



## Associations of androgens with health care utilization and costs in women—Perspectives of a population-based cohort study



Robin Haring<sup>a,b,\*</sup>, Henri Wallaschofski<sup>a</sup>, Henry Völzke<sup>c</sup>, Steffen Flessa<sup>d</sup>, Brian G. Keevil<sup>e</sup>, Matthias Nauck<sup>a</sup>, Sebastian E. Baumeister<sup>c,f</sup>

<sup>a</sup> Institute of Clinical Chemistry and Laboratory Medicine, University Medicine Greifswald, Germany

<sup>b</sup> European University of Applied Sciences, Faculty of Applied Public Health, Rostock, Germany

<sup>c</sup> Institute for Community Medicine, University Medicine Greifswald, Germany

<sup>d</sup> Faculty of Law and Economics, University Medicine Greifswald, Germany

<sup>e</sup> Department of Clinical Chemistry, University Hospital South Manchester, UK

<sup>f</sup> Department of Epidemiology and Preventive Medicine, University of Regensburg, Germany

### ARTICLE INFO

#### Article history:

Received 15 December 2015

Received in revised form 29 March 2016

Accepted 2 April 2016

#### Keywords:

Total testosterone

Androgens

Sex hormones

Women

Health care utilization

Costs

### ABSTRACT

**Objective:** Despite associations between total testosterone (TT) concentrations and increased cardiometabolic risk, the impact of serum androgens on health care utilization and costs among women is unknown.

**Methods:** We used data from 1521 women in the population-based cohort Study of Health in Pomerania (SHIP) to investigate the associations of serum TT (measured by liquid chromatography-tandem mass spectrometry), sex hormone-binding globulin (SHBG), and free testosterone (free T) with health care utilization and costs at baseline and five-year follow-up (N = 1210), implementing multivariable-adjusted econometric models.

**Results:** Cross-sectional analyses showed no association of TT, SHBG, or free T with hospitalization or total health costs (outpatient as well as inpatient costs). Prospective analyses revealed an inverse association of baseline SHBG with follow-up total health care costs (% change per standard deviation (SD): −26.2%, 95% confidence interval (CI): −42.2%; −8.9%) and inpatient costs (% change per SD: −26.5%, 95% CI: −45.5%; −2.5%). Baseline free T was positively associated with total health care costs at the five-year follow-up (% change per SD: +37.7%, 95% CI: +4.6%; +81.4%).

**Conclusions:** In this first cost analysis among women from the general population, we observed no association of androgen serum concentration with health care utilization and costs. However, baseline SHBG appeared to be inversely correlated and free T positively correlated with long-term health care costs.

© 2016 Elsevier Ireland Ltd. All rights reserved.

## 1. Introduction

Despite the emerging observational evidence suggesting independent associations of sex hormone concentrations, especially serum androgens, with increased cardiometabolic risk factor burden in women [1], no studies to date have specifically addressed the impact of androgens on health services utilization and costs. Given the observed associations of high total testosterone (TT) and low sex hormone-binding globulin (SHBG) with prevalent cardiometabolic risk factors including obesity, hypertension, metabolic syndrome, and type 2 diabetes mellitus [2,3], adverse

sex hormone profiles may hold the potential to cause considerable short- and long-term excess health care costs. Thus, we investigated cross-sectional and prospective associations of TT, SHBG, and free T concentrations with health care utilization and costs according to a well-established analytical protocol [4], using data from a large population-based sample of women from the general population.

## 2. Methods

Data from the population-based cohort Study of Health in Pomerania (SHIP) in north-eastern Germany were used, with details of the study design, recruitment procedure, and assessments being published previously [5]. The net baseline sample comprised 6265 eligible individuals (3160 women) with German citizenship and main residency in the study area, whereof 4308 (2192 women) aged 20–80 years finally participated between 1997 and 2001

\* Corresponding author at: Institute of Clinical Chemistry and Laboratory Medicine, University Medicine Greifswald, Ferdinand-Sauerbruch-Strasse, D-17475 Greifswald, Germany.

E-mail address: [robin.haring@uni-greifswald.de](mailto:robin.haring@uni-greifswald.de) (R. Haring).

(response 68.8%). Of the 2192 female baseline participants, we excluded women due to pregnancy (N = 18), self-reported bilateral oophorectomy (N = 52), missing hormone data and/or covariable data (N = 601), yielding a final baseline study population of 1521 women. At the five-year follow-up, 1210 repeatedly examined baseline participants were available for prospective analyses. All participants gave informed written consent. The study was monitored by an institutional review board of independent scientists. The study protocol is consistent with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the University of Greifswald.

Waist circumference (WC) was measured to the nearest 0.1 cm using an inelastic tape midway between the lower rib margin and the iliac crest in the horizontal plane, with the subject standing comfortably with weight distributed evenly on both feet. Systolic and diastolic blood pressures were measured using a digital blood pressure monitor (HEM-705CP, Omron Corporation, Tokyo, Japan). Hypertension was defined as systolic  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg or use of antihypertensive medication (ATC codes C02). Trained medical staff collected information on socio-economic characteristics, lifestyle, medication use, and health care utilization during a standardized personal interview. Participants responded to a list of 18 different types of physicians and specialists. Inpatient service was measured by asking the participants if they had been hospitalized at least once in the past year and were further probed for the number of hospitalized days during the past year if they answered affirmatively. Self-reported information on number of outpatient visits and inpatient days were used to estimate annual costs based on the recommendation of the German Working Group on Methods in Health Economic Evaluation with unit costs reported in year 2015 Euro [6]. Original costs were inflated to 2015 using the Consumer Price Indices for health care in Germany [7].

For the laboratory examinations, non-fasting blood samples were drawn from the cubital vein in the supine position between 07:00 a.m. and 07:00 p.m. Serum TT concentrations were measured from frozen aliquots using a validated routine liquid chromatography–tandem mass spectrometry (LC–MS/MS) method [8]. The lower limit of quantitation was 0.25 nmol/L and the intra- and inter-assay coefficients of variation were <10% over the measurement range of 0.3–35 nmol/L. Serum SHBG concentrations were measured on an Advia Centaur (Siemens, Eschborn, Germany) with an inter-assay coefficient of variation of 6.6% at the 27.1 nmol/L level, 7.6% at the 48.2 nmol/L level, and 7.7% at the 52.3 nmol/L level. Measured TT and SHBG concentrations were used to calculate free T according to the formula by Vermeulen et al. [9].

### 2.1. Statistical analysis

We used a generalized linear model (GLM) with gamma distribution and a log link to account for the skewness of total and outpatient costs [10]. Estimates were presented as percent changes (i.e.  $\exp[\text{coefficient}]$  per SD in TT, SHBG, and free T, respectively). Logistic regression models were used to estimate odds ratios (OR) and corresponding 95% confidence intervals (95% CI) for hospitalization. Two-part models with a logistic model of any hospitalization and a gamma–GLM for positive costs were used for inpatient costs [10]. Models were adjusted for age, WC, smoking status, years of education, and income. We performed sensitivity analyses to address missing values, drop-out, and deaths. Cross-sectional data were multiple imputed using chained equations, with 50 imputed datasets [11]. Possible informative censoring of follow-up costs from death was taken into account by using a joint model [12]. Results from multiple imputation and joint modelling did not substantially differ from complete-case analysis. Stata 13.1

**Table 1**  
Baseline characteristics of the study sample (N = 1521 women).

Characteristic	
Age, years	48.0 (35.0; 61.0)
Educational level, years of schooling	
<10	37.1
=10	47.0
>10	15.9
Equalized household income, Euro	2625 (1625; 3750)
Smoking	
Never-smoker	50.4
Ex-smoker	21.8
Current smoker	27.8
Daily alcohol consumption, g/d	3.29 (0.65; 7.86)
Physically active, %	37.7
Waist circumference, cm	81.5 (72.8; 92.0)
Systolic blood pressure, mmHg	127.3 (115.0; 144.0)
Diastolic blood pressure, mmHg	81.0 (73.7; 88.0)
Hypertension, %	42.6
Total testosterone, nmol/L	0.77 (0.55; 1.09)
Sex hormone-binding globulin, nmol/L	82.9 (57.8; 124.2)
Free testosterone, nmol/L	0.70 (0.45; 1.07)
Annual total costs, Euro <sup>a,b</sup>	298.5 (4.5), 1273.9 (4165.6)
Annual outpatient costs, Euro <sup>a,b</sup>	205.1 (2.6), 291.0 (321.2)
Annual inpatient costs, Euro <sup>a,b</sup>	4914.0 (2.4), 7364.3 (8753.9)
Hospitalizations (last year), %	13.4

<sup>a</sup> Data are median (p25, p75), geometric mean (standard deviation).

<sup>b</sup> Arithmetic mean (standard deviation) or percentages.

<sup>\*</sup> Inpatient costs of those with hospitalization during the last year.

SE/MP6 was used for all statistical analyses (Stata Corporation, College Station, TX, USA).

## 3. Results

Baseline characteristics of the study sample of 1521 women were presented in Table 1. Multivariable-adjusted cross-sectional analyses yielded no association of TT, SHBG, or free T with health care utilization and costs including total costs, outpatient costs, inpatient costs, and risk of hospitalization. In multivariable-adjusted prospective analyses of five-year follow-up data, baseline SHBG showed an inverse association with follow-up total health care costs (% change per SD: –26.2%) and inpatient costs (% change per SD: –26.5%). Additionally, baseline free T was positively associated with increased total health care costs at the five-year follow-up (% change per SD: +37.7%). Fig. 1 illustrates the associations of baseline SHBG and free T with long-term total health care costs. In contrast, TT was not associated with health care utilization and costs in neither cross-sectional, nor prospective analyses (Table 2 and Fig. 1). Sensitivity analyses including stratified analyses by menopausal status (pre- vs. post-menopausal women) did not change the results substantially (data not shown).

## 4. Discussion

The present study examined the association of TT, SHBG, and free T with health care utilization and costs in a population-based cohort of 1521 women aged 20–80 years. Although we detected no consistent associations across cross-sectional analyses, low SHBG and high free T concentrations at baseline predicted increased total costs and inpatient costs at five-year follow-up, independent of socio-economic and lifestyle factors.

The absent association of TT with health care utilization and costs in women adds to the conflicting results shown in more recent observational studies. While some studies related higher TT to adverse cardiovascular health [3], a 12-year follow-up study of 639 post-menopausal women reported an increased risk of coronary

Download English Version:

<https://daneshyari.com/en/article/1917010>

Download Persian Version:

<https://daneshyari.com/article/1917010>

[Daneshyari.com](https://daneshyari.com)