovascular Disease-related Interventions Among HIV-positive persons: D:A:D Study

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BACKGROUND

- There have been substantial reductions in the incidence of myocardial infarction (MI) and improvements in post-MI survival in the general population. However, these improvements have tended to lag in women compared to men (1, 2).
- Reasons for this gender difference remain unclear but may possibly be explained by less use of drug interventions and invasive cardiovascular procedures (ICPs) in women (2,3).
- There is a lack of corresponding data related to potential gender differences in the use of interventions to prevent and treat cardiovascular disease (CVD) among HIV-positive individuals.

STUDY AIM

To investigate whether gender differences exist in the use of CVD-related interventions among HIV-positive participants in the D:A:D study.

METHODS

- The D:A:D Study is an observational study of >49,000 HIV-positive persons from 11 cohorts across Europe, Australia and USA. The primary aim of the study is to investigate potential associations between the use of antiretroviral drugs (ARVs) and CVD (MIs, strokes, ICPs) and other clinical events. Data are collected prospectively; the standardized dataset includes information on socio-demographic, HIV-and CVD-related factors.

STATISTICAL METHODS

- Follow-up was from 01/02/99 until the earliest of death, six months after last visit or 01/02/13.
- Individuals with a MI/stroke at baseline were excluded.
- Rates of initiation of lipid-lowering drugs (LLDs), angiotensin-converting enzyme inhibitors (ACEIs), anti-hypertensives and receipt of ICPs (bypass, angioplasty, endarterectomy) were calculated overall and in groups determined to be at higher CVD risk (i.e periods of time in person years (PYRS) where individuals were at higher CVD risk) :
 - i. total cholesterol (TC) >6.2 mmol/l
 - ii. triglyceride (TG) >2.3 mmol/l
 - iii. hypertension
 - iv. previous MI
 - v. diabetes
 - vi. age >50 years
 - vii. 10-year Framingham CVD risk score >10%
- Poisson regression was used to assess whether rates of initiation of CVD-related interventions were higher in men than women, after adjustment for potential confounders.

RESULTS

- Baseline characteristics of men and women at enrolment in the D:A:D Study are shown in **Table 1**.
- Of 49,071 individuals without a MI/stroke at baseline, 0.6% women vs. 2.1% men experienced a MI while 0.8% women vs.1.3% men experienced a stroke.
- The overall rates of initiation of LLDs, ACEIs, anti-hypertensives and ICPs were all lower in women than in men (**Figure 1**). Within most high risk groups, initiation rates of CVD-related interventions were also lower in women than in men (**Figure 2**).
- With the exception of anti-hypertensives, the observed gender differences persisted after adjustment for potential confounders (**Table 2**).
- Additional adjustment for race, smoking status, AIDS, CVD family history and stroke as well as TC, TG, systolic/diastolic blood pressure as continuous covariates, had minimal effect on the observed associations with gender.

CONCLUSION

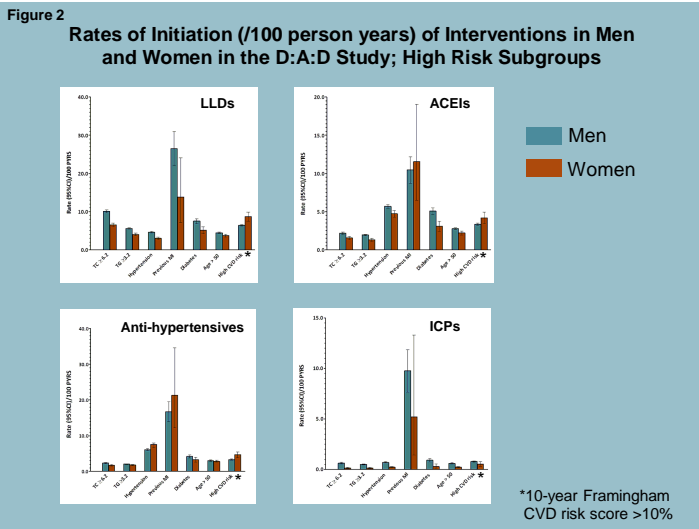
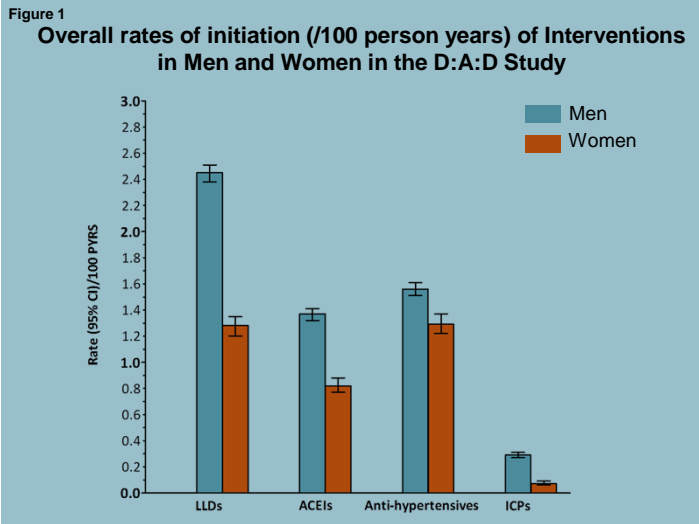
- The initiation rates of most CVD-related interventions, except for anti-hypertensives, were lower among HIV-positive women than men in the D:A:D study.
- Our findings suggest that actions should be taken to ensure that both men and women are monitored for CVD and, if eligible, receive appropriate CVD-related interventions.
- As women are most often found within low CVD risk groups, further investigation of the potential differences in monitoring of CVD risk factors between men and women are warranted as women may be less frequently and less sufficiently monitored.

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| Table 1 Baseline Characteristics of Men and Women in D:A:D | | | | |
|--|-------------------|----------------|----------------|---------|
| | | Men | Women | p-value |
| Number | | 36664 | 13039 | |
| Mode of infection | MSM | 21809 (59.5) | | |
| | IDU | 5187 (14.2) | 2428 (18.6) | |
| | Heterosexual | 7199 (19.6) | 8999 (69.0) | |
| | Other/not known | 2469 (6.7) | 1612 (12.4) | 0.0001 |
| White Race | White | 19335 (52.7) | 5825 (44.7) | |
| Age (years) | Median (IQR) | 39 (33, 46) | 34 (29, 40) | 0.0001 |
| BMI (kg/m²) | <18 | 875 (2.4) | 716 (5.5) | |
| | ≥18, ≤26 | 2444 (66.7) | 7808 (59.9) | |
| | >26, ≤30 | 4733 (12.9) | 1391 (10.7) | |
| | >30 | 1262 (3.4) | 934 (7.2) | |
| | Not known | 5351 (14.6) | 2190 (16.8) | 0.0001 |
| Smoking | Current | 13669 (37.3) | 3821 (29.3) | 0.0001 |
| | Ex- | 6497 (17.7) | 1810 (13.9) | |
| | Never | 8285 (22.6) | 4834 (37.1) | |
| | Not known | 8213 (22.4) | 2574 (19.7) | 0.0001 |
| Prior AIDS diagnosis | | 8332 (22.7) | 2723 (20.9) | 0.0001 |
| Exposed to ART | | 22461 (61.3) | 7885 (60.5) | 0.11 |
| CD4 (cells/mm³) | Median (IQR) | 400 (244, 590) | 405 (249, 591) | 0.07 |
| Family history of CVD | | 2403 (6.6) | 724 (5.6) | 0.0001 |
| Diabetes | | 1022 (2.8) | 230 (1.8) | 0.0001 |
| Dyslipidemia | | 14199 (38.7) | 3095 (23.7) | 0.0001 |
| Hypertension | | 4158 (11.3) | 931 (7.1) | 0.0001 |
| Predicted CVD risk score | Low (<10%) | 9919 (27.1) | 4172 (32.0) | |
| | Moderate (10-20%) | 2413 (6.6) | 149 (1.1) | |
| | High (>20%) | 1114 (3.0) | 56 (0.4) | |
| | Unknown | 23218 (63.3) | 8662 (66.4) | 0.0001 |



| Table 2 Relative rate (RR) of Receipt of Each Intervention in Women vs. Men in the D:A:D Study, Before and After Adjustment for Markers of High CVD Risk | | |
|--|---|---|
| Intervention | Before adjustment RR (95% CI); p-value | After adjustment* RR (95% CI); p-value |
| LLDs | 0.52 (0.49, 0.56); p=0.0001 | 0.80 (0.75, 0.86); p=0.0001 |
| ACEIs | 0.60 (0.56, 0.65); p=0.0001 | 0.80 (0.74, 0.87); p=0.0001 |
| Anti-hypertensives | 0.83 (0.78, 0.89); P=0.0001 | 1.21 (1.13, 1.30); p=0.0001 |
| ICPs | 0.25 (0.20, 0.32); p=0.0001 | 0.49 (0.38, 0.63); p=0.0001 |

*Adjustment for age, calendar year, body mass index, high total cholesterol, high triglycerides, hypertension, previous MI, diabetes and moderate/high predicted 10-year CVD Framingham risk score

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