INTRODUCTION

The Committee on Medical Aspects of Food and Nutrition Policy (COMA) recommended in 1998 that high consumption of red and processed meat should be reduced due to the risk of colorectal cancer (1). Similarly, the 2005 US Dietary Guidelines for Americans recommend that the intake of red and processed meat be moderated due to their impact on plasma cholesterol (2). The latter recommendation is based on the ‘diet-heart hypothesis’ from the 1930s (3). It states that a diet rich in high saturated fats and cholesterol and poor in low polyunsaturated fats leads to high plasma cholesterol levels, which favor the development of atherosomatous plaques, arterial narrowing and cardiovascular diseases (CVDs). Its major opposition is the fact that total cholesterol is present in serum not only as low-density lipoprotein (LDL) cholesterol, intermediate-density lipoprotein (IDL) cholesterol and very low-density lipoprotein (VLDL) cholesterol, which are positively correlated with the risk of CVDs, but also as high density lipoprotein (HDL) cholesterol, which is inversely related to the development of CVDs.

Ecological studies have discovered the association between low saturated fat intakes and low coronary death rates (CDRs) in less industrialized countries in comparison with high saturated fat intakes and high CDRs in highly industrialized countries (4-10). Migrant studies investigating CDRs in the populations of
Japanese living in Japan, Honolulu and San Francisco demonstrated the associations between their saturated fat intakes and their age adjusted incidence of CDRs (11,12). The Multiple Risk Factors Intervention Tri-
al showed the relationship between the rise in serum cholesterol levels and rise in CDRs (13-18). Case-con-
trol studies have reported an increased risk of myocardial infarction (MI) in Italian women taking high lev-
els of meat, butter and total fat and low levels of fish, vegetables and fruits (19) and in Greek women cook-
ing on margarine (20). On the contrary, various cohort studies found men and women with higher total en-
ergy intakes to have lower CDRs, which they tended to explain by confounding with their higher levels of physical activity (21-25).

A meta-analysis conducted by Lewington et al., based on 61 prospective observational studies from West-
nern Europe and North America and including 900,000 adults without previous disease has shown that age, sex, and blood pressure could modify the associations of total LDL and HDL cholesterol levels with vascular mortality (26). A prospective cohort study by Clarke et al. that included 5,360 men, mean age 77, followed for seven years, showed that vascular mortality was posi-
tively associated with logarithmic C-reactive protein, fibrinogen and total/HDL cholesterol, and inversely with albumin (27). Another study revealed that heart disease mortality was positively associated only in men without CVDs and inversely in men with CVDs (28).

Another prospective cohort study conducted by Clarke et al. in 18,863 men employed in civil service in Lon-
don, England, examined at entry in 1967-1970 and fol-
lowed for 38 years, showed an association of baseline smoking, blood pressure and serum cholesterol levels with 10- to 15-year shorter life expectancy from age 50 (29). Numerous epidemiological surveys of systol-
ic blood pressure (SBP) levels in different populations linked diets containing little meat and fish to low mean blood pressures (30).

Sacks et al. and Sacks and Kass have proposed a relation-
tion between SBP levels and intake of food from ani-
mal sources (31,32). Steffen et al. observed that plant food intake was inversely related, dairy intake was not related, while red and processed meat intakes were posi-
tively related to elevated blood pressure (33). Miura et al. examined relations of food intakes to SBP changes in the Chicago Western Electric Study and found that men with a higher intake of red and white meat had a significantly greater increase in blood pressure, while higher intakes of vegetables, fruits and fish were re-
lated to less of an increase in SBP and diastolic blood pressure (DBP) over time (34). Appel et al. designed a clinical trial called Dietary Approaches to Stop Hyper-
pertension (DASH) as a multicentre randomized feed-
ing study and thus managed to demonstrate that cer-
tain dietary patterns independently of their sodium content could favorably affect blood pressure in adults with average SBP of less than 160 mm Hg and DBP of 80 to 95 mm Hg (35).

In their case-control study, Kontogianni et al. demon-
strated the red meat intake to be strongly associated with 52% increased odds of acute coronary syndrome (ACS), while white meat intake seemed to be associat-
ed with only 18% likelihood of sustaining CVD events (36). Sinha et al. conducted a prospective cohort study called Diet and Health Study and showed that men and women in the highest versus lowest quintile of red and processed meat intakes had elevated risk of overall mortality and cause-specific mortality from cancer and CVDs (37). Micha et al. conducted a systematic review and meta-analysis of 17 prospective cohort and three case-control studies and showed that the intake of red meat was not associated with either chronic heart dis-
ese (CHD) or diabetes mellitus (DM), processed meat was associated with 42% higher risk of CHD and 19% higher risk of DM, and total meat intake showed in-
termediate associations, while neither meat type intake was associated with stroke (38).

The cited literature is mainly based on the assumption that the effect of meat on vascular risk is mediated only by the effect of saturated fats and dietary cholesterol on blood cholesterol levels. On this track, this paper will look at the associations between the intakes of differ-
ent meat types (red, processed, red + processed, total) and CVD risk factors (BMI, SBP, and plasma total cho-
lesterol (PTC)) according to the British National Diet and Nutrition Survey data set from 2000/1 (NDNS-
DS) (39).

**PATIENTS AND METHODS**

The NDNS public access data set on adults aged 19-
64 carried out in 2000/01 is available on request from the United Kingdom National Statistics Public En-
quiry Service (39). It is comprised of 312,631 individ-
ual food item records from a total of 12,068 person-
days of recording by 1,724 respondents (766 males and 958 females), recorded through weighted intakes for seven days. Records were coded using 4,612 differ-
ent food codes from the NDNS food database of 7,374 codes (39). The main NDNS-DS reports on food in-
takes were not based on full disaggregation of compos-
ite dishes and they were derived by Aston et al. (40).

Primary food constituents were identified according to a set of 45 project-specific food categories. Composite dishes like 'beef, veal and dishes', 'lamb and dishes' or 'meat, meat dishes and meat products' were fully disag-
gregated into primary ingredients (40).
Statistical analysis, which included 766 male and 958 female respondents aged 19 to 64 was conducted by the PASW version 18. Due to their observed adverse influence in the development of CVDs, red (meat from mammals) and processed (meat products) meat intakes were chosen for analysis rather than white (poultry) meat intakes. In order to assess their possible additive or multiplicative effects, the already created red + processed meat intake variable was also included. Finally, in order to evaluate the effects of meat by itself, total meat intakes were chosen as well. Sex and age were chosen as confounding factors due to their known effects on both meat intake and CVDs morbidity and mortality rates. Considering cardiovascular risk factors, BMI was chosen because of both its relevance and robustness. SBP was chosen rather than DBP due to its greater importance in the development of CVDs. PTC was chosen rather than adverse LDL cholesterol or protective HDL cholesterol. On the one hand, LDL cholesterol could not have been chosen because it was not directly measured during data collection, but was only later calculated from PTC by using Friedewald's formula, which has obviously affected its robustness. On the other hand, HDL cholesterol was dismissed because it is currently perceived as a protective factor against CVDs, while the purpose of this paper was to assess adverse factors for the development of CVDs and in this respect, it was not so relevant.

In order to assess the normality of distribution of the seven-day mean total, red + processed, red and processed meat intakes, Smirnov-Kolmogorov tests were performed and histograms of distributions produced. Only, after logarithm (ln) transformation of the cases that remained after dropping the mentioned zero values cases, it was possible to obtain normal distributions. Linear regression was performed in order to assess the potential impact of the red, processed, red + processed and total meat intakes on BMI (weight in kg/height in m²), SBP (mean of two systolic measurements in mm Hg) and PTC (plasma total cholesterol in mm/L) as cardiovascular risk factors, while paying attention to subject age and sex as potential confounders. The mentioned potential confounders were analyzed both independently and in combination and a new age by sex variable was created in order to assess their possible additive or multiplicative effects, while in order to reduce confounding by body size and energy turnover, the energy adjusted meat intakes were used, expressed as g/MJ (grams/mega joule) of total energy recorded over seven days of dietary recording; in order to respond to their lack of normal distribution, their interquartile ranges (IQRs) were used in calculations instead of their standard deviations (SDs). Results were described as significant if their p values were less than 0.05 and as highly significant if their p values were less than 0.01; all p values reported in this paper were obtained by two-tailed tests. Bearing in mind the general robustness of linear regression, it was decided to use the total, red + processed meat, red and processed meat intakes as recorded in the NDNS-DS in all cases, and ln transformations of the mentioned variables after dropping the cases with zero values in linear regression. Linear regression models were built for the mentioned cardiovascular risk factors as a dependent variable and each of the mentioned meat type intakes combined with sex, age and age by sex as independent variables. The preferred model was the one that had the greatest adjusted R² value for the least number of the confounding variables (sex, age, and age by sex). Descriptive statistical analysis showed that BMI had abnormal distribution, so it was ln transformed into lnBMI, while SBP and PTC had normal distributions. As mentioned above, the total, red + processed meat, red and processed meat intakes, and ln transformations of the mentioned variables after dropping the cases with zero values were used in linear regression.

**RESULTS**

Distributions and correlations of the intakes of different meat types are shown in Tables 1 and 2. After linear regression, the preferred models for lnBMI and PTC with particular meat type intakes were those that also included subject age, while for SBP they included both age and sex of respondent. Histograms and scatter plots of the preferred models were produced and showed normality of distribution and independence of residuals. Nonstandardized coefficients (B) for constant, meat type intakes and age and sex were extracted together with their p values. They were used to calculate the effects of IQRs of the meat type intakes on the CVD risk factors analyzed according to the formulas:

\[
\text{lnBMI} = B_0 + B_1 \times \text{age of respondent} \\
+ B_2 \times \text{IQR meat type intakes}
\]

\[
\text{SBP} = B_0 + B_1 \times \text{sex of respondent} \\
+ B_2 \times \text{age of respondent} \\
+ B_3 \times \text{IQR meat type intakes}
\]

\[
\text{PTC} = B_0 + B_1 \times \text{age of respondent} \\
+ B_2 \times \text{IQR meat type intakes}
\]

Results are shown in Table 3.
DISCUSSION

Considering BMI, it should be noted that the effects of different meat type intakes were almost the same for their IQRs with all cases included and for their IQRs after ln transformation of the remaining cases after excluding zero meat intake cases. The mentioned effects were greatest for total meat intake with 1.03 rise in kg/m^2 of the BMI and 1.03 rise in kg/m^2 for the ln transformed values. They were closely followed by the combined red and processed meat intakes with 1.03 and 1.03 rise in kg/m^2 of the BMI and 1.03 rise in kg/m^2 for the ln transformed values. They were closely followed by the combined red and processed meat intakes with 1.03 and 1.03 rise in kg/m^2 of the BMI, respectively, but one should bear in mind that the combined red and processed meat intakes were entirely included in the total meat intakes, of which they formed the greatest part, which explains the observed similarity in their effects. The red and processed meat intakes analyzed as separated categories had almost the same effects of around 1.02 or 1.02 and around 1.02 or 1.01 rises in kg/m^2 of the BMI, respectively, which could be interpreted as their influence just per se, regardless of the methods of their preparation and preservation. By looking at all meat intake effects together, there was no adding or multiplication of the effects between the red and processed meat intakes. As sex of respondents exerted no significant effect and subject age was included in the preferred model in order to address its potential confounding, the observed rise in BMI values by approximately 1 kg/m^2 per IQR of meat intakes could be ascribed to the effects of the mentioned meat intakes. Although the mentioned effects were not striking by their values, they all were statistically highly significant. The only nonsignificant result (p=0.125) was the one for the ln processed meat intake effects, which was also the only result that was slightly lower (1.01) than the others.

Meat intakes had greatest effects on SBP, with approximately 1.5 mm Hg rise per IQR of different meat type intakes. They were slightly bigger for IQRs of the combined red and processed meat intakes with around 1.7 and 1.5 mm Hg than for IQRs of the total meat intakes with around 1.7 and 1.4 mm Hg, respectively. One possible explanation for this discrepancy that a part had bigger effect than the whole could be the potential protective effect of white meat intakes, which were not analyzed separately, but were forming a part of the total meat intakes together with the other two meat types. One cannot continue without commenting that the IQRs of the red meat intakes had bigger effects of around 1.5 and 1.3 mm Hg than the IQRs of the processed meat intakes of around 1.02 and 0.37 mm Hg, respectively. It could be interpreted as a good evidence of the adverse effects of meat intakes on SBP.
just themselves as such and regardless of the contents of salt present in them. On this track, it should be noted that both age and sex of the respondents as potential confounders were included in the preferred models for SBP, which could be used as yet another evidence for the above statement. In this respect, it should be repeated that all the observed effects were statistically highly significant. The only nonsignificant result (p=0.548) was again the one for the ln processed meat intakes, which was now strikingly smaller (0.37) than the other results.

The observed influence of the red meat intake on SBP is in accordance with the cross-sectional epidemiological study conducted by Tzoulaki et al., which included 4680 adults aged 40-59 from 17 population samples from Japan, China, the United Kingdom, and the United States participating in the international collaborative study on macro-/micronutrients and blood pressure (INTERMAP). Their multiple linear regression analyses showed that 102.6 g/24 h (2 SD) higher red meat intake was associated with 1.25 mm Hg higher SBP (41). On this track, one should mention a prospective study conducted by Pan et al. on 37 698 men from the Health Professionals Follow-up Study (1986-2008) and 83 644 women from the Nurses’ Health Study (1980-2008), which proved that red meat consumption was associated with an increased risk of total, CVFs, and cancer mortality, while substitution of other healthy protein sources for red meat was associated with a lower mortality risk (42). A possible explanation for the mentioned connection was suggested by a cross-sectional study conducted by Azadbakhht et al., which included 482 Tehrani female teachers aged 40-60 (43). Their statistical analyses showed that the increased red meat consumption was cross-sectionally associated with a greater risk of metabolic syndrome and inflammation.

Although dyslipidemias are recognized as a risk factor for CVD development and the guidelines for their prevention and treatment propose reduction of red and processed meat intakes (44-46), our linear regression models revealed no association between the mentioned meat intakes and PTC level rise. Half of them even had negative signs, thus suggesting a possible protective influence of the mentioned meat intakes against PTC level rise. However, it should be highlighted that none of the results was statistically significant, except for the one for the ln processed meat intakes (p=0.027), which in this case was much bigger (-0.12) than the other results, and thus different as usual.

One should also take into account the robustness of the cardiovascular risk factors evaluated. BMI was most robust due to its calculation from weight and height, which were easily obtained from the study partici-
m² and SBP by around 1.5 mm Hg, although low, cannot be perceived as trivial effects at the population level. Thus, linear regression proved the existence of the mentioned effects on the individual level as well.

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REFERENCES


SAŽETAK

CRVENO I OBRADIO MESO KAO ČIMBENICI RIZIKA SRČANO-KRVOŽILNIH BOLESTI

B. ATALIĆ, J. TOTH¹, V. ATALIĆ², D. RADANOVIĆ³, M. MIŠKULIN i A. LUČIN⁴

Zavod za javno zdravstvo i primarnu zaštitu, Sveučilište u Cambridgeu, Cambridge, Velika Britanija, ¹Zavod za hitnu medicinu, Zagreb, ²Zavod za javno zdravstvo Osječko-baranjske županije, Osijek, ³Odjel za internu medicinu, Opća bolnica Vukovar i ⁴Dom zdravlja Zagreb Istok, Zagreb, Hrvatska

Cilj: Utvrđivanje mogućih utjecaja konzumacije crvenoga i preradenoga mesa na srčano-krvožilne rizične čimbenike na temelju podataka sadržanih u British National Diet and Nutrition 2000/1 Survey podatkovnome setu za 1724 ispitanika (766 muškaraca i 958 žena).

Metode: Provedena je statistička linearna regresija povezanosti između konzumacije crvenoga, preradenoga, kombinacije crvenoga i preradenoga, te ukupnoga mesa s jedne strane i indeksa tjelesne mase (BMI), sistoličkoga krvnog tlaka (SBP), te ukupnoga plazmatskog kolesterola (PTC) kao srčano-krvožilnih rizičnih čimbenika s druge strane, uz obraćanje pozornosti na dob i spol ispitanika kao moguće utjecajne čimbenike.

Rezultati: Linearna analiza je pokazala da konzumacija ukupnoga mesa, te kombinacije crvenoga i preradenoga mesa uzrokuju porast BMI za oko 1,03 kg/m², dok odvojena konzumacija crvenoga i preradenoga mesa uzrokuje porast SBP za oko 1,02 mm Hg. Najveći utjecaj je opažen kod porasta SBP koji je iznosio 1,7 mm Hg kod konzumacije ukupnoga mesa, te 1,5 mm Hg kod konzumacije crvenoga mesa, te 1,02 mm Hg kod konzumacije preradenoga mesa. Između konzumacije različitih vrsta mesa i razine PTC nije utvrđena nikakva povezanost.

Rasprava i zaključak: Dobiveni rezultati pokazuju da interkvartalni rasponi (IQR) konzumacije navedenih vrsta mesa poviseju BMI za oko 1 kg/m², a SBP za oko 1,5 mm Hg, dok na PTC nemaju nikakav utjecaj.

Ključne riječi: srčano-krvožilne bolesti; srčano-krvožilni rizični čimbenici; indeks tjelesne mase; sistolički krvni tlak; ukupni plazmatski kolesterol