Marked gender differences in mortality on ART in lower- and middle-income countries: a systematic review and meta-analysis

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Introduction

Across all low- and middle-income countries (LMIC), men and women comprise similar proportions of people living with HIV who are eligible for antiretroviral therapy (ART). However, men are only 41% of those receiving ART. 1 There has been limited study of men’s outcomes in ART programs, despite a number of studies suggesting that men have higher mortality rates than women. 2,3

Objective

Conduct a systematic review (SR) and meta-analysis (MA) to assess differential mortality between men and women living with HIV and on ART in LMIC.

Methods

Systematic Review Protocol

Populations: Adults ≥15 years of age in low- and middle-income countries as defined by the World Bank. Intervention: HIV treatment. Comparator: Men versus women. Outcome: All-cause mortality. Databases: PubMed, EMBASE, Ovid Global Health. Search Terms: Controlled vocabulary & keyword terms: HIV and AIDS, ART, LMIC, (not) children. Inclusion criteria: Observational studies (published 2006-2015) among people living with HIV and on ART before or at baseline, reporting hazard ratios of all-cause mortality for men and women, even if gender differences were not the main outcome. Exclusions: Included studies: ≥15 years old; sample size ≥50 males or ≥70 women; systematic reviews; mathematical modeling; drug studies; vaccination studies after their opportunistic infections; studies explicitly only focused on one sex. Review Process: Screening and abstraction was conducted by two independent reviewers. Conflicts were resolved by a third reviewer. The screening process and search results are outlined below in Figure 1.

Meta-Analysis

Random-effects meta-analysis of hazard ratios (HRs) (men vs. women) for all-cause mortality using Stata (8.0) random-effects command (College Station, Texas). Heterogeneity analyses 2,3 Adjusted hazard ratios were used when available.

Results

The characteristics of included studies are listed in Table 1. The majority of the studies were conducted in sub-Saharan Africa, with a minority from Asian countries (excluding one study from Eastern Europe). Median follow-up time was 33 months.

Table 1. Characteristics of Included Studies

Region n (male) n (female) Sample Size M F Follow-up Time (months)
Africa 53 66 597 57 3
Asia 14 13 1737 2011 33
Latin America & Caribbean 1 1 2808 5506 144
Total 70 97 37827 72667 2014

Pooled hazard ratios for all-cause mortality (men vs. women), shown in Table 2, below, indicate men have a statistically significant 37% increased hazard for mortality while on ART.

Table 2. Increased Hazard for Mortality for Men on ART vs. Woman

Region n (male) n (female) n (HRS) Pooled Hazard Ratio (95% CI)
All LMIC a 249,027 375,067 87 1.37 (1.31-1.43)
Africa 181,779 375,067 66 1.33 (1.26-1.39)
Asia 59,073 44,029 19 1.58 (1.42-1.75)

Pooled hazard ratios for all-cause mortality (men vs. women), shown in Table 2, below, indicate men have a statistically significant 37% increased hazard for mortality while on ART.

Table 3. Pooled HRs for Mortality, M vs. F, by Sub-region & Time (≤12 & >12 months)

Region n (male) n (female) n (HRS) Pooled Hazard Ratio (95% CI)
All Africa a 181,779 375,067 66 1.33 (1.26-1.39) 1.42 (1.34-1.50)
East 67,936 246,610 20 1.19 (1.09-1.29) 1.38 (1.25-1.50)
Southern 10,104 31,046 13 1.26 (1.15-1.37) 1.31 (1.21-1.44)
West/Central 7,386 14,807 10 No pooled data 1.57 (1.28-1.90)
Asia 59,973 44,029 19 1.43 (1.31-1.56) 1.64 (1.51-1.80) 4

Some studies from Asia reported 20-60% of their participants were people who use drugs (PWUD). Subgroup analysis shows differences between studies with and without reported PWUD, shown in Table 4.

Table 4. Pooled HRs for Mortality, M vs. F, by Drug Use & Time (≤12 & >12 months)

Country n (male) n (female) n (HRS) Pooled Hazard Ratio (95% CI)
All PWUD 4,613 9,084 12 0.66 (0.57-0.75) 0.65 (0.56-0.75)
Some PWUD 51,566 34,525 7 1.50 (1.38-1.63) 1.44 (1.36-1.55)

Conclusions

• Men living with HIV had significantly greater hazards of mortality compared to women while on ART in LMIC. 1
• This effect persisted and increased over time on treatment.
• Clinical and prevention benefits of ART will only be realized if programs can improve male engagement, diagnosis, and support better long-term retention and adherence.

Literature cited


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