



# Long-term processed and unprocessed red meat consumption and risk of heart failure: A prospective cohort study of women ☆,☆☆



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## ABSTRACT

**Background:** Epidemiologic studies of red meat consumption in relation to risk of heart failure (HF) are limited. We examined the associations between long-term unprocessed red meat and processed red meat consumption and incidence of HF in women.

**Methods:** The population-based prospective Swedish Mammography Cohort included 34,057 women, aged 48–83 years, with no history of HF or ischemic heart disease at baseline (in 1997). Meat consumption was assessed using a self-administered food-frequency questionnaire (FFQ) in 1997 as well as FFQ administered in 1987–90. Cox proportional hazard regression models were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs).

**Results:** During a mean follow-up of 13.2 years, 2806 women were diagnosed with HF. Consumption of processed meat (FFQ 1997) was statistically significant positively associated with HF incidence. Women who consumed  $\geq 50$  g/day processed red meat compared to those who consumed  $<25$  g/day had a 1.23 (95% CI: 1.09–1.39,  $P$ -trend = 0.003) higher risk of HF. Long-term high consumption of processed red meat (average from 1987 to 1997)  $\geq 50$  g/day in comparison to  $<25$  g/day was associated with HR: 1.30 (95% CI: 1.05–1.60,  $P$ -trend = 0.002). Women who consistently consumed (in both 1987 and 1997)  $\geq 50$  g/day vs.  $<25$  g/day had a 1.78 (95% CI: 1.00–3.16) higher risk of HF. Consumption of unprocessed meat was not associated with increased risk of HF incidence.

**Conclusions:** Findings from this prospective study of women indicate that processed red meat, but not unprocessed red meat, consumption is associated with an increased risk of HF incidence.

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## 1. Introduction

About 5.7 million people in the United States suffer from heart failure (HF) [1], the corresponding estimate for the UK is 800,000 people [2]. According to the American Heart Association forecasts, the number of incidence of HF will increase an additional 3 million from 2010 to 2030, and nation's cost of medical care, medications, and loss of productivity will increase almost 3-fold, from \$34 to \$95 billion [3]. Identification of

factors that affect the risk of HF and effective prevention of spreading the disease is necessary to limit the growing burden.

The results of recent systematic reviews and meta-analyses indicate that high consumption of red meat or processed red meat is related to increased risk of coronary heart disease (CHD) [4], stroke [5] as well as increased CVD [6] and all-cause mortality [7]. Three previous prospective studies [8–10] have examined total red meat consumption in relation to HF incidence with partly inconsistent results. To the best of our knowledge, only one study [10] assessed the association with HF incidence separately for unprocessed and processed meat, while none assessed this risk in women or considered long-term red meat consumption. Importantly, as only processed meat, but not unprocessed meat, was associated with increased risk of HF in the study on men [10] – possibly explaining previous inconsistent results for total meat – it is essential to explore this in women, also at high risk of developing HF.

Therefore, in the large population-based prospective Swedish Mammography Cohort we evaluated the associations of unprocessed red meat and processed red meat consumption with HF incidence in

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women. We also assessed the association based on long-term red meat consumption.

## 2. Methods

### 2.1. Study population

The Swedish Mammography Cohort (SMC) was established between 1987 and 1990. All women born between 1914 and 1949 and residing in Uppsala and Västmanland counties in central Sweden were invited to participate and asked to complete a questionnaire (response rate 74%). In 1997 to update the information about food consumption and life-style factors, the women who were still alive and living in the study area were sent a second questionnaire (response rate 70%). In the present study, the data collected in 1997 was used as baseline because information about certain risk factors important for HF development, e.g. smoking habits and physical activity, was not obtained in the first questionnaire in 1987–90.

Of the 39,227 women who returned the questionnaire in 1997, we excluded those with missing or incorrect national identification number, those with implausible values for total energy intake ( $>3$  standard deviations from the mean value for log-transformed energy), those with pre-baseline diagnosis of cancer (other than non-melanoma skin cancer), ischemic heart disease and HF ( $n = 3789$ ). Moreover, women with missing data for unprocessed red meat or processed red meat consumption ( $n = 1381$ ) were excluded. After these exclusions, a total of 34,057 women remained for the analysis. The study was approved by the ethics committees of Uppsala University Hospital and the Karolinska Institutet (Stockholm); women's response to the questionnaire constituted the participants' informed consent.

### 2.2. Assessment of diet and other exposures

The self-administered questionnaires completed at baseline (in 1997) included nearly 350 items on diet and other life-style factors. Diet was assessed with a 96-item food-frequency questionnaire (FFQ), which included questions about commonly consumed food items among others about consumption of unprocessed and processed red meat. Participants were asked to indicate how often, on average, they had consumed various foods over the previous year. Frequency of consumption was predefined from "never/seldom" to "3 or more times per day". The frequencies of red meat consumption were converted to gram per day by multiplying the frequency of consumption of each food item by appropriate age-specific portion sizes. We categorized meat consumption into unprocessed red meat or processed red meat. Unprocessed meat included three food items: pork, beef/veal and minced meat, while processed meat included four food items: sausages/hot dogs, cold cuts (ham/salami), blood pudding and liver pâté. The long-term consumption of red meat was estimated for each participant by calculating the average unprocessed, processed and total red meat consumption from the questionnaires in 1987–90 and in 1997. The FFQ has been validated for nutrients using fourteen 24-h recall interviews among 248 Swedish respondents aged 40–74 years from the study area [11]. The mean Spearman correlation coefficients between estimates from the FFQ and 24-h recall interviews were 0.65 for macronutrients and 0.62 for micronutrients.

We also collected data about education, smoking status, body weight and height, physical activity, history of hypertension and high cholesterol levels, aspirin use, family history of myocardial infarction before age 60 years, and alcohol drinking habits. Body mass index (BMI) was calculated by dividing the weight (kg) by the square of height (m). Pack-years of smoking were calculated by number of packs of cigarettes smoked per day multiplied by number of years smoking. The total physical activity score, measured as metabolic equivalents (MET h/day), was defined by time spent at various activities multiplied by their typical energy expenditure, as was described in detail by Norman et al. [12,13].

### 2.3. Case ascertainment

Cases of incident HF were ascertained by linkage of the study cohort with the Swedish Patient Register and the Cause of Death Register considered almost 100% complete [14]. Events of HF were defined according to the International Classification of Diseases and Related Health Problems, 10th Revision (ICD code I50 and I11.0). In the present study, we included the first HF event recorded in the registers listed either as the primary diagnosis or at any diagnosis position [15].

### 2.4. Statistical analysis

Study participants were followed from September 15, 1997, to the date of the first HF diagnosis, death or the end of the study follow-up period (December 31, 2011), whichever came first. We used Cox proportional hazard regression models to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) of HF incidence by three categories of unprocessed and processed red meat consumption ( $<25$ ,  $25$ – $49.9$  and  $\geq 50$  g/day) and three categories of total red meat consumption ( $<50$ ,  $50$ – $99.9$  and  $\geq 100$  g/day), and by 50 g/day-increment of consumption of unprocessed, processed and total red meat. Women in the lowest category of red meat consumption were used as the reference group.

The multivariate models included the following variables: age (continuous), education (less than high school, high school, or university), smoking status and pack-years of smoking (never; past  $<20$ ,  $20$ – $39$ ,  $\geq 40$  pack-years; current  $<20$ ,  $20$ – $39$ ,  $\geq 40$  pack-years), BMI ( $<20$ ,  $20$ – $24.9$ ,  $25$ – $29.9$ ,  $\geq 30$  kg/m<sup>2</sup>), total physical activity (MET h/day, quintiles), aspirin use (yes or no), family history of myocardial infarction before 60 years of age (yes or no), intake of energy (kcal/day, continuous) and consumption of alcohol, whole grain products, fruit, vegetables and fish (g/day, quintiles). Results for unprocessed red meat and processed red meat consumption were based on mutually adjusted models. All covariates were prespecified and included in the models because they are known risk factors of CVD including HF or potentially related to HF and red meat consumption.

The proportional hazards assumption was met for all variables by regressing scaled Schoenfeld residuals against survival time. To calculate  $P$ -values for linear trend, the continuous values of unprocessed, processed and total red meat consumption were used.

The statistical analyses were performed by using SAS version 9.2 (SAS Institute Inc, Cary, NC). All reported  $P$ -values are from two-sided statistical test, and statistical significance was taken as  $P \leq 0.05$ .

## 3. Results

During a mean of 13.2 years of follow-up (447,898 person-years), we ascertained 2806 cases of first event of HF diagnosis. The estimated mean of total red meat consumption was  $63 \pm 41$  g/day, unprocessed red meat was  $34 \pm 24$  g/day and processed red meat was  $30 \pm 26$  g/day in 1997. Of note, the consumption of unprocessed red meat in 1987 was higher (mean:  $47 \pm 29$  g/day) than in 1997, while consumption of processed red meat was lower  $12 \pm 11$  g/day. The Spearman's correlation between unprocessed and processed meat consumption in 1997 was 0.32. In general, women in the highest category of unprocessed, processed and total red meat consumption were younger and less likely to have a university education, but were more likely to have a history of hypertension compared with those in the lowest category (Table 1). Moreover, women who reported high unprocessed, processed and total red meat consumption also had higher intake of energy, whole grain products, fruit, vegetables and fish consumption.

Processed meat, but not unprocessed meat, consumption was positively associated with risk of HF (Table 2). Compared with women in the lowest category of processed red meat consumption ( $<25$  g/day), the multivariable-adjusted HR for those in the highest category ( $\geq 50$  g/day) was 1.23 (95% CI: 1.09–1.39,  $P$ -trend = 0.003); consuming moderate amount of processed meat ( $25$ – $49.9$  g/day) was not associated with risk

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