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The association between macronutrients and severe musculoskeletal pain in the Tromsø7 study

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1 Introduction

Musculoskeletal pain (MP) is a common public health problem that affects millions around the globe and is recognized as the leading cause of disability worldwide [1, 2]. MP is defined as any acute or chronic pain that affects the muscles, ligaments, tendons and bones [3]. This pain can occur in the neck, shoulder, back, knees, and anywhere else in the body and has a wide range of severity [1]. Musculoskeletal pain is commonly a consequence of muscle overuse or injury caused by daily life activities that can range from prolonged sitting in the workplace, participating in exercises or sports, or serving in the military. It can also be caused by traumatic injuries such as fractures, muscle sprain, which is an injury to the ligaments, and muscle strain; an injury to the tendons [1]. In addition, various medical conditions can lead to the development to musculoskeletal pain. These include conditions affecting the bones such as osteoporosis and osteopenia, those effecting the joints such as osteoarthritis and rheumatoid arthritis, and those affecting the muscles such as sarcopenia. Conditions causing systematic inflammation in the body, such as fibromyalgia and systemic lupus erythematosus, also trigger musculoskeletal pain [1]. Unfortunately, people affected by MP suffer several adverse consequences, including, but not limited to, increased drug consumption, a constant need to take time off work, limited activity, added financial strain, and overall diminished quality of life [4, 5]. It is no surprise that these individuals are also at a higher risk for developing mental health disorders [6]. All of these consequences, and likely much more, place a significant burden on society and healthcare systems in terms of psychological, physical, and socio-economic outcomes [1].

Low back and neck pain are the most prevalent forms of MP, with low back pain being the single leading cause of disability in 160 countries with an estimated 570 million cases worldwide as of 2019, according to the world health organization [1, 4, 7]. Moreover, age is considered a risk factor that is thought to greatly affect the prevalence of MP. For instance, the elderly population are more likely to have chronic MP compared to the younger population due to the inevitable deterioration of joints and muscles, decreased energy intake, and sedentary lifestyle [4]. In today's world, musculoskeletal pain is treated primarily through a combination of rehabilitation and pharmaceutical means; however, severe cases may require surgical intervention [4]. According to the clinical practice guideline developed by The American College of Physicians for the management of acute and chronic low back pain, using non-pharmaceutical means should be the first-line therapy for patients with acute or subacute low back pain. These can include massage therapy, acupuncture, heat therapy, or spinal manipulation [8]. In case patients desire pain relievers to manage symptoms, the use of nonsteroidal anti-inflammatory drugs (NSAIDs) or skeletal muscle relaxants is recommended. For individuals suffering from chronic low back pain, the initial treatment plan should also include the non-pharmaceutical means above in addition to multidisciplinary rehabilitation, exercise, and mindfulness-based stress reduction amongst others. The chronic use of these medications should always be practiced with caution due to their unfavorable side effects that include, but not limited to, dizziness, fatigue, constipation, weight gain, difficulty sleeping, and others [9, 10]. Despite current available treatments, data suggest that the number of individuals suffering from MP will continue to increase [1], further emphasizing the need for newer interventions. In recent years, new research investigating other alternatives to manage MP suggests a potential beneficial relationship between chronic pain and nutrient intake [11-14].

Nutrients, specifically macronutrients, are essential for providing energy to facilitate the growth and repair of various tissues in the human body [15]. some studies suggest that high consumption of energy-providing nutrients such as sugar, fat, and protein positively correlate with pain intensity in people with chronic musculoskeletal pain [16]. Moreover, Ketogenic diet therapy, where individuals follow a low carbohydrates, moderate protein, and high fat intake was shown to potentially reduce chronic pain [17]. Unfortunately, studies aiming to understand the relationship between macronutrients intake and severe musculoskeletal pain are very limited. Hence, investigating the relationship between macronutrients and severe musculoskeletal pain can potentially offer benefits to people suffering from this condition. Consequently, appropriate recommendations to these populations and provision of new guidelines to clinicians can significantly improve current healthcare practices for musculoskeletal pain management. Therefore, this cross-sectional study aims to investigate the relationship between self-reported consumption of different macronutrients and severe pain in a Norwegian population aged 40-89 years old.

2 Materials and methods

2.1 Study population and data collection

The Tromsø Study is a large population-based cohort study in Tromsø, Norway. The study is conducted in Tromsø municipality and included both urban and rural populations. The seventh survey, Tromsø7, was used for this study and was conducted from 2015 to 2016. The study invited 32,591 individuals aged 40 and above to participate, and a total of 21,083 attended the study representing a 65% participation rate [18]. However, for the purpose of this study, participants with incomplete Food Frequency Questionnaire (FFQ) (n=9620) and pain data (n=671) were excluded. Furthermore, those with missing education and physical activity data (n=314) and BMI (n=26) were also removed from the study. As a result, the study included a final total of 10,438 participants **Figure 1**.

Confounders

Confounding variables included in the analyses were age, sex, education, physical activity, and Body Mass Index (BMI). Variables were categorized as the following: Education as: primary/partly secondary education (up to 10 years in schooling), upper secondary education (a minimum of 3 years), short tertiary education (college/university less than 4 years), and long tertiary education (college/university 4 years or more). Physical activity and leisure time was categorized as sedentary (reading/watching tv or other sedentary activity), light (walking, cycling, or any other form of exercise at least 4 hours a week, including walking or cycling to a place of work, Sunday walking, etc.), and moderate-to-vigorous (participation in recreational sports: heavy gardening, snow shovelling, etc. at least 4 hours a week and participating in hard training or sports competitions, regularly). Physical activity and leisure time were reported based on the Saltin-Grimby Physical Activity Level Scale (SGPALS)[19]. Body mass index (BMI) was measured in kilograms (kg) divided by meters (m) squared (kg/m2) and categorized as follows: normal weight (<25 kg/m2), overweight (25-29.9 kg/m2), and obese (>30 kg/m2).

Macronutrients

Participants answered a comprehensive food frequency questionnaire (FFQ) to assess the intake of each macronutrient, the questionnaire can be found in detail on the Tromsø7 study website [18]. Macronutrients included in this study were as follows: protein, overall fat, alcohol, carbohydrates, sugar, and fiber **Table 1**. The intake of energy providing nutrients (macronutrients), energy percentages (E%) were calculated by The University of Oslo. Information regarding the variables of Tromsø7 study can be found in the Tromsø study website [18]. Macronutrients were measured as energy percentages (E%) and categorized according to the Nordic Nutrition Recommendation 2012 (NNR-2012), except for fiber, which was measured in grams per day (g/day) [20]. According to the NNR-2012, protein intake recommendations were based on age groups and divided into two categories: adults (18-64 years) and elderly (65> years), and each was further categorized into low (0-9.999%), optimal (10-20%), and high intake (20.001%+), and low (0-14.999%), optimal (15-20%,) and high intake (20.001%+), respectively. Overall fat was categorized as low (0-24.9%), optimal (25-40%), and high (40.001%+), while alcohol was categorized as optimal (<5%) and high intake (>5%). Carbohydrates was categorized as low (0-44.999%) and optimal/high (≥45%); data for optimal and high carbohydrate intake were combined as only few participants (n=36) had high intake. Sugar was categorized as optimal (<10%) and high (>10%), and fiber (g/day) was categorized based on gender as optimal for females (> 25 g/d) and optimal for males (>35g/d).

Musculoskeletal pain

To study the phenomenon of pain, this study included two pain variables. The first one was regarding neck and shoulders where participants were asked if they suffered from pain and/or stiffness in muscles or joints in the neck/shoulders area lasting for at least 3 consecutive months. The second was if they suffered from pain and/or stiffness in muscles or joints in the lumbar regions lasting for at least 3 consecutive months. The study aimed to understand the relationship between severe pain and macronutrients intake. The time period of at least 3 months was used to identify if the pain was chronic. Consequently, pain data were divided into two categories: "no/moderate" pain and "severe" pain for the neck/shoulder and low back (lumbar regions) pain.

2.2 Statistical analysis

A descriptive analysis of macronutrients among different confounders was presented using counts (n=#) and percentages (%) according to the intakes of NNR-2012. Pearson's chi-square test with a $P \leq .05$ significance was used to test the difference in the distribution of the categorical variables. For fiber, mean and standard deviation were used to present data. An independent T-test and ANOVA were used to test the p-value for continuous variables, as shown in **Table 1**. Moreover, a descriptive analysis of neck/shoulder and lumbar pain among different confounders was also presented using counts (n=#) and percentages (%) and displayed according to severe pain; P-value of $P \leq .05$ significance was tested using Pearson's chi-square test **Table 2**.

Binary logistic regression analysis was used to determine the relationship between neck/shoulder, lumbar pain, and macronutrients. Ordinal logistic regression was not used due to a violation of the assumption. Two binary logistic regression models were applied to assess the relationship between macronutrients and severe pain; the first model (model 1) tested pain variable with each macronutrient separately (with confounders), the second model (model 2) tested pain variable with all macronutrients and all confounders together. The optimal intake of all macronutrients was used as the reference in the regression analysis, except for carbohydrates where the low intake was used as a reference as shown in **Table 3** and **Table 4**. High carbohydrate intake was combined with optimal as its values were very low; hence, low was used as a reference. All statistical analyses were performed using IBM SPSS program version (29.0.0.0 (241)) for Mac, released in 2022.

2.3 Ethical consideration

The data from the Tromsø7 study was anonymous and approved by the data protection authority (DPU).

3 Results

3.1 Study sample

In this study, female participants make up majority of the population with a percentage of 52.7%, while males account for 47.3%. Over half of participants (53%) completed a university education defined as tertiary education, both short and long, as observed in **Table 1**. In terms of physical activity, over half the population (58.6%) engage in light exercises such as walking, cycling, or other forms of exercise at least 4 hours a week. Obese and overweight individuals account for two-thirds (66.7%) of the total study population **Table 1**.

3.2 Study Confounders and Macronutrients

In this study sample, age was found to be significantly associated with all macronutrients with a p-value of <.001; results show that people with the lowest protein intake were among participants over the age of 60 (62.8%) **Table 1**. Sex was significantly associated with all macronutrients except for carbohydrates (*P*.089); females were observed to consume more protein than men in all protein categories, as presented in **Table 1**. Education showed a significant association with all macronutrients (*P*<.001). Overall, long tertiary education had the highest optimal protein (33.9%) and sugar (33.1) intakes as well as the highest distribution in all fat, carbohydrates, alcohol, and fiber categories **Table 1**. Physical activity was found to be significantly associated with protein (*P*.002), sugar and fiber (*P*<.001); participants who engage in light exercises were found to have the highest distribution in protein and sugar intakes (57.9%) amongst other physical activity and leisure time categories. BMI was found to be significant with all macronutrients except for sugar (*P*.090); overweight participants were shown to have the highest distribution in all categories of macronutrients, as shown in **Table 1**.

3.3 Pain and Confounders

In this study sample, age was found to be significantly associated with neck/shoulder pain (*P*<.001) but not with lumbar pain (*P*.231); participants who are 59 years and younger had the highest severe neck/shoulder pain (36.4%) **Table 2**. On the other hand, all remaining confounders; sex, education, physical activity, and BMI, were found to be significantly associated with neck/shoulder and lumbar pain with a p-value of <.001, as shown in **Table 2**. In this sample, women were found to have the highest neck/shoulder (67%) and lumbar (62%) severe pain compared to men. Participants with 10 years of schooling who finished upper secondary level education had the highest percentage of severe neck/ shoulder and lumbar pain combined (58.7% and 59.2%, respectively) **Table 2**. Individuals who participated in light exercises had the highest severe neck/shoulder (61%) and lumbar (59.8%) pain, as presented in **Table 2**. In terms of BMI, individuals who are overweight or obese had the highest combined percentage of severe neck/shoulder (70.9%) and lumbar (73.1%) pain.

3.4 Regression

3.4.1 Neck/Shoulder Pain

When testing neck/shoulders pain with each macronutrient individually and all confounders (model 1), high protein intake was significantly associated with increased odds of severe neck/shoulder pain (OR 1.196,95% CI 1.011-1.416) in comparison to optimal intake **Table 3**. Similarly, a high overall fat intake was significantly associated with increased odds of severe neck/shoulder pain (OR 1.225, 95% CI 1.032-1.453) compared to optimal intake. High sugar intake was also significantly associated with increased odds of severe neck/shoulder pain (OR 1.300, 95% CI 1.055-1.602) compared to optimal intake **Table 3**. In addition, when testing all macronutrients and all confounders with neck/shoulder pain together (model 2), high protein intake was also significantly associated with increased odds of severe neck/shoulder pain (OR 1.234, 95% CI 1.037-1.467) compared to optimal intake

Table 3. Similarly, High overall fat intake was also significantly associated with increased odds of severe neck/shoulder pain compared to optimal intake in model 2, which included all macronutrients (OR 1.235, 95% CI 1.029-1.482) **Table 3**. High intake of sugar is also significantly associated with increased positive odds of severe neck/shoulder pain compared to optimal intake (OR 1.465, 95% CI 1.171-1.834) as shown in **Table 3**. Lastly, a higher intake of fiber is associated with an increased odds for severe neck/shoulder pain with an OR of 1.002 95% CI 1.000-1.004 as presented in Table 3. Both alcohol and carbohydrates were not significantly associated with neck/shoulder pain in both models.

3.4.2 Lumbar Pain

When testing lumbar pain with each macronutrient individually and all confounders (model 1), a low intake of protein was associated with reduced odds of experiencing severe lumbar pain compared to the recommended intake (OR 0.649, 95% CI 0.43-0.981) **Table 4**. However, high protein intake was associated with increased odds of severe lumbar pain compared to recommended intake levels of protein (OR 1.282, 95% CI 1.065-1.544) **Table 4**. Additionally, optimal/high intakes of carbohydrates were associated with reduced odds of experiencing severe lumbar pain compared to low intakes of carbohydrates (OR 0.847, 95% CI 0.722-0.995) **(model 1, Table 4)**. Finally, in model 1, increased fiber intake was significantly associated with positive odds of experiencing severe lumbar pain (OR 1.003, 95% CI 1.001-1.005) **Table 4**. Furthermore, when testing lumbar pain with all macronutrients and all confounders together as shown in model 2, low protein intake was significantly associated with reduced odds of experiencing severe lumbar pain compared to the recommended intake with an OR of 0.629 with 95% CI 0.413-0.957. On the contrary, high protein intake was associated with an increased odds for severe lumbar pain compared to the recommended intake (OR 1.304, 95% CI 1.078-1.578) **Table 4**. Finally, a higher grams per day of fiber intake was associated with increased odds for severe lumbar pain, with an OR of 1.003 with 95% CI 1.002-1.005, as shown in model 2 **Table 4**. Sugar, alcohol, and overall fat were not significantly associated with lumbar pain in both models.

4 Discussion

In this study, consuming high amounts of protein was significantly associated with increased odds of severe neck/shoulder and lumbar pain compared to the recommended intake. Additionally, low protein intake was significantly associated with lower odds off severe lumbar pain compared to the recommended intake. Similar to these findings, a recent systematic review assessing nutrient intake and pain severity found a significant positive correlation between protein intake and pain [16]. Moreover, a cohort study evaluating food intake and female patients suffering from fibromyalgia found that vegetarian diets composed of low protein and low-fat help in alleviating pain[21].

Contrary to this study, a cross-sectional study investigating chronic spinal pain and diet quality found that people suffering from chronic spinal pain consume less protein [22]. In addition, a systematic review of dietary interventions for managing fibromyalgia revealed that the consumption of protein, specifically soy protein, can effectively reduce inflammatory markers and alleviate pain sensations [23]. Moreover, a pilot randomized control trial investigating the ketogenic diet's effect on chronic pain found that this diet, where protein is 10-20% of the total energy requirements, improves chronic pain[17]. While some studies indicate that a high-protein diet may have pain-relieving benefits for chronic pain sufferers, this study did not take into account the particular sources or type of protein consumed. It is plausible that the higher odds of severe pain associated with excessive protein intake in our study could be attributed to the consumption of red meat or processed meat, which have been associated with adverse health outcomes [24].

In this paper, a high fat intake was associated with increased odds of severe neck/shoulder pain compared to the optimal fat intake. Similar to our findings, a cross-sectional study assessing spinal pain, which included (back, neck, and hip) and diet quality, found that people who report having chronic pain consume higher amounts of saturated fat [22]. Moreover, another cross-sectional study assessing the relationship between fatty acid intakes and chronic neck/shoulder pain found that high intakes of specific fatty acids were associated with chronic neck/shoulder pain [25]. However, despite similar findings, it is important to note that in this study, the types of fat consumed by participants were not assessed; only overall fat’s association with pain was assessed.

High sugar consumption was associated with an increase in odds of severe neck/shoulder pain compared to low sugar intakes in this study. Most studies have found that high sugar intake is associated with chronic pain [22, 24, 26]. Similarly, a cross-sectional study found that added sugar was associated with increased odds of having spinal pain [22]. Another cross-sectional study assessing chronic low back pain and dietary patterns found that consuming high amounts of sugar was also associated with chronic low back pain[24]. In addition, another study found that adhering to sugary foods decreases muscle strength, which can ultimately lead to musculoskeletal pain [26].

In this study, we found that fiber was significantly associated with increased odds of experiencing severe neck/shoulders and lumbar pain. However, the odds ratios for both types of pain were only slightly higher than 1 (1.002 for severe neck/shoulder pain and 1.003 for severe lumbar pain), indicating that the association between fiber and pain is weak. Although the p-value indicates statistical significance, the results suggest that the difference in pain levels is negligible. Nevertheless, many studies have found that consuming at least the daily recommended fiber intake was significantly associated with chronic pain relief [21-23, 27].

4.1 Strengths & Limitations

Strengths of this study include the large sample size, inclusion of multiple confounder variables, and the inclusion of six macronutrients to understand their individual effects on severe pain. The findings can be shared with healthcare providers to direct patients or educate the public on the effects of high or low intake of certain macronutrients to better manage severe pain. Limitations included the study design being cross-sectional, which makes it difficult to derive a cause-and-effect relationship between variables. In addition, the time period of obtaining the data might not truly represent the population as it is a snapshot measure of exposure and outcome. The method for data collection, specifically food frequency questionnaires (FFQ), is also subjected to recall bias and under- or over-reporting as it is retrospective in nature. In addition, FFQ consists of pre-specified food lists, which may not accurately represent the eating habits of different populations. Thus, one must practice caution when applying the findings to other populations. The findings are also limited due not including smoking habits, occupation, and income in the study, all of which are likely to affect the results due to their known negative consequences on pain[28-30].

In addition, data used in this study included protein and overall fat, without specifying the source of protein (i.e animal vs plant protein) and what type of fat is consumed. Recent studies show that consumption of plant-based protein and/or vegetarian diets carry more pain-relieving effects [16]. Specific types of unsaturated fats, most notably the essential omega-3 fatty acid, was found to be inversely associated with worsening pain in the elderly population while high levels of omega-6 were found to have a linear associated with pain[31, 32]. These findings warrant further research to understand the effects of specific macronutrient types on pain, which was not addressed in this study. Moreover, the definition of moderate and severe pain differs from one participant to another due to tolerance and pain being a highly individualized experience. The study aimed to address severe pain; however, the definition of severe pain differs from one person to another and is difficult to measure uniformly across all populations. Musculoskeletal pain was also limited to only two questions in the Tromso7 survey with a pain scale of "no pain, little, or severe." The use of gold standard pain questionnaires such as the Numerical Rating Scale (NRS) or a more detailed questionnaire might have produced different results. In addition, logistic regression was used to measure the association between macronutrients and severe neck/shoulders and lumbar pain. Ordinal logistic regression model was not feasible for this study because the assumptions were violated; hence, binary logistic regression was used instead. Consequently, pain was categorized as "no/moderate" and "severe" to satisfy the assumptions for binary logistic regression to measure the relationship between the variables.

5 Conclusion

In conclusion, several macronutrients were found to be associated with severe pain in our population. Most notably, high protein intake and overall fat intake were found to be associated with severe neck/shoulders and lumbar pain. Nevertheless, these associations cannot be applied or recommended to the general public due to the nature of cross-sectional studies where they do not allow inferring causality between the studied variables. Further studies in a more controlled setting that perhaps include both micronutrient and macronutrients together are needed to truly understand and determine the cause-and-effect relationship of these nutrients and severe musculoskeletal pain.

Figures and Tables

Table 1 –Characteristics of study sample and macronutrients intake. The Tromsø study 2015-2016

Characteristics	*Total N (%)*	Macronutrients: Protein			*P*-value	Overall Fat			*P*-value	Alcohol		*P*-value
		Low	Opt	High		Low	Opt	High		Opt <5	ETC	
Age					<0.001				<0.001			<0.001
40-49	3126 (29.9%)	8(1.5%)	2760(33.3)	358(22.4)		88 (22.2%)	2469 (29.1%)	569 (36.8%)		2608 (32.5%)	518 (21.4%)	
50-59	3065 (29.4%)	6(1.1%)	2550(30.7)	509(31.8)		119 (30%)	2474 (29.1%)	472 (30.6%)		2285 (28.5%)	780 (32.3%)	
60-69	2840 (27.2%)	342 (62.8%)	1982(23.9)	516(32.3)		108 (27.2%)	2362 (27.8%)	370 (23.9%)		2020 (25.2%)	820 (33.9%)	
70-79/80-89	1407 (13.5%)	189 (34.7%)	1002(12.1)	216(13.5)		82 (20.7%)	1191 (14%)	134 (8.7%)		1108 (13.8%)	299 (12.4%)	
Sex					<0.001				<0.001			<0.001
Female	5498 (52.7%)	217 (39.8%)	4334 (52.3%)	947(59.2)		174 (43.8%)	4431 (52.2%)	893 (57.8%)		4447 (55.4%)	1051 (43.5%)	
Male	4940 (47.3%)	328 (60.2%)	3960 (47.7%)	652(40.8)		223 (56.2%)	4065 (47.8%)	652 (42.2%)		3574 (44.6%)	1366 56.5%)	
Education Level[a]					<0.001				0.003			<0.001
Up to 10 years of schooling	2044 (19.6%)	166 30.5%)	1507 (18.2%)	371(23.2)		97 (24.4%)	1699 (20%)	248 (16.1%)		1698 (21.2%)	346 (14.3%)	
Upper-secondary education	2854 (27.3%)	140 (25.7%)	2233 (26.9%)	481(30.1)		101 (25.4%)	2327 (27.4%)	426 (27.6%)		2268 (28.3%)	586 (24.2%)	
Tertiary education, short	2164 (20.7%)	91 (16.7%)	1739 (21%)	334(20.9)		78 (19.6%)	1751 (20.6%)	335 (21.7%)		1608 (20%)	556 (23%)	

Tertiary education, long	3376 (32.3%)	148 (27.2%)	2815 (33.9%)	413(25.8)		121 (30.5%)	2719 (32%)	536 (34.7%)		2447 (30.5%)	929 (38.4%)	
Physical activity level[b]					0.002				0.069			0.060
Sedentary	1371 (13.1%)	85 (15.6%)	1103 (13.3%)	183(11.4)		59 (14.9%)	1078 (12.7%)	234 (15.1%)		1051 (13.1%)	320 13.2%)	
Light	6116 (58.6%)	335 (61.5%)	4800 (57.9%)	981(61.4)		222 (55.9%)	5016 (59%)	878 (56.8%)		4746 (59.2%)	1370 (56.7%)	
Moderate/Vigorous	2951 (28.3%)	125 (22.9%)	2391 (28.8%)	435(27.2)		116 (29.2%)	2402 (28.3%)	433 (28%)		2224 (27.7%)	727 (30.1%)	
BMI[c]					<0.001				0.049			<0.001
Normal	3470 (33.3%)	221 (40.6%)	2855 (34.4%)	394(24.6)		114 (28.7%)	2804 (33%)	552 (35.7%)		2712 (33.8%)	758 (31.4%)	
Overweight	4555 (43.6%)	223 (40.9%)	3641 (43.9%)	691(43.2)		178 (44.8%)	3737 (44%)	640 (41.4%)		3412 (42.5%)	1143 (47.3%)	
Obese	2413 (23.1%)	101 (18.5%)	1798 (21.7%)	514(32.1%)		105 (26.4%)	1955 (23%)	353 (22.8%)		1897 (23.7%)	516 (21.3%)	

Table 1– Cont.

		Macronutrients								
Characteristics	*Total N (%)*	Carbohydrates		*P*-value	Sugar		*P*-value	Fiber		*P*-value
		Low	Optimal/High		Optimal	Higher		Mean (g/day)	SD (+/-)	
Age				<0.001			<0.001			<0.001
40-49	3126 (29.9%)	2060 (29.1%)	1066 (31.8%)		2801 (29.4%)	325 (35.8%)		114.2	40.91	
50-59	3065 (29.4%)	2203 (31.1%)	862 (25.7%)		2832 (29.7%)	233 (25.7%)		118.01	43.4	

60-69	2840 (27.2%)	1994 (28.1%)	846 (25.3%)		2618 (27.5%)	222 (24.4%)		114.35	41.07	
70-79/80-89	1407 (13.5%)	833 (11.7%)	574 (17.1%)		1279 (13.4%)	128 (14.1%)		106.86	39.02	
Sex				0.089			<0.001			0.003
Female	5498 (52.7%)	3775 (53.2%)	1723 (51.5%)		5086 (53.4%)	412 (45.4%)		113.24	40.45	
Male	4940 (47.3%)	3315 (46.8%)	1625 (48.5%)		4444 (46.6%)	496 (54.6%)		115.63	42.78	
Education Level[a]				<0.001			<0.001			<0.001
Up to 10 years of schooling	2044 (19.6%)	1284 (18.1%)	760 (22.7%)		1815 (19%)	229 (25.2%)		107.43	41.51	
Upper-secondary education	2854 (27.3%)	1948 (27.5%)	906 (27.1%)		2564 (26.9%)	290 (31.9%)		112.95	42.53	
Tertiary education, short	2164 (20.7%)	1532 (21.6%)	632 (18.9%)		2001 (21%)	163 (18%)		115.4	40.18	
Tertiary education, long	3376 (32.3%)	2326 (32.8%)	1050 (31.4%)		3150 (33.1%)	226 (24.9%)		119.12	41.08	
Physical activity level[b]				0.714			<0.001			<0.001
Sedentary	1371 (13.1%)	921 (13%)	450 (13.4%)		1192 (12.5%)	179 (19.7%)		98.5	37.76	
Light	6116 (58.6%)	4172 (58.8%)	1944 (58.1%)		5627 (59%)	489 (53.9%)		113.61	40.44	
Moderate/Vigorous	2951 (28.3%)	1997 (28.2%)	954 (28.5%)		2711 (28.4%)	240 (26.4%)		123.32	43.21	
BMI[c]				0.049			0.90			<0.001
Normal	3470 (33.3%)	2324 (32.8%)	1146 (34.2%)		3168 (33.2%)	302 (33.3%)		116.95	42.25	

Overweight	4555 (43.6%)	3079 (43.4%)	1476 (44.1%)		4164 (43.7%)	391 (43.1%)		113.74	40.99	
Obese	2413 (23.1%)	1687 (23.8%)	726(21.7%)		2198 (23.1%)	215 (23.7%)		111.85	41.55	

Overall differences between macronutrients and confounders were tested by Pearson's chi-square test for categorical variables, independent t-test and ANOVA for continuous variables, and mean/standard deviation for the scale variable. Significance is defined as a p-value <0.05. [a]Education Levels: Up to 10 years of schooling, Upper-secondary education: a minimum of 4 years, Tertiary education short: less than 4 university years, Tertiary education, long: 4 or more university years. [b]Physical Activity: Sedentary: reading/TV, Light: walking/cycling, or other forms of exercise at least 4 hours a week, and Moderate/Vigorous (at least 4 hours a week of recreational sports/hard training more than 4h a week). [c]BMI (Body Mass Index): Normal: (BMI < 25.0 kg/m2), Overweight (BMI 25.0–29.9 kg/m2), Obesity (BMI ≥ 30 kg/m2).

Table 2-Charactarestics of study sample and musculoskeletal pain. The Tromsø study 2015-2016

Characteristics	Total N(%)	Neck/Shoulders No/Moderate	Neck/Shoulders Sever	Neck/Shoulders *P*-value	Lumbar Region No/Moderate	Lumbar Region Sever	Lumbar Region *P*-value
Age				<0.001			0.231
40-49	3126 (29.9%)	2806 (29.9%)	320 (29.9%)		2903 (30.1%)	223 (27.9%)	
50-59	3065 (29.4%)	2676 (28.6%)	389 (36.4%)		2806 (29.1%)	259 (32.4%)	
60-69	2840 (27.2%)	2571 (27.4%)	269 (25.2%)		2631 (27.3%)	209 (26.2%)	
70-79 80-89	1407 (13.5%)	1316 (14%)	91 (8.5%)		1299 (13.5%)	108 (13.5%)	
Sex				<0.001			<0.001
Female	5498 (52.7%)	4782 (51%)	716 (67%)		5003 (51.9%)	495 (62%)	
Male	4940 (47.3%)	4587 (49%)	353 (33%)		4636 (48.1%)	304 (38%)	
Education[a]				<0.001			<0.001
Up to 10 years of schooling	2044 (19.6%)	1777 (19%)	267 (25%)		1825 (18.9%)	219 (27.4%)	
Upper-secondary education	2854 (27.3%)	2494 (26.6%)	360 (33.7%)		2600 (27%)	254 (31.8%)	
Tertiary education, short	2164 (20.7%)	1966 (21%)	198 (18.5%)		2018 (20.9%)	146 (18.3%)	
Tertiary education, long	3376 (32.3%)	3132 (33.4%)	244 (22.8%)		3196 (33.2%)	180 (22.5%)	
Physical activity[b]				<0.001			<0.001
Sedentary	1371 (13.1%)	1182 (12.6%)	189 (17.7%)		1220 (12.7%)	151 (18.9%)	
Light	6116 (58.6%)	5464 (58.3%)	652 (61%)		5638 (58.5%)	478 (59.8%)	
Moderate/vigorous	2951 (28.3%)	2723 (29.1%)	228 (21.3%)		2781 (28.9%)	170 (21.3%)	
BMI[c]				<0.001			<0.001
Normal	3470 (33.3%)	3159 (33.7%)	311 (29.1%)		3255 (33.8%)	215 (26.9%)	
Overweight	4555 (43.6%)	4110 (43.9%)	445 (41.6%)		4237(44%)	318 (39.8%)	

Obese	2413 (23.1%)	2100 (22.4%)	313 (29.3%)	2147 (22.3%)	266 (33.3%)

Overall differences between pain variables and confounders were tested by Pearson's chi-square test for categorical variables. Significance is defined as a p-value <0.05. [a]Education Levels: Up to 10 years of schooling, Upper-secondary education: a minimum of 4 years, Tertiary education short: less than 4 university years, Tertiary education, long: 4 or more university years. [b]Physical Activity: Sedentary: reading/TV, Light: walking/cycling, or other forms of exercise at least 4 hours a week, and Moderate/Vigorous (at least 4 hours a week of recreational sports/hard training more than 4h a week). [c]BMI (Body Mass Index): Normal: (BMI < 25.0 kg/m2), Overweight (BMI 25.0–29.9 kg/m2), Obesity (BMI ≥ 30 kg/m2).

Table 3-Regression analysis of neck/shoulder musculoskeletal pain and macronutrients

	Model 1				Model 2			
Macronutrient	Odds ratio	CI 95% Lower	CI 95% Upper	*P-value*	Odds ratio	CI 95% Lower	CI 95% Upper	*P-value*
Protein								
Low	1.053	0.759	1.46	0.757	0.956	0.684	1.336	0.791
Optimal	Reference							
High	1.196	1.011	1.416	0.037	1.234	1.037	1.467	0.018
Overall fat								
Low	1.284	0.931	1.77	0.128	1.281	0.917	1.789	0.147
Optimal	Reference							
High	1.225	1.032	1.453	0.02	1.235	1.029	1.482	0.023
Carbohydrates								
Low	Reference							
Optimal/High	0.918	0.798	1.055	0.227	0.902	0.765	1.062	0.215
Alcohol								
Optimal	Reference							
High	1.009	0.86	1.184	0.915	1.059	0.892	1.256	0.515
Sugar								
Optimal	Reference							
	1.3	1.055	1.602	0.014	1.465	1.171	1.834	<0.001
Fiber (grams/day)	1.002	1	1.003	0.056	1.002	1	1.004	0.015

Results shown in Odds ratios with 95% confidence interval and p-value with <0.05 significance level. Model 1: Regression analysis of pain with each macronutrient separately (with all confounders). Model 2: Regression analysis of pain and all macronutrients and all confounders together. The optimal intake of all macronutrients was used as a Reference except for Carbohydrates where the low intake was used as a Reference.

Table 4- Regression analysis of lumbar musculoskeletal pain with macronutrients.

Macronutrient	Model 1				Model 2			
	Odds ratio	CI 95%		*P-value*	Odds ratio	CI 95%		*P-value*
		Lower	Upper			Lower	Upper	
Protein								
Low	0.649	0.43	0.981	0.04	0.629	0.413	0.957	0.03
Optimal	Reference							
High	1.282	1.065	1.544	0.009	1.304	1.078	1.578	0.006
Overall Fat								
Low	1.258	0.881	1.796	0.207	1.29	0.89	1.871	0.179
Optimal	Reference							
High	1.216	0.999	1.479	0.051	1.23	0.999	1.515	0.051
Carbohydrates								
Low	Reference							
Optimal/high	0.847	0.722	0.995	0.043	0.893	0.741	1.076	0.233
Alcohol								
Optimal	Reference							
High	1.064	0.89	1.271	0.496	1.139	0.941	1.378	0.182
Sugar								
Optimal	Reference							
High	0.92	0.708	1.195	0.53	1.125	0.852	1.486	0.406
Fiber (grams/day)	1.003	1.001	1.005	<0.001	1.003	1.002	1.005	<0.001

Results shown in Odds ratios with 95% confidence interval and p-value with <0.05 significance level. Model 1: Regression analysis of pain with each macronutrient separately (with all confounders). Model 2: Regression analysis of pain and all macronutrients and all confounders together. The optimal intake of all macronutrients was used as a Reference except for Carbohydrates where the low intake was used as a Reference.

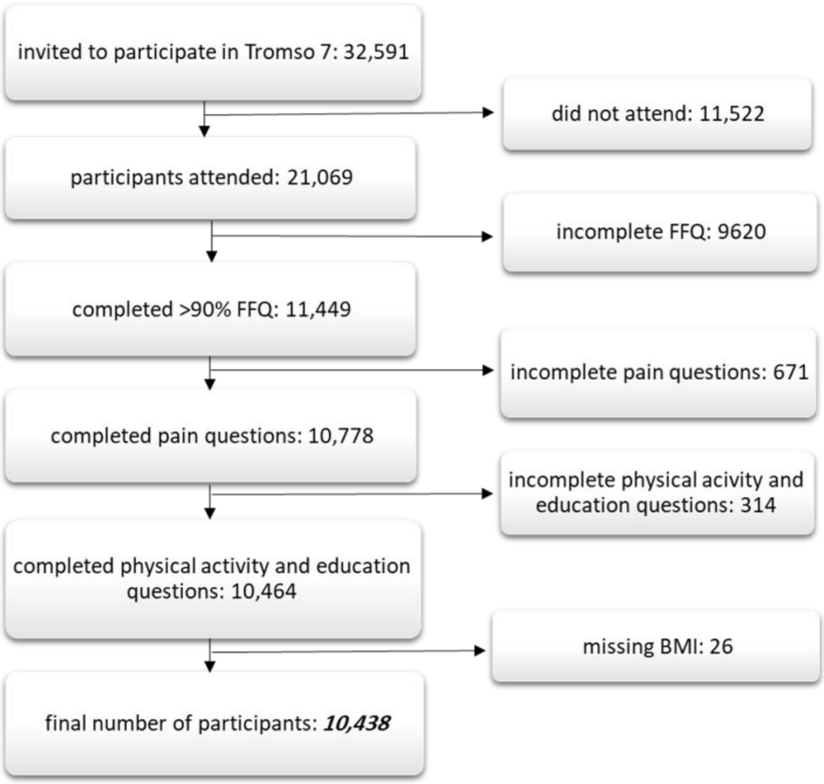

Figure 1 – flowchart of study sample.

References

1. W.H.O. *Musculoskeletal Health Fact sheet* 2022; Available from: https://www.who.int/news-room/fact-sheets/detail/musculoskeletal-conditions.
2. *Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016.* Lancet, 2017. **390**(10100): p. 1211-1259.
3. Arendt-Nielsen, L., C. Fernández-de-Las-Peñas, and T. Graven-Nielsen, *Basic aspects of musculoskeletal pain: from acute to chronic pain.* J Man Manip Ther, 2011. **19**(4): p. 186-93.
4. El-Tallawy, S.N., et al., *Management of Musculoskeletal Pain: An Update with Emphasis on Chronic Musculoskeletal Pain.* Pain Ther, 2021. **10**(1): p. 181-209.
5. Hoy, D., et al., *The Epidemiology of low back pain.* Best Pract Res Clin Rheumatol, 2010. **24**(6): p. 769-81.
6. Garnæs, K.K., et al., *Mental health among patients with chronic musculoskeletal pain and its relation to number of pain sites and pain intensity, a cross-sectional study among primary health care patients.* BMC Musculoskelet Disord, 2022. **23**(1): p. 1115.
7. Cieza, A., et al., *Global estimates of the need for rehabilitation based on the Global Burden of Disease study 2019: a systematic analysis for the Global Burden of Disease Study 2019.* Lancet, 2021. **396**(10267): p. 2006-2017.
8. Qaseem, A., et al., *Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians.* Ann Intern Med, 2017. **166**(7): p. 514-530.
9. Clinic, D.O.R.S.E.-M. *Drugs and Supplements*

Duloxetine (Oral Route). 2023; Available from: https://www.mayoclinic.org/drugs-supplements/duloxetine-oral-route/side-effects/drg-20067247?p=1.

10. Clinic, T.O.R.S.E.-M., *Drugs and Supplements*

Tramadol (Oral Route). 2023.

11. Mendonça, C.R., et al., *Effects of Nutritional Interventions in the Control of Musculoskeletal Pain: An Integrative Review.* Nutrients, 2020. **12**(10).
12. Noh, H.M., et al., *Association between Dietary Protein Intake, Regular Exercise, and Low Back Pain among Middle-Aged and Older Korean Adults without Osteoarthritis of the Lumbar Spine.* J Clin Med, 2022. **11**(5).
13. pain, I.a.f.t.s.o. *Nutrition and Chronic Pain*. Fact sheet 2020; Available from: https://www.iasp-pain.org/resources/fact-sheets/nutrition-and-chronic-pain/.
14. Field, R., et al., *Dietary Interventions Are Beneficial for Patients with Chronic Pain: A Systematic Review with Meta-Analysis.* Pain Med, 2021. **22**(3): p. 694-714.
15. Kumar, V., et al., *ROLE OF MACRONUTRIENT IN HEALTH.* 2017. **6**: p. 373-381.
16. Elma, Ö., et al., *Do Nutritional Factors Interact with Chronic Musculoskeletal Pain? A Systematic Review.* J Clin Med, 2020. **9**(3).
17. Field, R., F. Pourkazemi, and K. Rooney, *Effects of a Low-Carbohydrate Ketogenic Diet on Reported Pain, Blood Biomarkers and Quality of Life in Patients with Chronic Pain: A Pilot Randomized Clinical Trial.* Pain Med, 2022. **23**(2): p. 326-338.
18. Study, T.T. *The Tromsø Study: Tromsø7 / Tromsøundersøkelsen: Tromsø7*. 2015-2016; Available from: https://uit.no/research/tromsostudy/project?pid=708909.

19. Grimby, G., et al., *The "Saltin-Grimby Physical Activity Level Scale" and its application to health research.* Scand J Med Sci Sports, 2015. **25 Suppl 4**: p. 119-25.
20. Ministers, N.C.o. *Nordic Nutrition Recommendations 2012* © Nordic Council of Ministers 2014; Available from: https://norden.diva-portal.org/smash/record.jsf?pid=diva2%3A704251&dswid=-3793.
21. Batista, E.D., et al., *Food intake assessment and quality of life in women with fibromyalgia.* Rev Bras Reumatol Engl Ed, 2016. **56**(2): p. 105-10.
22. Zick, S.M., S.L. Murphy, and J. Colacino, *Association of chronic spinal pain with diet quality.* Pain Rep, 2020. **5**(5): p. e837.
23. Lowry, E., et al., *Dietary Interventions in the Management of Fibromyalgia: A Systematic Review and Best-Evidence Synthesis.* Nutrients, 2020. **12**(9).
24. Pasdar, Y., et al., *Major dietary patterns in relation to chronic low back pain; a cross-sectional study from RaNCD cohort.* Nutr J, 2022. **21**(1): p. 28.
25. Asai, A., et al., *Relationship between fatty acid intake and chronic neck/shoulder/upper limb pain without elevated CRP in a Japanese population: a cross-sectional analysis of the Shika study.* J Nutr Sci, 2022. **11**: p. e38.
26. Pasdar, Y., et al., *Better muscle strength with healthy eating.* Eat Weight Disord, 2021. **26**(1): p. 367-374.
27. Elma, Ö., et al., *Chronic Musculoskeletal Pain and Nutrition: Where Are We and Where Are We Heading?* Pm r, 2020. **12**(12): p. 1268-1278.
28. Green, B.N., et al., *Association Between Smoking and Back Pain in a Cross-Section of Adult Americans.* Cureus, 2016. **8**(9): p. e806.
29. Schneider, S., S. Lipinski, and M. Schiltenwolf, *Occupations associated with a high risk of self-reported back pain: representative outcomes of a back pain prevalence study in the Federal Republic of Germany.* Eur Spine J, 2006. **15**(6): p. 821-33.
30. Ikeda, T., et al., *Socioeconomic inequalities in low back pain among older people: the JAGES cross-sectional study.* Int J Equity Health, 2019. **18**(1): p. 15.
31. Carballo-Casla, A., et al., *Fish consumption, omega-3 fatty acid intake, and risk of pain: the Seniors-ENRICA-1 cohort.* Clin Nutr, 2022. **41**(11): p. 2587-2595.
32. Tokuyama, S. and K. Nakamoto, *Unsaturated fatty acids and pain.* Biol Pharm Bull, 2011. **34**(8): p. 1174-8.