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Evaluation of the relationship between nutrition and the risk of fatal outcomes from cardiovascular diseases in people with type 2 diabetes

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ABSTRACT

Aim. To evaluate the relationship between nutrition and the risk of fatal outcomes from cardiovascular diseases in individuals with type 2 diabetes mellitus (T2DM).

Materials and methods. The baseline study was conducted within the HAPIEE project in 2002–2005. The follow-up period for the observed cohort, including individuals with T2DM, lasted from 2003–2005 to December 31, 2018 and reached on average 12.8 years (1.1 ± 16.0 years). Within the study, 2 groups were formed: the treatment group which included persons with T2DM who "developed fatal events" and the control group which encompassed individuals with T2DM who "did not develop fatal events" during the follow-up. The treatment group included 207 people (107 men, 100 women), the average age for both sexes was 62.4 ± 5.9 years; the control group consisted of 474 people (177 men, 297 women), the average age for both sexes was 58.1 ± 6.6 years. The data on actual nutrition were obtained from a survey of the participants using the Food Frequency Questionnaire and included information on consumption of 147 foods. Statistical processing of the data was carried out using the SPSS 13.0 software package. The data were presented as $M \pm SD$, where M is the arithmetic mean and SD is the standard deviation. An analysis of the association between nutrition and the risk of death from cardiovascular diseases was performed using the Cox regression model. The differences were considered statistically significant at $p < 0.05$.

Results. In the studied sample, we identified a significant relationship between the consumption of a number of foods and the risk of death from cardiovascular diseases in people with T2DM over a 15-year follow-up. It was shown that increased consumption of fruits (by 80 g / day) and nuts (by 2 g / day) was significantly associated with a decreased risk of death in men: hazard ratio (HR) = 0.726, $p = 0.044$ and HR = 0.826, $p = 0.011$, respectively. Increased consumption of eggs in men (by 50 g / day) was associated with an increased risk of death: HR = 1.728, $p = 0.003$. In women, a decreased risk of death was observed only with the consumption of meat products: HR = 0.786, $p = 0.036$.

Conclusion. The results of the study showed a clear relationship between the consumption of a number of foods and the risk of death from cardiovascular diseases. Thus, increased consumption of fruits, nuts, and meat products was significantly associated with a decreased risk of death from cardiovascular diseases in people with T2DM, while the consumption of eggs and dairy products, on the contrary, was associated with an increased risk of mortality. These data indicate the importance of dietary control in individuals with carbohydrate metabolism disorders.

Keywords: type 2 diabetes, death from cardiovascular diseases, nutrition, hazard ratio

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Оценка связи питания с риском фатальных исходов от сердечно-сосудистых заболеваний у лиц с сахарным диабетом 2-го типа

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РЕЗЮМЕ

Цель. Изучить связь питания с риском фатальных исходов от сердечно-сосудистых заболеваний у лиц с сахарным диабетом 2-го типа (СД2).

Материалы и методы. Базовое исследование проведено в рамках проекта HAPIEE в 2002–2005 гг. Период наблюдения за наблюдаемой когортой, в том числе за лицами с СД2, длился с 2003–2005 гг. по 31 декабря 2018 г. и составил в среднем 12,8 лет (1,1 ± 16,0 лет). В рамках исследования были сформированы две группы: основная – лица с СД2, у которых «Развились фатальные события», и группа сравнения – лица с СД2, у которых «Не развились фатальные события» за период наблюдения. В основную группу были включены 207 человек (107 мужчин, 100 женщин), средний возраст для лиц обоего пола 62,4 ± 5,9 лет; в группу сравнения – 474 человека (177 мужчины, 297 женщин), средний возраст для лиц обоего пола 58,1 ± 6,6 лет. Данные по фактическому питанию были получены при опросе 681 участника с использованием вопросника по оценке частоты потребления пищевых продуктов и включали информацию о потреблении 147 продуктов. Статистическую обработку данных проводили с использованием пакета прикладных программ SPSS 13.0. Описание данных представлено в виде $M \pm SD$, где M – среднее арифметическое значение, SD – стандартное отклонение. Оценка отношения рисков проведена с использованием регрессии Кокса. Критический уровень статистической значимости различий принимался при $p < 0,05$.

Результаты. Получены данные, что увеличение потребления фруктов (на 80 г/сут) и орехов (на 2 г/сут) связано со снижением рисков сердечно-сосудистой смерти: отношение рисков (HR) = 0,726; $p = 0,044$ и HR = 0,826; $p = 0,011$ соответственно; увеличение потребления яиц (на 50 г/сут) – с повышением риска смерти: HR = 1,728; $p = 0,003$ у мужчин. У женщин при потреблении мясных продуктов наблюдалось снижение риска смерти: HR = 0,786; $p = 0,036$.

Заключение. Результаты исследования показали определенную ассоциацию потребления ряда продуктов с риском смерти от сердечно-сосудистых заболеваний у лиц с СД2. Так, более высокий уровень потребления фруктов, орехов, мясных продуктов был связан со снижением риска сердечно-сосудистой смертности, а увеличение потребления куриных яиц, наоборот, с повышением риска фатального исхода. Эти данные указывают на важность контроля питания у лиц с нарушениями углеводного обмена.

Ключевые слова: сахарный диабет 2-го типа, сердечно-сосудистая смерть, питание, отношение рисков

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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INTRODUCTION

Currently, cardiovascular diseases (CVDs) are the main cause of death among patients with type 2 diabetes mellitus (T2DM) in the Russian Federation [1]. The traditional risk factors for death in T2DM are gender, age, dyslipidemia, obesity, arterial hypertension (AH), smoking, low physical activity, marital status, and factors associated with the disease itself (the duration of T2DM, the presence of macro- and microvascular complications, hyper- and hypoglycemia) [2, 3]. The inclusion of foods rich in bioactive substances (antioxidants, phenolic acids, isoflavones, anthocyanins, carotenes, unsaturated fatty acids), which improve the parameters of carbohydrate metabolism, in the diet of T2DM patients may be one of the factors for preventing cardiovascular complications [4, 5]. The assessment of the actual nutrition of the population (aged 45–69 years) in Novosibirsk showed that the diet in general, among persons both with and without T2MD, is unbalanced and does not correspond to the recommendations [6].

The aim of the study was to investigate the relationship between nutrition and the risk of fatal outcomes from cardiovascular diseases in people with T2MD.

MATERIALS AND METHODS

The research was carried out on the material of the Russian branch of the international HAPIEE (Health, Alcohol and Psychosocial factors In Eastern Europe) study "Determinants of Cardiovascular Diseases in Eastern Europe". The object of the HAPIEE study was a population sample including residents (aged 45–69 years) of two administrative districts of Novosibirsk, typical both of Novosibirsk and other large industrial cities of Siberia. The sample was formed on the basis of the electoral register using random number tables. The total sample size from the general population was determined by the protocol of the HAPIEE project. From 2003 to 2005, the staff of the Research Institute of Internal Medicine of the Siberian Branch of the Russian Academy of Medical Sciences (since 2017 – Research Institute of Internal and Preventive Medicine – Branch of the Institute of Cytology and Genetics of the Siberian Branch of the Russian Academy of Sciences) examined 9,360 men and women of the specified age (the principal researchers – the Academician Yu. P. Nikitin and Prof. S. K. Malyutina). The response made 61% [7].

Out of 9,360 examined individuals, T2DM was detected in 982 people (for the first time, during screening and before screening). In total, 301 people were excluded from the study: persons with T2DM who reported nonfatal myocardial infarction and / or stroke in their medical history during the baseline survey (139 people), persons whose cause of death was not CVD during the follow-up (123 people), and 39 people about whom no information was received during the follow-up. Thus, the analysis included the data from the baseline survey of 681 people with T2DM (284 men, 397 women).

The follow-up period for the observed cohort, including persons with T2DM, lasted from 2003–2005 to December 31, 2018 and made on average 12.8 years (1.1 ± 16.0 years). Fatal outcomes in the study cohort were identified by combining several sources of information. We copied the data from the Medical Certificates of Cause of Death for the period from 01.02.2003 to 31.12.2018, obtained at the Civil Registry Office in the city of Novosibirsk. Information about fatal events was also collected during repeat screenings in 2006–2008 and 2015–2017 and two postal surveys. The causes of overall and cardiovascular (CV) death were established in accordance with the codes of the International Classification of Diseases, 10th revision

(ICD-10). Cardiovascular death was established according to the ICD codes I (0–99).

Within the study, 2 groups were formed: the treatment group which included persons with T2DM who "developed fatal events" – 207 people (107 men, 100 women) and the control group which encompassed individuals with T2DM who "did not develop fatal events" during the follow-up – 474 people (177 men and 297 women).

All project participants underwent a baseline screening, which included anthropometric measurements (height, weight, body mass index calculation) and collection of information using the structured questionnaire of the HAPIEE project on the presence of T2DM and its duration, as well as on the presence of AH, education, marital status, smoking status, and the level of physical activity. To assess actual nutrition, the adapted Food Frequency Questionnaire was used to determine the frequency of food consumption [8]. 147 products were included in the questionnaire. Nutrition was assessed over the previous 3 months according to answers to 9 questions on the frequency of consumption of a certain product. The answers ranged from "never or less than once a month" to "up to six or more times a day". The survey was conducted by a trained interviewer [9].

Statistical processing of the data was carried out using the SPSS v.13.0 software package. The data were presented as $M \pm SD$, where M is the arithmetic mean, and SD is the standard deviation. Hazard ratio (HR) was calculated using the Cox regression model. The differences were considered statistically significant at $p < 0.05$.

RESULTS

The men in the treatment group were 4 years older than in the control group (60.78 ± 6.52 vs. 56.88 ± 6.53 years; $p < 0.001$), and the women in the treatment group were 5 years older than in the control group (64.15 ± 6.14 vs. 58.81 ± 6.13 years; $p < 0.001$). Body mass index (BMI) among men (29.55 ± 4.86 vs. 29.66 ± 4.88 kg / m^2; $p = 0.857$) and women (33.81 ± 5.56 vs. 32.62 ± 5.51 kg / m^2; $p = 0.064$) did not differ significantly between the groups. The total energy intake from nutrition both among men (2,562 ± 799 vs. 2,777 ± 803 kcal / day; $p = 0.030$) and women (2,084 ± 633 vs 2,262 ± 632 kcal / day; $p = 0.016$) was lower in the treatment group.

Table 1 presents the data on food consumption (g / day) among the residents of Novosibirsk (aged 45–69 years) with T2DM (baseline screening within the HAPIEE study, $M \pm SD$) who developed / did not develop fatal cardiovascular events during the follow-up. The men from the treatment group consumed less fruits and nuts and more chicken eggs and dairy products than those in the control group. For the rest of the products, no significant difference in consumption was revealed. Increased consumption of white bread and decreased consumption of meat products were observed among the women of the treatment group.

Table 2 shows the results of the Cox regression analysis on the relationship between the risk factors (consumption of the studied products, g / day) and death from CVD among the people with T2DM, adjusted for age, BMI, total energy intake, educational level, marital status, smoking status, AH, and the level of physical activity. Using this method, we estimated the hazard ratio (HR) of fatal CV event development with an increase in individual food item consumption calculated by a certain amount (g / day) [10]. It was found that the risk of a fatal CV event among men decreased by 27.4% with an increase in the consumption of some fruits (by 80 g / day) ($p = 0.044$). The "fruits" group included apples, pears, oranges, grapefruits, tangerines, peaches, apricots, and bananas. The risk of a fatal CV event among men also decreased by 17.4% with an increase in the consumption of nuts (by 2 g / day) ($p = 0.011$). The increased consumption of meat products (by 80 g / day) reduced the risk of fatal CV events among women by 21.4% ($p = 0.036$).

An increase in the consumption of chicken eggs by men (by 50 g / day – one more egg on average) increased the risk of CV death by 1.7 times ($p = 0.003$). The consumption of dairy products (excluding milk) increased the risk of CV death by 1.1 times ($p = 0.029$). No such correlations were observed for women (Table 2). Previously, the authors presented the relationships of such factors as AH, abdominal obesity, low level of physical activity, current smoking, and marital status with CV mortality among people with T2DM living in Novosibirsk [3].

DISCUSSION

The results of the study showed that the increased consumption of fruits and nuts was associated with a decreased risk of death from CVD among men. The data obtained are consistent with the results of a number of population-based studies. The article by G. Liu et al. (2019) presents the results of two prospective, cohort studies that included 16,217 men and women with T2DM, which showed that the consumption of nuts (the consumption was more than 20 g / day in the

highest quintile and less than 0.9 g / day in the lowest quintile) was associated with significant reduction of a risk for CVD death (the relative risk in the highest quintile compared with the lowest one was HR = 0.66; 95% confidence interval (CI) 0.52–0.84). The effect was greater with the consumption of hazelnuts (walnuts, almonds, Brazil nuts, cashews, pistachios, cobnuts, pine nuts) and peanuts (legumes).

As the authors of the work note, the mechanism of the positive effects of nut consumption among the persons with T2DM is currently not clear [11], although this can be primarily determined by the rich nutritional composition of nuts (polyunsaturated fatty acids, dietary fiber, vitamins, minerals (calcium, potassium, magnesium), and phytochemicals (flavonoids, phytosterols)) [12]. The study on the relationship between the consumption of fruits, vegetables, and legumes in the diet of Europeans with T2DM (10,449 participants) and fatal outcomes from CVDs showed a significant decrease in the relative risk of death with increased consumption of legumes (RR = 0.72; CI 0.60–0.88) and fruits (relative risk (RR) = 0.90; 95% CI 0.81–0.99) (adjusted for gender, age, total energy intake, smoking status, history of heart diseases, cancer, and AH). At the same time, no significant relationship with vegetable consumption was revealed (RR = 0.85; 95% CI 0.85–1.07) [10].

The data from a number of prospective meta-analyses also show the positive impact of fruits and nuts. Thus, the meta-analysis of 15 prospective studies showed that the increased consumption of fruits and vegetables was associated with a 10% decrease in the all-cause mortality (RR = 0.90, CI 0.87–0.93) [13]. The analysis of 17 studies on the consumption of vegetables and nuts found that nut consumption was associated with a reduced risk of death (all nuts: RR = 0.78, 95% CI 0.72–0.84; hazelnuts: RR = 0.82, 95% CI 0.75–0.90; peanuts: RR = 0.77, 95% CI 0.69–0.86) [14]. The meta-analysis (15 studies) on the consumption of nuts [15] showed 20% reduction of a risk of all-cause mortality (consumption of nuts: RR = 0.81, 95% CI 0.77–0.85; hazelnuts: RR = 0.80, 95% CI 0.74–0.86; peanuts: RR = 0.85, 95% CI 0.82–0.89), which indicates a positive effect of the increase in the consumption of these products in the diet.

In our study, we obtained the data that the increase in the meat product consumption (by 80 g / day) reduced the risk of a fatal CV event among women with T2DM. A number of studies including a big population sample showed a significant increase in the risk of all-cause mortality and mortality from CVDs with the consumption of red meat and processed meat products (sausages, ham, canned meat) [16, 17]. However, it was also shown that the consumption of meat products which included chicken, turkey, fish, poultry cuts, lean sausages, and poultry hot dogs was associated with the decrease in the all-cause mortality and mortality from CVDs [17]. It was noted that the increase in the proportion of animal protein in relation to plant protein was associated with an increased risk of death, also among the persons with T2D [18]. In a large, prospective cohort study of Japanese residents (70,696 participants aged 45–74 years), higher consumption of plant protein was associated with a lower risk of all-cause mortality and death from CVDs [19].

Increased egg consumption was associated with an increased risk of death from CVDs among men. The association between egg consumption and the risk of death is supported by the results of a prospective cohort study in the United States (21,327 participants aged 40–86 years), which found the relationship of chicken egg consumption with the relative risk of all-cause mortality when comparing the highest quintile of consumption (≥ 7 eggs/ week) with the controls (< 1 egg / week) (HR = 1.22; 95% CI 1.09–1.35); among the people with T2DM, the risk of death was 2 times higher (HR = 2.01; 95% CI 1.26–3.20) [20]. In another study of US residents (29,615 participants), higher egg consumption was associated with an increased risk of all-cause mortality (by 8%) (HR = 1.08; 95% CI 1.04–1.11) [21].

Our analysis also showed that the increase in the consumption of dairy products (sour cream, kefir, dairy desserts, cottage cheese, and cheese) by 50 g / day ($p = 0.029$) increased the risk of fatal CVDs by 1.1 times among men ($p = 0.029$), which requires further research.

CONCLUSION

The results of the study indicate a certain role of the consumption of particular foods as an “unconventional” factor in the development of a fatal CV event among persons with T2DM, when taking into account traditional risk factors, such as age, BMI, total energy intake, smoking status, educational level, marital status, AH, and the level of physical activity. It can be noted that there are differences between men and women. While the observed relationships between fruit and nut consumption and the decrease in the risk of death from CVD, as well as between the increase in the consumption of eggs and the increased risk of death from CVDs among men comply with the find-

ings of current population-based studies, the relationship between the consumption of meat products and the decrease in the risk of death from CVDs among women requires a more thorough analysis.

The complexity of evaluating the relationship between the consumption of meat products and the risk of death is determined by the difference and diversity of the consumed meat products (beef, lamb, pork, sausages, chicken, rabbit meat, offal, ham, loin, pates, canned meat), the method of meat preparation (boiled, fried, smoked, canned, salted), and the plant protein / animal protein ratio. Evaluation of the relationship of dairy products with the risk of fatal outcomes among men also requires further research because of the weakly expressed association.

It should be noted that the average consumption of nuts was almost 4 times lower than the recommended level. Since there are no definite recommendations for the inclusion of nuts in the diet of people with T2DM, the results obtained indicate their potential positive role in mortality reduction among people with carbohydrate metabolism disorders and should be taken into account when developing and updating dietary recommendations.

Table 1

Data on nutrition of Novosibirsk residents (aged 45–69 years) with T2DM (baseline screening within the HAPIEE study, *M* ± *SD*) who developed / did not develop fatal cardiovascular events during the follow-up (men and women – adjustment for age, BMI, and total energy intake; both genders – adjustment for gender, age, BMI, and total energy intake)

Food groups, g / day	Both genders		*p*	Men		*p*	Women		*p*
	Fatal cardiovascular events have developed, *n* = 207	Fatal cardiovascular events have not developed, *n* = 474		Fatal cardiovascular events have developed, *n* = 107	Fatal cardiovascular events have not developed, *n* = 177		Fatal cardiovascular events have developed, *n* = 100	Fatal cardiovascular events have not developed, *n* = 297	
Fruits	78.76±86.40	99.38±83.78	0.006	63.59±75.38	90.53±74.65	0.005	99.56±93.08	111.31±89.61	0.284
Vegetables	259.63±164.9	281.64±159.8	0.132	246.15±138.2	271.66±136.8	0.141	281.26±183.9	298.06±177.1	0.438
Cereals	79.31±55.89	79.88±54.38	0.906	79.15±50.56	79.61±50.12	0.942	80.82±60.90	81.55±58.58	0.919
Legumes	12.37±12.58	12.04±12.27	0.767	10.82±10.89	10.52±10.78	0.822	14.15±14.01	13.82±13.78	0.837
Nuts	2.51±8.91	4.95±8.68	0.002	2.19 ± 10.68	5.82±10.58	0.007	3.22±7.53	4.33±7.25	0.212
White bread	72.75±50.98	62.36±49.66	0.019	85.83±53.60	80.20±53.06	0.401	60.96±50.04	46.47±48.17	0.014
Black bread	40.89±51.23	46.40±45.35	0.173	42.61±48.60	44.42±48.10	0.766	39.19±46.07	48.46±44.37	0.088
Sweets	79.01±55.54	81.00±53.97	0.667	88.21±59.97	91.67±59.35	0.645	75.55±52.52	75.62±50.57	0.991
Meat products	176.64±69.34	190.95±67.31	0.017	205.97±79.10	219.94±78.29	0.158	152.24±60.73	168.09±58.48	0.027
Fish	38.41±27.30	39.70±26.47	0.581	39.97±29.06	41.29±28.77	0.715	38.11±26.37	39.24±25.40	0.717
Eggs	20.40±19.80	15.50±19.21	0.004	27.11±25.49	19.37±25.19	0.016	13.90±14.34	12.29±13.80	0.339
Dairy products	143.23±119.4	121.66±115.7	0.036	152.40±129.0	114.94±127.7	0.021	138.68±113.4	131.68±109.2	0.600
Milk	127.68±166.9	107.22±161.5	0.154	146.56±199.6	123.72±201.6	0.365	112.21±138.0	93.59±132.8	0.252
Fats, oil	36.30±15.97	33.12±15.59	0.021	37.08±17.26	33.68±17.08	0.117	36.25±15.01	33.50±14.46	0.120

Table 2

Results of the Cox regression analysis on the relationship between the risk factors (consumption of the studied products) and fatal outcomes from CVD among people with T2DM (* adjustment for age, BMI, total energy intake, educational level, marital status, smoking status, arterial hypertension, and physical activity)

Food groups, g / day	Both genders, *n* = 681	Men, *n* = 284	Women, *n* = 397
Fruits (by 80 g / day)			
HR	0.786 (*p* = 0.011)	0.726 (*p* = 0.044)	0.852 (*p* = 0.228)
95% CI	0.670–0.923	0.570–0.990	0.670–1.083
Vegetables (by 80 g / day)			
HR	0.923 (*p* = 0.220)	1.000 (*p* = 0.571)	0.923 (*p* = 0.299)
95% CI	0.852–1.000	0.852–1.083	0.852–1.083
Cereals (by 50 g / day)			
HR	1.000 (*p* = 0.821)	1.051 (*p* = 0.662)	1.000 (*p* = 0.965)
95% CI	0.905–1.162	0.860–1.283	0.818–1.221
Legumes (by 10 g / day)			
HR	1.030 (*p* = 0.624)	1.127 (*p* = 0.305)	0.990 (*p* = 0.944)
95% CI	0.904–1.184	0.904–1.397	0.834–1.184
Nuts (by 2 g / day)			
HR	0.895 (*p* = 0.006)	0.826 (*p* = 0.011)	0.939 (*p* = 0.178)

Table 2 (continued)

Food groups, g / day	Both genders, *n* = 681	Men, *n* = 284	Women, *n* = 397
95% CI	0.828–0.968	0.662–0.956	0.857–1.028
White bread (by 50 g / day)			
HR	1.105 (*p* = 0.234)	1.000 (*p* = 0.874)	1.221 (*p* = 0.060)
95% CI	0.951–1.283	0.818–1.221	1.000–1.489
Black bread (by 50 g / day)			
HR	0.951 (*p* = 0.601)	1.105 (*p* = 0.372)	0.778 (*p* = 0.054)
95% CI	0.818–1.105	0.905–1.349	0.605–1.000
Sweets (by 50 g / day)			
HR	1.000 (*p* = 0.739)	0.951 (*p* = 0.707)	1.000 (*p* = 0.840)
95% CI	0.860–1.105	0.818–1.162	0.778–1.221
Meat products (by 80 g / day)			
HR	0.852 (*p* = 0.083)	0.923 (*p* = 0.318)	0.786 (*p* = 0.036)
95% CI	0.726–1.000	0.726–1.083	0.618–0.990
Fish (by 30 g / day)			
HR	1.000 (*p* = 0.938)	1.000 (*p* = 0.938)	0.942 (*p* = 0.671)
95% CI	0.835–1.196	0.786–1.270	0.696–1.270
Eggs (by 50 g / day)			
HR	1.728 (*p* = 0.001)	1.728 (*p* = 0.003)	1.815 (*p* = 0.097)
95% CI	1.283–2.223	1.221–2.440	0.905–3.437
Dairy products (by 50 g / day)			
HR	1.051 (*p* = 0.036)	1.051 (*p* = 0.029)	1.051 (*p* = 0.537)
95% CI	1.000–1.105	1.000–1.162	0.951–1.105
Milk (by 80 g / day)			
HR	1.000 (*p* = 0.523)	1.000 (*p* = 0.789)	1.083 (*p* = 0.431)
95% CI	0.923–1.083	0.923–1,083	0.923—1.173
Fats, oil (by 15 g / day)			
HR	1.094 (*p* = 0.197)	1.078 (*p* = 0.438)	1.178 (*p* = 0.150)
95% CI	0.956–1.250	0.900–1.288	0.942–1.491

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