



Habitual chocolate consumption and the risk of incident heart failure among healthy men and women

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Abstract *Background:* We aimed to examine the association between chocolate intake and the risk of incident heart failure in a UK general population. We conducted a systematic review and meta-analysis to quantify this association.

Methods and results: We used data from a prospective population-based study, the European Prospective Investigation into Cancer (EPIC)-Norfolk cohort. Chocolate intake was quantified based on a food frequency questionnaire obtained at baseline (1993–1997) and incident heart failure was ascertained up to March 2009. We supplemented the primary data with a systematic review and meta-analysis of studies which evaluated risk of incident heart failure with chocolate consumption. A total of 20,922 participants (53% women; mean age 58 ± 9 years) were included of whom 1101 developed heart failure during the follow up (mean 12.5 ± 2.7 years, total person years 262,291 years). After adjusting for lifestyle and dietary factors, we found 19% relative reduction in heart failure incidence in the top (up to 100 g/d) compared to the bottom quintile of chocolate consumption (HR 0.81 95%CI 0.66–0.98) but the results were no longer significant after controlling for comorbidities (HR 0.87 95%CI 0.71–1.06). Additional adjustment for potential mediators did not attenuate the results further. We identified five relevant studies including the current study ($N = 75,408$). The pooled results showed non-significant 19% relative risk reduction of heart failure incidence with higher chocolate consumption (HR 0.81 95%CI 0.66–1.01).

Conclusions: Our results suggest that higher chocolate intake is not associated with subsequent incident heart failure.

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Introduction

Cocoa, one of the main ingredients in plain chocolate, is an important dietary source of flavonoids which are believed to have cardiovascular benefits. Both observational and trial evidence have shown that chocolate consumption is associated with a reduction in blood pressure [1–4]. This reduction in blood pressure is thought to be due to enhancement of endothelial nitric oxide production [5,13] and inhibition of angiotensin converting enzyme [6,7]. Flavonoids also increase antioxidant capacity and diminish the production of oxidative products in the plasma [8] and cocoa (one of the ingredients) has been shown to inhibit oxidation of low density lipoprotein (LDL) [9]. Moreover, the intake of chocolate and cocoa-based products increases high density lipoprotein (HDL) cholesterol [10], reduces inflammation [11,12] and inhibits platelet aggregation [13]. Indeed, we have recently reported that habitual chocolate consumption is associated with lower cardiovascular risk [14]. These factors in combination may reduce the incidence of heart failure with higher chocolate consumption.

Existing observational studies evaluating the risk of heart failure with chocolate consumption show conflicting results and are not directly applicable to the general population. They were conducted in highly selective populations such as women who underwent mammography [15], older women who received calcium therapy [16], in those after myocardial infarction [17], and among male physicians [18]. To date, there has not been a study on the general population which evaluates the relationship between habitual chocolate intake and subsequent risk of heart failure.

In this paper, we report results from a large prospective UK population study, the European Prospective Investigation into Cancer-Norfolk (EPIC-Norfolk), and quantify the effect of chocolate consumption on heart failure incidence by conducting a systematic review and meta-analysis, including the current study.

Methods

EPIC-Norfolk cohort study

The study methods of the European Prospective Investigation into Cancer (EPIC)-Norfolk have been previously described in detail [19]. In brief, this is a prospective population study of 25,639 men and women, resident in Norfolk, United Kingdom (99.6% white Caucasian). A baseline survey was conducted between 1993 and 1997. Participants completed a health and lifestyle questionnaire and attended a health examination at their general practitioner's clinic where a non-fasting venous blood sample was taken and stored.

The data collection methods are described in [Appendix 1](#). Measurements of height, weight, body mass index; laboratory methods; ascertainment of education status, social class, self-reported physical activity, smoking status, alcohol consumption, and identification of participants'

co-morbid conditions using questionnaires have been described in previous studies [19–22]. A food frequency questionnaire (FFQ) was used to assess overall diet in the past year [23,24].

A one year recall of chocolate consumption was estimated using three questions from the FFQ and these questions were consumption of: “Chocolates singles or squares” (average portion size of 8 g), “Chocolate snack bars, e.g. Mars, Crunchie” (average portion size of 50 g) and “Cocoa, hot chocolate (cup)” (average portion size of 12 g powder weight). The amount of chocolate product eaten (grams/day) was derived from multiplying the frequency categories by the portion size. The sum of the weights of these food items consumed, rather than their flavonoid or cocoa content, formed the measure of exposure. Chocolate intake ranged from 0 to 348 g/d. We excluded participants with chocolate intake greater than 100 g/d ($n = 68$), since generalization of the results to such high quantities seemed unjustified. Equally, errors (i.e. outliers) relating to participant's poor comprehension of FFQs in general, or specifically the questions on chocolate products, were hereby minimized.

Ascertainment of heart failure incidence

Hospital admissions for participants were identified using the participant's unique National Health Service number and linking this to the ENCORE (East Norfolk Commission REcord) database. All participants were flagged for death certification at the UK Office of National Statistics, ascertaining vital status for the entire cohort. Incident heart failure cases were ascertained by using death certificate data and hospital record linkage using the “International Classification of Disease-10” (ICD10) code I50 with virtually complete follow up [22]. Heart failure ascertainment has been previously validated and reported [25]. We reported data with follow-up up to March 2009, an average of 12.5 years. The study was approved by the Norwich District Health Authority Ethics Committee. All participants provided signed informed consent.

Statistical analysis

Statistical analysis was conducted using STATA 14.0 (StatCorp, College Station, USA). We categorized chocolate consumption into quintiles. The participants in the first quintile consumed no chocolate. Baseline characteristics were compared between the quintile groups of chocolate consumption using one-way analysis of variance (ANOVA) for continuous variables and chi-squared test for categorical variables. We excluded participants with prevalent baseline heart failure (where prevalent heart failure was defined using self-reported intake of drugs recommended for heart failure at the time of the survey, essentially loop diuretics in combination with digitalis or angiotensin converting enzyme inhibitors [22,26]), cancer as well as participants with missing data on any of the variables included in the models. The bottom quintile (i.e. non-consumers) was used as the reference category for all

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