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Original Paper

Diet and Prostate Cancer: a Case–Control Study

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A case–control study, performed in two towns of Serbia (Yugoslavia) from 1990 to 1994, comprised 101 patients with histologically confirmed prostate cancer and 202 hospital controls individually matched by age (±2 years), hospital admittance and place of residence. Dietary information was obtained by using a standard questionnaire. After adjustment for possible confounders, risk factors for prostate cancer appeared to be the highest tertile of protein (odds ratio (OR) = 13.54, 95% confidence interval (CI) = 2.38–77.13), saturated fatty acid (OR = 3.63, 95% CI = 1.03–12.79), fibre (OR = 4.02, 95% CI = 1.38–11.73), and vitamin B12 intake (OR = 2.07, 95% CI = 1.08–3.97); a protective effect was found for the highest tertile of α-tocopherol (OR = 0.15, 95% CI = 0.05–0.53), calcium (OR = 0.37, 95% CI = 0.14–0.99) and iron intake (OR = 0.34, 95% CI = 0.12–0.95). There were significant ($P < 0.05$) linear trends in the odds ratios for α-tocopherol, vitamin B12, calcium and iron. According to logistic regression step by step analysis, risk factors for prostate cancer were dietary intake of retinol equivalent (OR = 1.64, 95% CI = 1.01–2.67) and vitamin B12 (OR = 1.87, 95% CI = 1.15–3.05), and a protective effect was found for dietary intake of iron (OR = 0.40, 95% CI = 0.27–0.58).

Key words: prostate cancer, diet, case–control study

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INTRODUCTION

LITTLE IS known about the aetiology of prostate cancer. A number of risk factors have been identified in past epidemiological studies, although the findings have not always been reproducible. The plausibility of diet having a major role in the aetiology of prostate cancer is supported by certain observations based on descriptive epidemiology of the disease [1], but the results of analytical epidemiological studies have been inconsistent.

This report describes results relating to dietary factors, obtained in a case–control study carried out in Serbia. A quantitative dietary history was used to estimate the weekly intake of different nutrients. Results related to non-dietary factors will be reported separately.

MATERIALS AND METHODS

The study was conducted in two towns of Central Serbia (Kragujevac and Ćuprija) from January 1990 to December 1994. Of 141 patients with histologically confirmed clinical prostate cancer, 12 patients could not be interviewed as they gave incorrect addresses, 9 patients refused to participate, 10 patients were too ill to be interviewed and 9 patients died before we were able to contact them. The final group consisted of 101 prostate cancer patients.

For each case, two hospital controls (202 controls in total) were chosen among patients confirmed as having neither prostate cancer nor other prostate diseases. Those with other malignancies were also excluded. The majority of controls—154 patients, were treated at the hospital because of physical injuries, 11 had asthma, 8 had pneumonia, 8 had a peptic ulcer, 7 had cholecistitis, 6 had angina pectoris, 4 had cirrhosis, 3 had pleuritis and 1 had pancreatitis. All selected controls were interviewed—no one refused to participate. Cases and controls were individually matched by age (±2 years), hospital admittance and place of residence.

Demographic, epidemiological and dietary data were obtained using a standard questionnaire. Dietary information was obtained by a quantitative history approach in which subjects were asked about their usual frequency of

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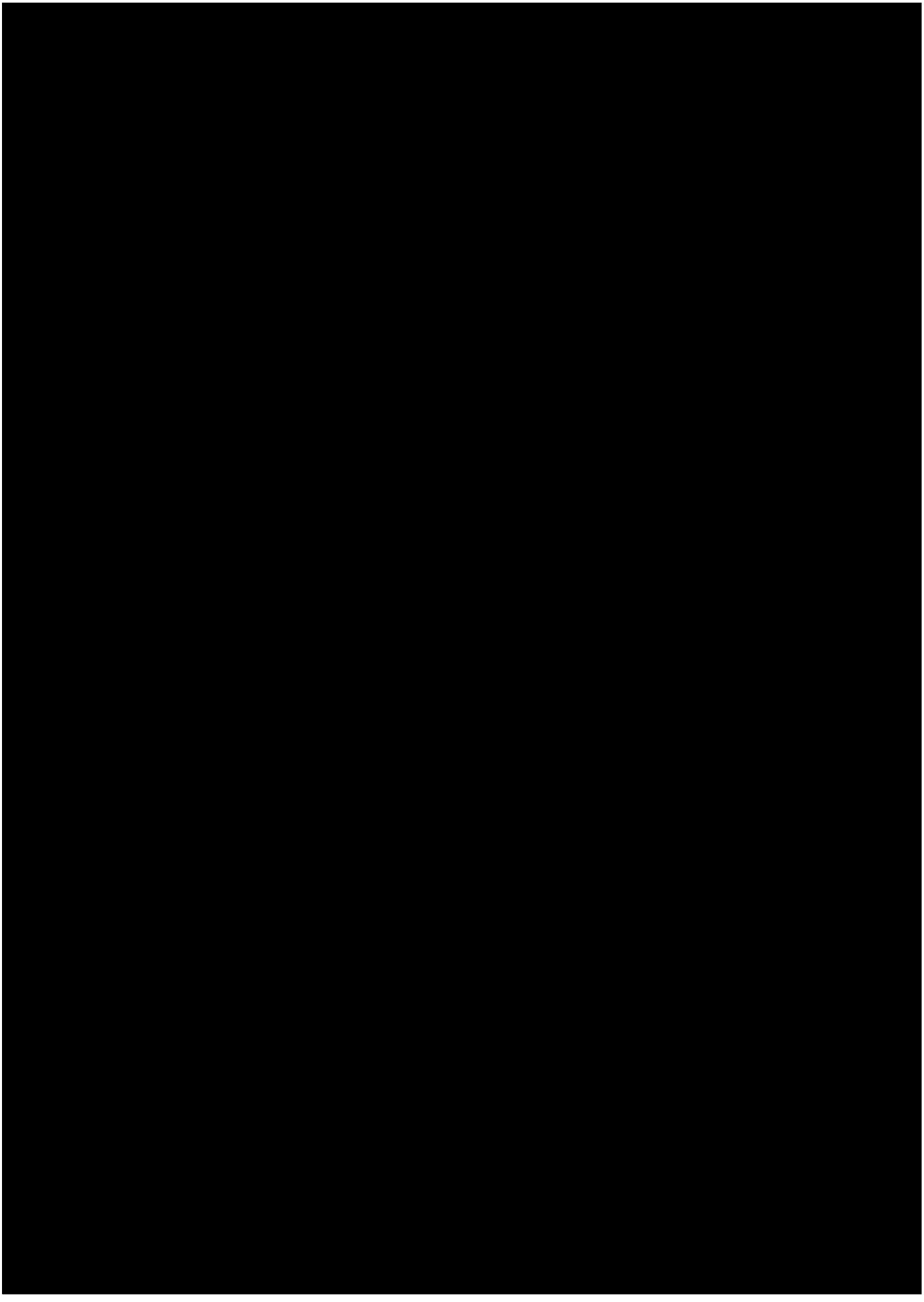

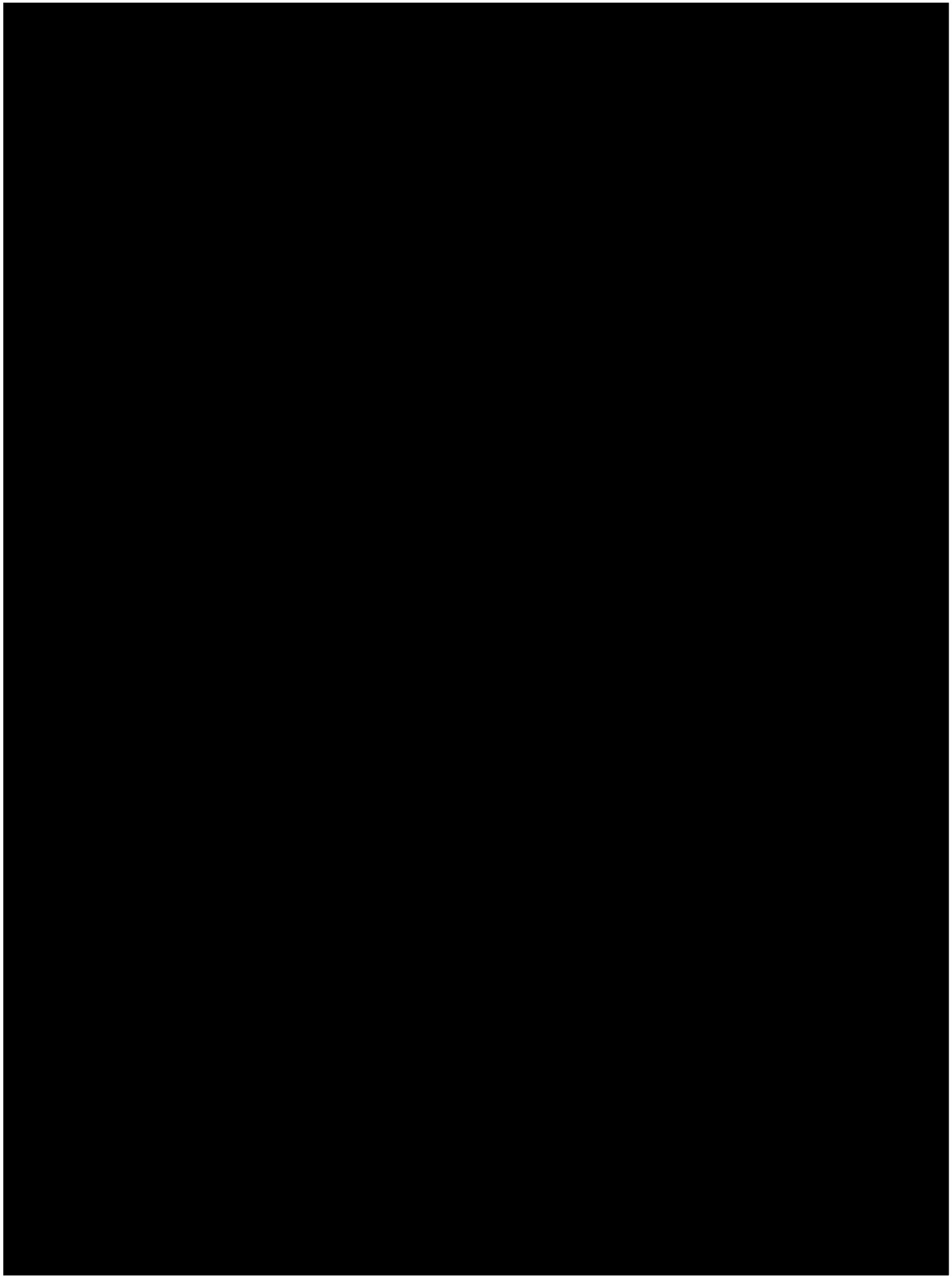

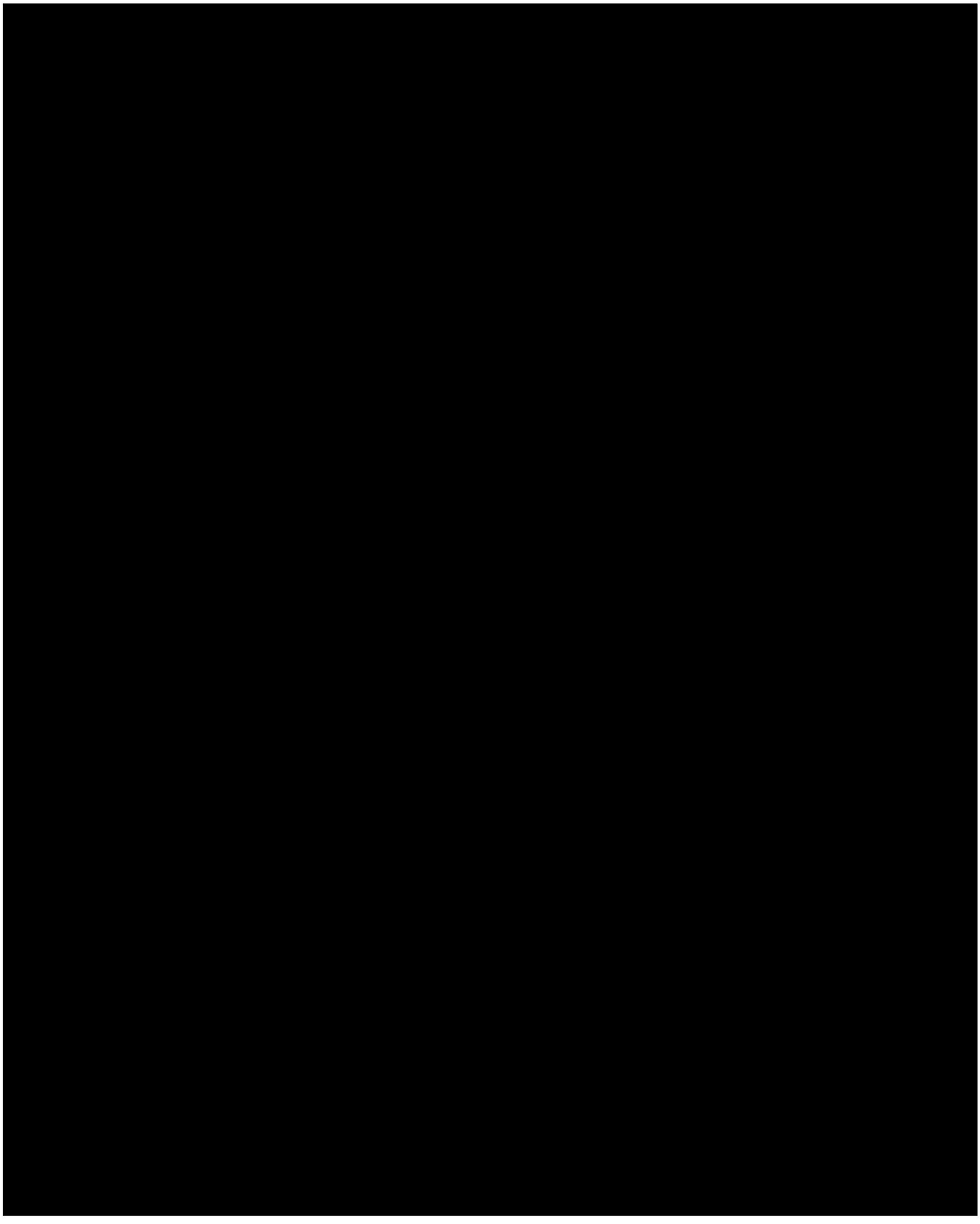

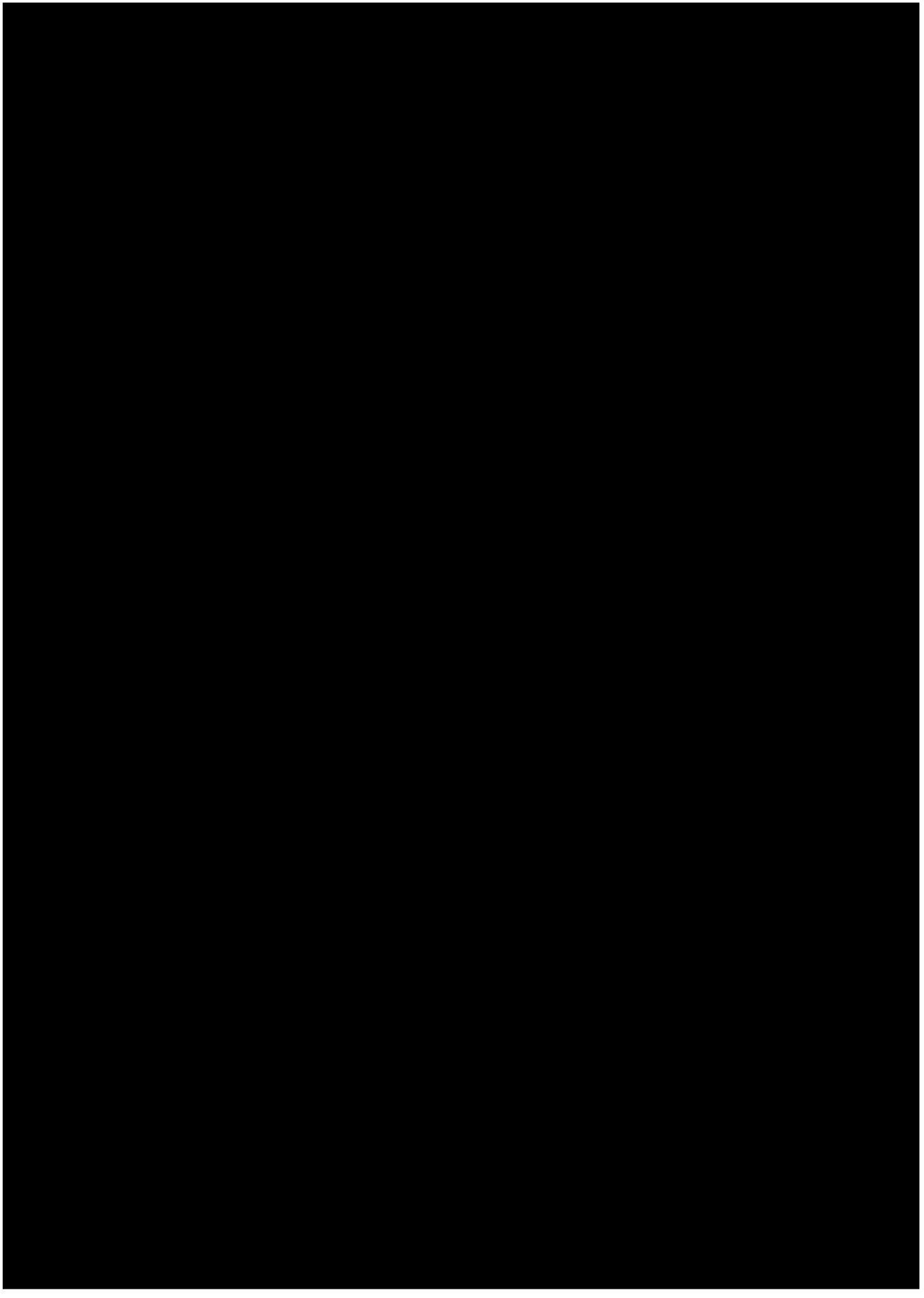

cer, and Hsing and associates [13] also observed no association with consumption of meat, eggs or dairy products.

It has been hypothesised that dietary fat affects cancer occurrence via alteration in the hormone environment. Some experimental data [14, 15] and analysis of hormone levels in the human population provide some corroborative information. A Western diet fed to black South African men increased the urinary excretion of oestrogen and androgens, while the excretion of oestrogen and androgens decreased in black North American men fed a vegetarian diet [16]. Bishop and associates [17] correlated differences in sex hormone levels in 171 twin pairs with differences in reported dietary habits. They found differences in fat intake correlated with differences in testosterone levels.

Which fat component in particular may be responsible for the association with prostate cancer has not yet been established [1]. The association with saturated fat observed in our study had been most frequently found [18, 19] or suggested by the association with animal fat and with meat or dairy products [20]. However, West and associates [21] found a relationship with saturated and unsaturated fat. Giovannucci and associates [11] found that saturated fat, unsaturated fat and α-linolenic acid were associated with advanced prostate cancer risk, but only an association with α-linolenic acid persisted when saturated fat, unsaturated fat, linolenic acid and α-linolenic acid were modelled simultaneously.

Data about the relationship of vitamin A or its precursors, especially beta-carotene, to prostate cancer risk, are also inconsistent both in epidemiological and in animal studies [1]. Our findings that retinol and retinol equivalent are risk factors for prostate cancer, with an odds ratio of around 2.00, is in accordance with many case–control [22–25] studies and some cohort studies [12, 13, 26]. Studies in which an inverse association has been found are also numerous [20, 27, 28]. Methodological differences in study design and dietary survey methods might, in part, explain these inconsistencies, but opposite results were obtained even in studies using the same method for dietary data collection. The suggestion that the effect of vitamin A or its precursors depends on fat intake [28] is not supported by our data, showing a positive effect of retinol equivalent and no effect of carotene, independently of quantity and type of fat consumed. Nevertheless, it is possible that moderate amounts of vitamin A might protect against prostate cancer, while large amounts could enhance the risk [28]. According to a recent report, a trial in the United States involving 18 000 smokers has been discontinued 2 years early after initial results showed that taking vitamin A and beta-carotene as supplements may increase the risk of cancer [29].

Data on the effect of energy intake are also inconsistent. Severson and associates [12] did not find that total energy intake caused an increased risk of prostate cancer. According to the study of Rose and associates [30], prostate cancer mortality rates were only weakly associated with total calorie intake in the 28 countries, due to a strong positive correlation with calories of animal origin. In the study of West and associates [21], energy intake had an odds ratio of 2.5 (95% CI = 1.0–6.5). In our study the highest tertile of total energy intake was a risk factor for prostate cancer after adjustment for possible confounders including protein, total fat, carbohydrate and total sugar.

The positive association between prostate cancer and protein intake found in our investigation was noted in studies of Kolonel and associates [31], Heshmat and associates [32] and Metlin and associates [20], but was not found in other studies [12, 27].

The effect of total caloric intake as well as protein would most likely be through hormones. The positive relationship between prostate cancer and fibre intake found in this investigation would also most likely be through hormones. Lubin and associates [33] found that breast cancer risk decreases with a higher consumption of food rich in fibre, even in those with a high intake of fat and protein. Adlercreutz [34] suggested that breast cancer risk may be favourably influenced by lignans, precursors of which occur in the diet and are associated with fibre component. He hypothesised that the fibre had an anti-oestrogen effect. Since oestrogen has a beneficial effect in the treatment of prostate cancer, it is postulated that a decrease in the oestrogen level could increase the risk of prostate cancer [35]. At the same time, the lower risk of prostate cancer in cirrhotic patients could be the result of hyperoestrogenism that is present in subjects with cirrhosis [36, 37].

There is no literature data on vitamin B12 as a risk factor for prostate cancer. Vitamin B12 is involved in all metabolic processes, but at present we have no adequate explanation for its positive connection with prostate cancer.

The protective effect of vitamin E and iron, observed in the present study, could have a plausible explanation. Vitamin E is known as an intracellular antioxidant [38]. It also stimulates T cells and increases immunological reactions [39]. *In vitro* and *in vivo* vitamin E inhibits the synthesis of *N*-nitroso compounds, nitrosamine and nitrosamide, which are known to be carcinogenic in laboratory animals [40]. The protective effect of vitamin E has been reported for different cancers including colon cancer, head and neck cancers, cervical cancer [41] and breast cancer [42]. A study is ongoing to investigate whether α-tocopherol will increase the DNA repair capacity in patients at risk of head, neck and colon cancer [43]. The fact that iron is involved in oxidation–reduction processes makes it plausible that iron may decrease the risk of cancer by inhibition of free radical reactions.

There are no data about the relationship of prostate cancer and calcium intake, but the protective effect of calcium has been reported for some other cancers [44, 45]. Two clinical trials are ongoing to investigate the effect of calcium supplementation in colon cancer chemoprevention [46] and in preventing recurrences of neoplastic polyps of the large bowel [47].

The relationship of prostate cancer with vitamin B12, vitamin E, fibre, calcium and iron should be corroborated by other investigations.

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