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## Identifying optimal doses of heart failure medications in men

## compared with women: a prospective, observational, cohort study

Bernadet T Santema, MD • Wouter Ouwerkerk, PhD • Jasper Tromp, MD • Izhah E Sama, PhD • Alice Ravera, MD •

Prof Vera Regitz-Zagrosek, MD • et al. [Show all authors](#) • [Show footnotes](#)Published: August 22, 2019 • DOI: [https://doi.org/10.1016/S0140-6736\(19\)31792-1](https://doi.org/10.1016/S0140-6736(19)31792-1) •

## Summary

## Background

Guideline-recommended doses of angiotensin-converting-enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), and  $\beta$  blockers are similar for men and women with heart failure with reduced ejection fraction (HFrEF), even though there are known sex differences in pharmacokinetics of these drugs. We hypothesised that there might be sex differences in the optimal dose of ACE inhibitors or ARBs and  $\beta$  blockers in patients with HFrEF.

## Methods

We did a post-hoc analysis of BIOSTAT-CHF, a prospective study in 11 European countries of patients with heart failure in whom initiation and up-titration of ACE inhibitors or ARBs and  $\beta$  blockers was encouraged by protocol. We included only patients with left ventricular ejection fraction less than 40%, and excluded those who died within the first 3 months. Primary outcome was a composite of time to all-cause mortality or hospitalisation for heart failure. Findings were validated in ASIAN-HF, an independent cohort of 3539 men and 961 women with HFrEF.

## Findings

Among 1308 men and 402 women with HFrEF from BIOSTAT-CHF, women were older (74 [12] years *vs* 70 [12] years,  $p < 0.0001$ ) and had lower bodyweights (72 [16] kg *vs* 85 [18] kg,  $p < 0.0001$ ) and heights (162 [7] cm *vs* 174 [8] cm,  $p < 0.0001$ ) than did men, although body-mass index did not differ significantly. A similar

number of men and women reached guideline-recommended target doses of ACE inhibitors or ARBs (99 [25%] *vs* 304 [23%],  $p=0.61$ ) and  $\beta$  blockers (57 [14%] *vs* 168 [13%],  $p=0.54$ ). In men, the lowest hazards of death or hospitalisation for heart failure occurred at 100% of the recommended dose of ACE inhibitors or ARBs and  $\beta$  blockers, but women showed approximately 30% lower risk at only 50% of the recommended doses, with no further decrease in risk at higher dose levels. These sex differences were still present after adjusting for clinical covariates, including age and body surface area. In the ASIAN-HF registry, similar patterns were observed for both ACE inhibitors or ARBs and  $\beta$  blockers, with women having approximately 30% lower risk at 50% of the recommended doses, with no further benefit at higher dose levels.

### Interpretation

This study suggests that women with HFrEF might need lower doses of ACE inhibitors or ARBs and  $\beta$  blockers than men, and brings into question what the true optimal medical therapy is for women versus men.

### Funding

European Commission.

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