NC JSC "WEST KAZAKHSTAN MARAT OSPANOV MEDICAL UNIVERSITY"

ABSTRACT

The dissertation thesis "The effect of consumption of polyunsaturated fatty acids on the development of cardiovascular diseases in the Kazakh population" submitted for the degree of Doctor of Philosophy (PhD) by the specialty 6D110100 – "Medicine"

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Abstract of the dissertation by Tuleuova Raushan Shakirbekovna on the topic "Impact of the consumption of polyunsaturated fatty acids on the development of cardiovascular diseases in the Kazakh population" submitted for the degree of Doctor of Philosophy (PhD) in specialty 6D110100 – "Medicine"

Relevance. In most developed countries, cardiovascular diseases (CVDs) occupy the highest place in the mortality structure, they are the main cause of disability, and the issue of their prevention is related to solutions to medical and social problems (WHO, 2017; Mozaffarian D, 2016). In 2016, more than 17 million deaths were attributable to CVD worldwide, an increase of 14.5% compared with 2006 (Benjamin EJ, 2019). With the aging of society, the burden of CVD is constantly increasing, their importance has also increased in terms of life expectancy for people with disabilities (Global Burden of Disease Study, 2016), coronary heart disease (CHD) and stroke, which ranked first and second in frequency mortality rate in 2015 (Engelgau MM, Rosenthal JP, 2018), and this trend still persists in most Western countries (Beratarrechea A, Moyano D, 2017).

Cardiovascular disease is a complex of heterogeneous diseases, the main reason for the development of which is most often atherosclerosis (Francula-Zaninovic S, 2018). Numerous epidemiological studies have revealed many risk factors for developing atherosclerosis, such as dyslipidemia, smoking, hypertension, diabetes, chronic kidney disease (CKD), aging, male gender, a family history of coronary artery disease, non-cardiogenic cerebral infarction, peripheral artery disease, abdominal aortic aneurysm, hyperuricemia, nocturnal apnea syndrome, as well as metabolic syndromes, which are caused by the accumulation of visceral fat and insulin resistance (Leone A, Landini L., 2017). CVD is also closely associated with lifestyle, unhealthy diets, lack of physical activity, and psychosocial stress (Francula-Zaninovic S, 2018). The World Health Organization (WHO) has stated that more than three-quarters of all CVD deaths can be prevented. Both prophylaxis and treatment of atherosclerosis have reduced the death rate from CVD by about half (Wickramasinghe K, Wilkins E, 2018). Prevention of CVD, depending on the population, health workers and politicians, is defined as a coordinated set of actions at the state and individual levels aimed at eradicating, eliminating or minimizing the consequences of CVD. The basics of prevention are rooted in cardiovascular epidemiology and evidence-based medicine (Saeed A, 2017).

It is important for public health to find effective and easily applicable ways to manage modifiable risk factors (RF), including dietary, for the prevention of CVD. Studies have shown that, for example, high consumption of potassium, fruits and vegetables (Aburto NJ, 2013, Kinoshita M, 2018), as well as low consumption of salt and saturated fats (Aburto NJ, 2013, Hooper L, 2015) reduce the risk of cardiovascular disease.

The consumption of nutrients positively or negatively affecting the health of the population, including the development of CVD, in different countries is characterized by national eating habits. In the United States, the average American consumes more than the optimal amount of saturated fatty acids (EFAs), added sugars, and refined starches (DGA report, 2016). A FEEDCities study in Central Asia showed high consumption of salt, trans fats, and sugar in popular foods purchased by the local population (WHO, 2017). Unfortunately, in this study, which included Kazakhstan, the actual consumption of nutrients by the general population and patients with CVD in particular was not studied.

Worldwide recommendations for primary and secondary prevention of CVD recommend the use of polyunsaturated fatty acid (PUFA) sources (Piepoli MF, Hoes AW, Agewall S, et al. 2016). However, debates about the effects of omega-3-, omega-6-PUFAs continue. At the beginning of the 20th century, an active study of the biological significance of PUFAs began, it was shown that PUFAs have cardioprotective properties (Colussi G, Catena C, 2017), however, with the development of medical science and research methodology, it has been established that there are subspecies of fatty acids and their role in the human body significantly different from each other. Early epidemiological studies showed that high levels of omega-6 fats can worsen cardiovascular risk due to increased inflammation, while taking omega-3 PUFAs, on the contrary, have anti-inflammatory effects, have antioxidant and metabolic effects, and high consumption of omega-3 PUFAs reduces CVD risk (Yagi S, Fukuda D, 2017). Other studies have shown that a high intake of omega-6 PUFAs compared with EFAs or carbohydrates is associated with a lower risk of CVD, cardiovascular and overall mortality. In experimental studies, it was shown that omega-6 PUFAs lower LDL cholesterol concentrations in a dose-dependent manner compared to carbohydrates in the diet and have a neutral effect on blood pressure (Maki KC, 2018). An increase in omega-6 fat may be beneficial for people at high risk for myocardial infarction (MI). Elevated omega-6 fats lower total serum cholesterol (Hooper L, 2018). Abdelhamid A.S. (2018) suggested that omega-6 fatty acids may reduce the risk of CVD by lowering triglycerides (TG) without affecting total cholesterol, low or high density lipoproteins, while increasing PUFA intake “has little or no effect on mortality from all causes or from cardiovascular disease. "

In general, conflicting research results do not yet provide conclusive evidence of the benefits or harms of omega-6 fats in CVD or other conditions (Wang DD. 2018). A recent meta-analysis of cohort studies showed that the total amount of fats, EFAs, monounsaturated fatty acids (MFAs) and PUFAs was not associated with a risk of CVD, but the authors found that high intake of trans fats dose-dependently increased cardiovascular morbidity and cardioprotective the effect of PUFA is evident in studies conducted over 10 years (Zhu Y, 2019).

There is no direct evidence that only one diet suppresses the development of CVD, however, lifestyle changes, including eating behavior, have a positive effect on CVD risk factors, including serum lipid levels, which, in turn, can suppress cardiovascular risk (Kinoshita M, 2018).

Most of the epidemiological studies were conducted in Europe and America, by analogy with them, the results of these studies were confirmed for Japanese (Yamagishi K, 2013) and other Asian cohorts, as well as for the population of other continents (PURE study, Dehghan M, 2017). However, Kazakhstan was not included in this study. Although we assume that the patterns obtained apply to the residents of our country, it is important to obtain our own data, taking into account traditional Kazakh food preferences and changing dietary components in recent years. In addition, to develop dietary recommendations, it is necessary to understand the current level of intake of nutrients, in particular fats. For example, in the clinical protocol of the Republic of Kazakhstan for the treatment and rehabilitation of patients after acute myocardial infarction with ST segment elevation (2017), it is recommended to follow the Mediterranean diet and DASH, which do not have a convincing evidence base. Therefore, it is advisable to conduct an epidemiological study of the actual nutrition of the local population to develop recommendations that are adequate for the local population and take into account the nature of their nutrition.

Purpose of the study.

To study the relationship between the consumption of polyunsaturated fatty acids and the frequency of cardiovascular diseases in the Kazakh population.

Research Objectives:

1. Validate and adapt the Food Frequency Questionnaire (FFQ) translated into the state and Russian languages;
2. To study the actual nutrition in the Kazakh population;
3. To determine the levels of omega 3-index and apolipoprotein A1 in groups of patients with cardiovascular diseases ("cases") and healthy participants ("controls")
4. Compare the frequency and volume of consumed sources of fatty acids with a subsequent analysis of their impact on the development of CVD.

The objects of study are adults living in the city of Aktobe; in the validation study - adults over 18 years of age who do not have dietary restrictions, who do not have diseases that require a special diet at the time of the study, not pregnant or lactating women; in a cross-sectional study - adults randomly selected by the cluster method and agreed to participate in the study; in the case-control study, patients in the acute period of myocardial infarction (AMI), cerebrovascular accidents or with acute coronary syndrome (ACS), who were admitted to the emergency departments of Aktobe hospitals from February to March 2018 (“Cases”) and couples selected for them according to covariates, but without AMI, acute stroke, acute coronary syndrome (“controls”).

The subject of the study are laboratory indicators of the omega-3 index, apolipoprotein A1, blood glucose, total blood cholesterol, triglycerides, anthropometric indicators, the volume and frequency of consumption of basic foods, macro- and micronutrients.

Theoretical and practical significance of the subject of the dissertation:

1. A validated questionnaire can be used for further epidemiological studies of nutritional assessment in Kazakh and Russian-speaking populations.

2. Analysis of the actual nutrition and content of omega 3-index and apolipoprotein A1 in the population of Kazakhstan will allow the development of preventive measures at the public level.

3. The data obtained on the consumption of nutrients and the effect of fatty acids on the development of CVD can be used in practical health care: to update recommendations in the clinical protocols for the diagnosis and treatment of cardiovascular diseases; to compile a menu of hospitals, review dietary tables; to develop informational materials for the population on the promotion of a healthy lifestyle (HLS).

4. The results of the study can be used to plan new scientific work in nutrition, in the field of public health and clinical medicine.

The scientific novelty of the dissertation research:

1. For the first time, a validation study of the questionnaire for assessing the frequency and volume of nutrition for use in populations with the Kazakh and Russian languages was conducted.

2. The content of omega-3 index and apolipoprotein A1 was studied for the first time in healthy people and patients with CVD in the Kazakh population

3. For the first time, the relationship between the content of the omega-3 index in the blood and the consumption of PUFA sources in the Kazakh population was studied.

4. For the first time, the nutritional characteristics of patients with acute cardiovascular diseases in the presence of a control group of healthy patients are analyzed.

The main provisions of the dissertation research submitted to the defense:

1. The adaptation of the FFQ questionnaire, borrowed and translated into Kazakh and Russian, showed its validity for use in epidemiological studies of nutritional assessment.

2. The nutritional behavior of the Kazakh population does not provide the human body with an adequate content of nutrients necessary for maintaining health, including PUFA, in accordance with the 2017 WHO recommendations for good nutrition.

3. The percentage of omega-3 PUFAs in red blood cells is critically low in the Kazakh population.

4. Adequate intake of sources of omega-3 PUFAs reduces the risk of cardiovascular disease in the Kazakh population.

5. The intake of saturated fatty acids reduces the risk of cardiovascular disease in the Kazakh population.

Approbation of work. The main provisions of the thesis were presented at an expanded meeting of the scientific problem committee of the West Kazakhstan Medical University named after Marat Ospanov.

The results of the study were reported at scientific conferences:
1. At the international conference: 20th International Conference on Nutrition, Food Science and Technology with an oral report on the topic “Adaptation and validation of the Russian and Kazakh versions of the Food Frequency Questionnaire” (Dubai, UAE, April 16, 17, 2018);
2. at the international conference WONCA with a report on the topic “Frequencies of Food Consumption in Patients with Cardiovascular Diseases”, (Korea, Seoul 10.2018);
3. At the International Scientific and Practical Conference of Young Scientists “Science and Health” with a report on the topic “Change in eating behavior after myocardial infarction” (Semey, Kazakhstan, December 8, 2018),
4. at the international conference “Internationalization of Continuing Medical Education. A look into the future ”with a poster report on the theme“ Assessment of micronutrient consumption of Kazakh population ”(Aktobe, Kazakhstan, April 27, 2019).

Information about publications:

Based on the materials of the thesis, 9 scientific papers were published, 4 of them in publications recommended by the Committee for Quality Assurance in the Field of Education and Science of the Ministry of Education and Science of the Republic of Kazakhstan; 1 - in a publication indexed in the Scopus information base (Cite Score 54th percentile, SJR 0.296): - “Systematic reviews in pharmacy”, 4 abstracts in international scientific conferences, 2 of which are foreign conferences.

Practical implementation

The results of the study have been introduced into the practical activities of the family medicine clinic at ZKMU named after Marat Ospanov, and into the educational process at the center of family medicine and primary care research at the ZKMU after M. Ospanov for fifth-year students of the undergraduate specialty in General Medicine.

Guidelines for doctors “Nutrition recommendations for primary and secondary prophylaxis of cardiovascular diseases”, approved by the UMC NAO “ZKMU named after Marat Ospanov” (minutes of the meeting of the Academic Council No. 6 of June 27, 2019) were published.

Volume and structure of the dissertation

The work is presented on 81 pages of computer text in accordance with GOST 7.32-2017, GOST 7.12-93, GOST 15.101-98, GOST 8.417-2002. The dissertation consists of an introduction, an analytical review of the literature, materials and research methods, research results, conclusions, conclusions and practical recommendations.

The text is illustrated by 9 tables and 12 figures. The list of sources used includes 237 sources, of which 10 in Russian and 227 in English.

This work was carried out in the framework of the program for financing intra-university grants of the ZKMU named after Marat Ospanov on the topic “Personification of recommendations on food consumption for the prevention of cardiovascular diseases” R / N No. 12 / 4-1-17 / 133 O / D dated 01/30/2018

Materials and methods:

The study was carried out in 3 stages: stage 1 - a validation study, stage 2 - a study of the actual nutrition of the population, stage 3 - a study - “case control”.
Belonging to the Kazakh nationality was established by questioning and checking with the data of the birth certificate, which indicates the nationality of the respondent and his parents. The study did not include persons with a parent or parents of non-Kazakh nationality.

Stage 1. Conducting a study for adaptation and validation translated into Russian and Kazakh Food frequency questionnaire (FFQ).
To adapt the original FFQ, 90 subjects randomly selected were included in the validation study, which was conducted from December 2017 to January 2018. Exclusion criteria - children and adolescents, diseases that require a special diet or food restrictions, pregnant or breastfeeding. Written informed consent was obtained from all entities. The average age of the study participants was 55.6 ± 14.9 years, 43 (47%) men, and an average BMI of 26.4 ± 5.3 kg / m². Almost all participants (83%) were considered conditionally healthy, 15 participants (17%) had mild arterial hypertension (AH), coronary heart disease (CHD).

FFQ_KZ was translated from The European Prospective Investigation into Cancer (EPIC) Norfolk FFQ. The development of FFQ_KZ took place in four stages, clearly following the methods described by Willett (1990) and Coulston et al. (2015). The original FFQ, translated into Russian and Kazakh, was adapted by replacing some foods that the local population does not consume, the composition, calorie content and servings of local products were adjusted, for example, positions such as “lamb”, “salted meat”, “salted pies” were replaced by "lamb", "horsemeat" and "pies (with different fillings)", respectively.

The frequency of consumption took into account how many times a day, week or month the respondent takes certain foods or drinks. Thus, the adapted FFQ_KZ began to contain 11 food groups with 119 positions consumed by the local population. We also left 5 open questions with which you can find out the types of milk (fat content, origin or other specific milk), how to prepare main dishes (meat), the intake of food additives during the year, as well as their frequency and quantity. According to the participants, the questionnaire was filled in by the main researcher (interviewer) to reduce the likelihood of a systematic memory error (recall bias).

The interview was conducted on the basis of informed consent (meeting of the ethics committee No. 1 of the Oskanov State Medical University named after M. Ospanov on January 29, 2018), at the request of the participant in Kazakh or Russian. For comparison and validation, FFQ_KZ used the 24-hour recall (24 HR) reference diet assessment tool, which allows you to determine the amount of actually consumed food and dishes through a survey, when the respondent reproduces from memory what he ate the day before the survey. The interviewer actively participated in the survey and, together with the respondent, gave a description of the nature and set the amount of food taken during the previous day. The obtained characteristics and values were recorded by the interviewer in a

special questionnaire form. The information in the form was processed to obtain data on energy and nutrient consumption.

Survey results, i.e. the frequency and volume of consumed staple foods obtained by two methods (non-adapted FFQ and 24HR) were compared with the survey results obtained by the adapted questionnaire FFQ_KZ and 24 HR.

2 stage. The study of the actual nutrition of the population was attended by 300 people selected by the cluster sampling method. The clusters were 14 outpatient clinics in Aktobe, of which 3 organizations were randomly selected, in each of which 1 section was randomly selected. The inclusion criterion was Kazakh nationality, exclusion criteria: refusal to participate, absence at the moment in the city, the presence of severe somatic pathology, requiring a special diet or associated with dietary restrictions. All study participants signed an informed consent (protocol of the meeting of the LEK ZKGMU named after M. Ospanov No. 1 dated 01/28/2018). Adapted FFQ_KZ was used to evaluate eating habits.
The nutrient intake of food per day is calculated using the FETA for Windows version 2.53 computer program. All food products were grouped as follows: cereal products (including rye), eggs, fish and fish products, fruits, meat and meat products, milk and dairy products, soft drinks (fruit juices, berry juices, coffee and tea), nuts, potatoes, soups, sugar and sweet snacks, vegetables (except potatoes). Nutrient composition calculated on 43 macro- and micronutrients.

The study of the actual nutrition of the population involved 138 men and 162 women. The average age was 44 ± 15.3 years, BMI 26.5 ± 3.9 kg / cm2, waist (OT) 85.2 ± 14.7 cm, 2% of women and 70% of men smoked.

3 stage. Case-Control Study

The case-control study involved 195 people. The “cases” were 98 people with acute myocardial infarction (AMI), acute coronary syndrome (ACS) or acute cerebrovascular accident (Stroke), urgently hospitalized in hospitals in Aktobe (Kazakhstan): cardiology department of the Medical Center of the West Kazakhstan Medical University named after M Ospanova, cardiology department with interventional surgery of Aktobe Medical Center (AMC), cardiology department with interventional surgery of emergency hospital (BSMP) and stroke center at BSMP. All patients, on the basis of informed consent (IS), completed FFQ_KZ, an individual registration card (IRF), handed over biomaterial for determining the Omega-3 index and the CVD biomarker of apolipoprotein A1 (ApoA1).

Participants in the control group were selected by cluster sampling from an attached population of 14 clinics in Aktobe. The inclusion criteria were Kazakh nationality, the absence of a history of acute forms of CVD. Exclusion criteria were refusal to participate, absence for the period of research in the city. Three polyclinics of the city were selected by random sampling, 1 section in each of them, and 120 sections corresponding to the inclusion criteria for each person from each section. Of the selected 360 people from 3 clinics, 97 “controls” were selected, suitable by sex, age, BMI, cholesterol (cholesterol), triglycerides (TG),

smoking status, social status “cases”, but without AMI, ACS, Stroke in history (table 1).

Table 1 - Patient characteristics in the case-control study

Risk factors	Cases (n=98)	Controls (n=97)	P level
Age, years , middle (SD)	61,4 ±10,8	61,2±10,7	=0,602
Proportion of men, %	78	78	=0,938
Patients with diabetes mellitus, %	18	6	=0,01
Patients with AH 3 extent, %	45	16	=0,01
Patients with a BMI 25-29,9 кг/м2, %	52	47	=0,436
Patients with a BMI ≥ 30 кг/м2, %	31	19	= 0,547
Patients with a level of Cholesterol ≥6.5 mmol/l, %	15	30	=0,731
Patients with a level of TH ≥1,2 mmol/l	56	50	=0,389
Proportions of smokers, %	52	41	=0,802
Men with a WC ≥102 см, %	66	41	=0,144
Women with a WC ≥88 см, %	10	13	=0,935

At 195 participants of the 3rd stage, venous blood was taken to determine the omega 3 index and apolipoprotein A1 (apoA1). Whole venous blood was taken on an empty stomach (at least 3 hours after the last meal) in test tubes with a purple cap and a white or black ring in a sterile tube containing the EDTA anticoagulant. Blood samples were separated by centrifugation for 5 minutes at 3000 rpm immediately after collection and stored at -40 ° C in the INVIVO laboratory (Aktobe). Then the samples were packed with dry ice and carefully delivered to an external laboratory for analysis (Moscow, Russian Federation). Serum phospholipids were extracted using a mixture of chloroform-methanol (2: 1 by volume) followed by acid hydrolysis. After esterification in boron trifluoride-methanol, the serum fatty acid composition was analyzed by gas chromatography using an Agilent GC-7890B gas chromatograph, Germany equipped with an Omegawax capillary polyethylene glycol column (length 30 m, internal 0.25 mm) diameter, film thickness 0.25 μm , Sigma-Aldrich Co. LLC, St. Louis, Missouri, USA). The concentrations of each fatty acid were expressed as the proportion of all whey fatty acids.

Statistical analysis of the results

To analyze the results, we used the Statistica 10 statistical software package (Statsoft.inc). The study population was described using frequencies and percentages for categorical variables, to which 95% confidence intervals (CI) were calculated, and mean, standard deviation, medians (Me), interquartile range (IQR) for continuous variables. Statistical comparisons were made using chi-square or Fisher for categorical data, and Student or Mann-Whitney test for continuous data.

The normality of the distribution was checked by the Kolmogorov-Smirnov test. The relationship between continuous data was determined using Spearman correlation. A weak correlation was considered r, which is in the range of 0.01-0.29, medium - 0.3-0.69, strong - 0.7-0.99. Results were considered statistically significant at $p < 0.05$. To compare the measurements performed in two ways (FFQ and 24HR before adaptation; FFQ_KZ and 24HR after adaptation), the Bland-Altman method was used. For each pair of measurements performed by one or the other methods, the difference between the extreme values was calculated. The smallest spread of the variables was considered as satisfactory consistency, that is, the location along the midline is closer to zero, and the correlation coefficient is ≥ 0.7. In this case, the studied questionnaire is reliable. Descriptive statistics, frequency analysis, and the relationship between the consumption of PUFA sources and cardiovascular events were performed using logistic regression. For comparison of groups with quantitative variables, t-test of Student or Mann-Whitney was used, for binary and ordinal - chi-square.

The results of the study.

Validation study. Comparison of FFQ with a reference 24HR before adaptation showed high and statistically significant correlation coefficients for milk and dairy products ($r = 0.96$; $p = 0.05$), medium strength bonds are shown for meat and meat products ($r = 0.34$, $p = 0.86$), tea / coffee, potatoes and nuts (0.64; 0.6 and 0.63, respectively, $p = 0.05$). Fish and fish products ($r = 0.24$, $p = 0.68$), bread, and eggs showed a weak connection ($r = 0.26$, $p = 0.54$).

According to the nutrient composition, high correlation coefficients were obtained for proteins and energy ($r = 0.9$, $p \leq 0.05$), while for total fats ($r = 0.54$, $p < 0.001$), EFAs and PUFAs ($r = 0$, 36, $p = 0.27$), iron ($r = 0.3$, $p = 0.46$), vitamins B1 ($r = 0.34$, $p = 0.56$) and B2 ($r = 0.34$, $p = 0.42$), cholesterol ($r = 0.2$, $p = 0.56$), medium and low correlation coefficients were obtained. Thus, before adaptation (product replacement), FFQ showed a significant discrepancy from 24HR.

After adapting the questionnaire, Spearman's correlation coefficients between FFQ_KZ and 24HR were obtained high for meat and meat products ($r = 0.9$, $p = 0.09$), fish and fish products ($r = 0.7$ $p = 0.04$), milk and dairy products ($r = 0.9$, $p = 0.22$), and also for nutrients: proteins ($r = 0.99$, $p = 0.94$), fats ($r = 0.91$, $p = 0.56$) carbohydrates ($r = 0.91$, $p = 0.51$). And this means that after the adaptation of the frequency questionnaire (replacing uncharacteristic products with specific ones for the local population), the results on the frequency and volume of products and nutrients obtained using FFQ_KZ coincide with the results of the reference tool (24HR).

Bland-Altman plots calculated for proteins, carbohydrates, fats and energy, evaluated by FFQ and 24HR before adaptation, with large differences from the "zero" line did not show acceptable agreement: for proteins from 12.56 to -2 g / day, for fats from 42.75 to -19.21 g / day, for carbohydrates from 35.37 to -5.56 g / day.

The Bland-Altman plots after adaptation of FFQ_KZ showed no systematic discrepancy: for carbohydrates from 5.41 to -3.39 g / day, for proteins from 3.3 to -3.3 g / day, and fats from 22.03 to - 22.97 g / day.

2. **Actual nutrition of the population.**

Frequency analysis showed that the population consumes large quantities of cereals - pasta and bakery products (959 (324) g / day - men, 843 (308) g / day - women), milk and dairy products 364 (37) g / day, and the lowest consumed are nuts (0 (1.2) g / day), fish (59 (20) g / day) and fruits (80 (49) g / day).

For macronutrients, a significant excess of consumption was revealed compared with the recommended WHO standards, 2017, carbohydrates (392 g / day) at least 1.5 times, total fats (200 g / day) at least 2.5 times, and NLC separately (70, 39 g / day) 4 times.

For trace elements, large deviations from the norm were shown by alpha-carotene (299 g / day at a rate of 1000 g / day according to WHO recommendations, 2017), iron (15.6 g / day at a rate of 30 g / day according to WHO recommendations, 2017), folic acid (314 g / day at a rate of 400-1000 g / day according to WHO recommendations, 2017), magnesium (367 g / day at a rate of 800 g / day according to WHO recommendations, 2017), potassium (3790 g / day at a rate of 2000 g / day according to the recommendations of WHO, 2017), selenium (123 g / day at a rate of 70 g / day according to the recommendations of WHO, 2017), vitamin C (67.2 g / day at a rate of 150 g / day, according to the recommendations of WHO, 2017) .

3. Case-control.

On average, in 195 participants of the third stage of the case-control study, the content of Apolipoprotein A1 was 1.28 ± 0.28 g / l, the omega-3 index was 2.08 ± 0.92%, with a recommended target range of 8-11% (Berliner D, 2019).

In the main group (cases), the content of the omega-3 index was 2.18 ± 1.07 (95% CI 1.15; 1.6), in the control group 2.0 ± 0.74 (95% CI 1.41; 2.5), statistically significant differences between the groups were not found ($p = 0.377$).

The content of Apo A1 in the blood of participants in the control group was higher (1.39 ± 0.31 g / l) than in patients with CVD (1.17 ± 0.21 g / l, $p < 0.001$). The control range of Apo-A1 varies by gender as follows: in men more than 120 mg / dl (1.2 g / l), in women more than 140 mg / dl (1.4 g / l). A low level of Apo-A1 indicates an increased risk of CVD.

A positive but weak correlation was found between the ApoA1 and omega3 indices ($r = 0.26$, $p = 0.401$), probably associated with low consumption of PUFA sources.

According to the frequency and volume of consumption of the main food groups, there were no differences between the control and the main groups (Table 2).

Table 2 - Consumption of basic food products in the cases and control groups

Product name	Cases (g per day)	Control group (g per day)	p level
Grain products	875,5±189,09	874,4±185,1	=0,986
Eggs	11,2±25,4	14,7±29,7	=0,801
Fish and fish products	112,2±14,4	106,6±22,3	=0,149
Fruits	97,2±55,8	97,5±54,8	=0,674
Meat and meat products	148,4±91,1	159,6±89,7	=0,165
Milk and milk products	295,5±178,7	321,6±162,6	=0,313
Nuts	1,1±2,3	1,2±2,6	=0,745
Vegetables	158,03±41,5	159,04±41,9	=0,863

By the volume of consumption of macro- and micronutrients, there were no differences between the control and the main (cases) groups, except for vitamin D (14.00 ± 2.642 μg / day main, 10.53 ± 2.335 μg / day control, p = 0.041), PUFA (15.82 ± 4.635 g / day basic, 16.77 ± 4.788 g / day control, p = 0.028) and magnesium (358.02 ± 49.3 μg / day basic, 373.92 ± 53.559 μg / day control, p = 0.046).

As a result of studying the relationship between the consumption of PUFA sources and the development of CVD, regardless of gender, age, smoking, alcohol consumption, OT, GARDEN and BMI, a clinically and statistically significant positive effect was found (OR 0.591 (95% CI 0.41-0.852), p = 0.005).

A strong direct relationship was found between NLC consumption and CVD development (OR 0.661 (95% CI 0.442-0.988), p = 0.043), taking into account the above covariates.

The body saturation index with PUFA sources (omega-3 index) and CVD development showed statistically insignificant directly proportional relationships (OR = 0.8 (95% CI 0.504-1.272) p = 0.346). Also, no relationship was found between the consumption of PUFAs and the content of the omega-3 index (r = -0.07, p = 0.314), PUFA and ApoA1 (r = -0.06, p = 0.401), NFA and Apo A1 (r = 0,02, p = 0.785)

Correction for potential confounding factors during the logistic regression analysis showed that, first of all, there are stronger factors whose variability is less

(OT, systolic blood pressure, BMI), since statistically significant relationships in many indicators after correction to the above indicators were not preserved .

Blood omega-3 levels may vary depending on lifestyle (e.g. fish consumption), geographic and genetic causes (Superko HR, 2014). The omega-3 levels of the red blood cell index are lower than in other countries: in Russia from 1.12% to 6.4%, averaging 3.74% (Gavva E.M., 2012), in Germany 3.7 ± 1 , 0% (Berliner D, 2019). Our results on the content of apoA1 are similar to the results of a study in Russia, where the content of apoA1 was in the range of 1.99-2.34 g / l (Vorobev R.I., 2017).

The positive association between PUFA and CVD development in our study is supported by the Cochrane Systematic Review (Abdelhamid AS, 2018), which shows a decrease in cardiovascular morbidity due to an increase in PUFA intake (RR 0.89 (95% CI 0.79-1.01)

The unexpected positive relationship between NLC and the development of CVD in our study is also similar to the results of recent studies in the world, which are still perceived critically. Cohort studies among American women and Japanese have shown that cerebral hemorrhage increases with a low intake of animal fat and protein (Kinoshita M, 2018). A Japan Collaborative Cohort (JACC) study found an inverse relationship between EFA intake and mortality from stroke, brain hemorrhage, and ischemic stroke (Yamagishi K, 2010). A study by the Japan Public Health Center (JPHC) found a positive association between EFA intake and myocardial infarction (Yamagishi K, 2013). However, evidence is insufficient to establish the recommended intake of EFAs (Kinoshita M, 2018).

Our results allow us to draw the following conclusion. Eating behavior in the Kazakh population differs from the dietary traditions of Western countries. Replacement of 4 positions was required, 3 positions on food products were added, the biochemical composition of the products was adjusted. Adaptation of borrowed questionnaires is required for epidemiological studies in the field of nutrition. Our validation study showed its acceptability for the Kazakh population.

A study of the actual nutrition in the sample of the Kazakh population showed an imbalance in the consumption of nutrients, sources of useful macro- and micronutrients. We found a high consumption of harmful carbohydrates and saturated fats, including trans fats, in large quantities found in confectionery products, and a low consumption of healthy fish, nuts, raw fruits and vegetables. During our conduct, we also discovered the absence of modern tables for calculating the chemical composition of local food products, which would be regularly updated.

We found a low content of omega-3 index in all case-control study participants, regardless of the presence of CVD, and reflecting a low consumption of omega-3 PUFA sources, which weakly correlated with the consumption of a well-known source of PUFA (fish). No association was found between the level of the omega-3 index and the development of CVD, probably due to the large variability of the independent trait.

We found an acceptable level of apoA1 in 30% of the studied, without statistically significant differences between patients with CVD and healthy. No relationship was found between this biomarker and consumption of either PUFAs or NFAs.

We also revealed the beneficial effect of PUFA on the development of CVD, which will allow us to confidently formulate practical recommendations on diet for practitioners. The found positive relationship between NLC and the development of CVD, although supported by many other and larger studies, requires careful interpretation and dissemination in connection with the relevant recommendations still existing in international clinical guidelines, as well as in connection with their effect on obesity. In addition, local studies are needed on the dose-dependent protective or causal effects of EFAs.

Findings:

1. FFQ_KZ after adaptation showed reliability and validity. The consistency with the 24 HR reference tool was high: the correlation coefficient for the main nutrients was high (for proteins r = 0.99, p = 0.94, for fats r = 0.91, p = 0.56, for carbohydrates r = 0 , 91, p = 0.51), Bland-Altman graphs showed the absence of a systematic discrepancy in the average value for carbohydrates (from 5.41 to -3.39 g / day), proteins (from 3.3 to -3.3 g / day), and fats (from 22.03 to -22.97 g / day).

2. In assessing the actual nutrition of the population, an excess of consumption compared to the WHO norm (2017) of carbohydrates (392 g / day) by 1.5 times, total fat (200 g / day) by 2.5 times and EFA (70, 39 g / day) 4 times, and a critically low consumption of fruits and vegetables (97.1) 4 times lower than nuts (1.3 g / day) at a rate of 30 g / day. Only 4% of respondents consume fish 1 time per week, instead of the recommended 2 times a week.

3. The average content of the omega-3 index in the Kazakh population was 2.08 ± 0.92%, which is below the recommended target range, without statistically significant differences (p = 0.377) between patients with CVD and the control group. The average content of Apolipoprotein A1 in the participants of both groups was 1.28 ± 0.28 g / l; in the control group, the indicator was found to be higher (1.39 ± 0.31 g / l) than in patients with CVD (1.17 ± 0 , 21 g / l, $p<0.001$).

4. It was found that PUFAs (OSH = 0.591 (95% CI 0.41-0.852), p = 0.005) and SFAs (OSH = 0.661 (95% CI 0.442-0.988), p = 0.043) are associated with a reduced risk of CVD in the studied population.

Practical recommendations

The results of the study can be used in scientific research, practical health care and medical education:

- FFQ_KZ, adapted for the local population and validated, can be used in epidemiological studies to evaluate nutrition for other diseases and clinical conditions;

- the results obtained on the consumption of food products and nutrients can be used to develop dietary recommendations for primary and secondary prevention of cardiovascular diseases;

- the results obtained on the consumption of food products and nutrients can be used to develop dietary recommendations for the prevention and treatment of diseases that depend on the nature of the diet (oncological, etc.);

- the used methodology for assessing nutrition and calculating the chemical composition of food products is applicable for the preparation of dietary tables, the menu of hospitals, hospices, children and adolescents, and other groups of the population, for the compilation of information materials for the population to promote a healthy lifestyle;

- the obtained data can be used as input for subsequent studies, in particular, to determine the dose-dependent effect of fatty acids, as well as other nutrients, on the development of cardiovascular and other diseases in the Kazakh population;

- the results of the study can be used as educational material in educational programs for the training and professional development of medical workers.