



**Karolinska  
Institutet**

**Institutet för Miljömedicin**

# Antioxidants from Diet and Supplements in Relation to Cardiovascular Disease

**AKADEMISK AVHANDLING**

som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i Hillarpsalen, Retzius väg 8

**Fredagen den 15 juni, 2012, kl 13.30**

av

**Susanne Rautiainen Lagerström**

*Huvudhandledare:*

Professor Alicja Wolk  
Karolinska Institutet  
Institutet för Miljömedicin

*Fakultetsopponent:*

Professor Serge Hercberg  
University of Paris XIII  
Conservatoire National des Arts et Métiers

*Bihandledare:*

Professor Ralf Morgenstern  
Karolinska Institutet  
Institutet för Miljömedicin

*Betygsnämnd:*

Professor Yudi Pawitan  
Karolinska Institutet  
Institutionen för Medicinsk Epidemiologi och Biostatistik

Professor Mai-Lis Hellénius  
Karolinska Institutet  
Institutionen för Medicin

Professor Åke Bruce  
Uppsala Universitet  
Professor Emeritus

**Stockholm 2012**

## **Abstract**

Many epidemiological studies have reported an inverse association between fruit and vegetable consumption and cardiovascular diseases (CVD). Because fruits and vegetables are high in antioxidants they were hypothesized to be one the factors responsible for the protective mechanisms. However, studies focusing on single antioxidants such as vitamin C, vitamin E and beta-carotene have reported inconsistent results. In diet there is a wide range of substances present with antioxidant properties. Total Antioxidant Capacity is a concept aiming to measure the capacity from all present antioxidants in reducing reactive species by taking into account synergistic and antagonistic interactions. Multivitamin supplements are another source of antioxidants including vitamins and sometimes minerals usually in doses close to recommended daily allowances. A common belief is that multivitamin are good substitute for dietary derived nutrients and may help prevent CVD.

The aims with this thesis were to: 1) examine the validity and reproducibility of food-frequency questionnaire (FFQ)-based Total Antioxidant Capacity estimates. 2) examine whether Total Antioxidant Capacity of diet is associated with the risk of myocardial infarction and stroke among women and if the association is different between CVD-free women and women with CVD history at baseline. 3) examine whether multivitamin supplement use is associated with the risk of myocardial infarction and if the association is different between CVD-free women and women with CVD history at baseline. 4) examine whether multivitamin supplement use is associated with coronary heart disease (CHD) by quantitatively summarizing accumulated evidence with a meta-analytic approach.

The main contributors to Total Antioxidant Capacity of diet were fruits and vegetables (44%), whole grains (18%) and coffee (14%). The FFQ-based Total Antioxidant Capacity estimate, as measured with Oxygen Radical Absorbance Capacity (ORAC) assay, correlated with ORAC in whole plasma ( $r=0.29$ ) and ORAC in the lipophilic part of plasma ( $r=0.32$ ). Total Antioxidant Capacity of diet was inversely associated with the risk of myocardial infarction (HR in the highest quintile as compared to the lowest = 0.80, 95% CI: 0.67-0.97) and total stroke (HR in the highest quintile as compared to the lowest = 0.83, 95% CI: 0.70-0.99) among women who were CVD-free at baseline. Among women with CVD history Total Antioxidant Capacity of diet was not associated with myocardial infarction and total stroke. Multivitamin use was inversely associated with the risk of myocardial infarction only among CVD-free women and not among women with CVD history. The summarized evidence from 5 prospective cohort studies indicated a 21% (95% CI: 10-30%) decreased CHD risk among CHD/CVD-free study populations at baseline.

Taken together, these results suggest that Total Antioxidant Capacity may be of importance in primary prevention of myocardial infarction and stroke. Multivitamin supplement use may be of importance in primary prevention of CHD.