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Abbreviations and acronyms

- ADF Asymptotically Distribution Free
- AMD Age-Related Macular Degeneration
- AP Abdominal perimeter
- BMI Body mass index
- CATPCA Categorical Principal Components Analysis
- CFA Confirmatory Factor Analysis
- DM Diabetes Mellitus
- EFA Exploratory Factor Analysis
- GLS Generalized least squares
- HT Hypertension (High blood pressure)
- ML Maximum Likelihood
- NSI National Statistic Institute
- PYU Pack year unit
- RMSEA Root Mean Square Error of Approximation
- SEM Structural Equation Models

Abstract

Age-related macular Degeneration (AMD) is one of the main causes of blindness worldwide. A healthy diet and exercise have been referred to as protective factors whereas smoking is considered a risk factor. Many treatments recommend vitamin and mineral supplements because of their antioxidant properties. The Mediterranean diet and lifestyle, namely in Portugal, have never been tested.

Therefore, the aim of this study is to find a nutritional profile and risk factors for AMD that will allow us to recommend lifestyles that help prevent this disease.

Citizens of Lousã, aged 55 or older, were recruited. They underwent an eye exam consisting of a fundus color photograph which was graded by an Ophthalmologist. The same patients answered a questionnaire on food frequency, lifestyle habits, possible chronic illnesses, medication and the intake of diet supplements. The answers were analyzed with regards to the different nutrients and foods in order to identify a Mediterranean diet pattern.

The statistical analysis was composed both of descriptive and inferential tests using SPSS Statistics and SPSS Amos.

The final sample consisted of 884 patients, 451 of which did not suffer from AMD and 433 of which did. These groups were compared with each other. The results revealed that there are significant differences in the consumption of some nutrients and specific foods in both groups.

It was concluded that patients without AMD have a similar dietary pattern to the Mediterranean diet. When the consumption of wine is considered, however, this difference ceases to exist. Fast food, readymade meals, dairy products and meat are ingested more frequently by individuals suffering from AMD.

The consumption of fish, dark green leafy vegetables, fruit and pulses are different in both groups but without statistical difference.

Exercise was another factor that allowed inference that those who did not practice much would have a greater risk of suffering from AMD.

Even though the sample was relatively homogenous, it was possible to conclude from our findings that factors which can work as protectors for AMD are food such as carrots, tea, biscuits, chocolate and soup which carry protective nutrients, namely antioxidants.

Protection against AMD was found to be related to the ingestion of nutrients such as fiber, caffeine, vitamins C and E and carotenoids.

The 'Mediterranean diet' pattern and exercise were more common factors in the group without AMD.

Therefore, it is important to reinforce the interest of Mediterranean diet and exercise in the prevention of AMD since these characteristics are more than likely associated with a healthy Mediterranean lifestyle.

Keywords: Age-Related Macular Degeneration; Mediterranean diet; Antioxidants; Diet; Exercise; Smoking; Food(s); Food supplements

Resumo

A Degenerescência Macular Relacionada com a Idade (DMI) é uma das principais causas de cegueira a nível mundial. A alimentação saudável e a actividade física têm sido referidas como factores protectores e o tabagismo como factor de risco. No tratamento, muitos trabalhos preconizam a suplementação com vitaminas e minerais pelo seu efeito antioxidante. A alimentação mediterrânea e os estilos de vida a ela associados nunca foram testados, nomeadamente, em Portugal.

Assim, este trabalho tem como objectivo principal encontrar um perfil nutricional e de factores de risco para a DMI que nos permita dar indicações sobre estilos de vida, que previnam a doença.

Foram recrutados habitantes da Lousã, com idades superiores a 55 anos que fizeram exame oftalmológico com fotografia do fundo ocular, posteriormente avaliada por um "grader" Oftalmologista, para definir a existência ou não de DMI. Os mesmos utentes responderam a um inquérito alimentar de frequência e a questões sobre hábitos de vida e eventuais doenças crónicas presentes, medicação e a toma ou não de suplementos alimentares. As respostas foram analisadas relativamente aos diferentes nutrientes e alimentos, tentando também encontrar um padrão de dieta mediterrânea.

A análise estatística englobou testes descritivos e inferenciais através do SPSS Statistics e SPSS Amos.

A amostra final foi de 884 utentes, dos quais 451 não apresentavam DMI e 433 tinham DMI. Estes dois grupos foram comparados entre si. Os resultados mostraram que existem diferenças significativas no consumo de alguns nutrientes e alimentos específicos, entre os dois grupos. Verificou-se que as pessoas sem DMI têm um padrão alimentar mais próximo da dieta do tipo mediterrâneo, contudo, se lhe associarmos o consumo de vinho, essa diferença deixa de existir. Os alimentos *fastfood*, pré-confeccionados, derivados lácteos e carne são consumidos com maior frequência pelos indivíduos com DMI.

O consumo de peixe, vegetais de folha verde escura, frutas e leguminosas tem diferenças entre os dois grupos mas sem significado estatístico.

O exercício físico foi outro factor que permitiu inferir que quem o pratica menos tem maior probabilidade de sofrer de DMI.

Apesar de se tratar de uma amostra bastante homogénea foi possível concluir que os factores que podem funcionar como protectores para a DMI, de acordo com os nossos resultados, são alimentos como cenoura, chá, bolachas e chocolate em associação e sopa, veiculando nutrientes protectores, nomeadamente os antioxidantes.

A protecção para a DMI está também relacionada com os nutrientes como a fibra, a cafeína, as vitaminas C e E e os carotenos.

O padrão de "dieta mediterrânea" e o exercício físico foram mais frequentes no grupo de indivíduos sem DMI.

Assim, é importante reforçar o interesse da alimentação mediterrânea e do exercício físico, que muito provavelmente se associam aos hábitos saudáveis característicos do estilo de vida mediterrâneo.

Palavras-chave: Degenerescência Macular Relacionada com a Idade; Dieta mediterrânea; Antioxidantes; Nutrição; Exercício; Tabaco; Alimentos; Suplementos alimentares

Introduction

Age related macular degeneration (AMD) is the leading cause of irreversible blindness in developed countries [1] and ranks third worldwide. [2] There are two types of AMD: wet or exudative and dry. In Portugal, according to estimates, [3] there were approximately 84,000 cases of late onset AMD in 2010. 83,000 of these were in people over 55. The early stages of AMD are usually asymptomatic, with drusens and pigmentation alterations near the fovea.

Currently, existing pharmacological options are not very effective. Available treatments for exudative AMD help improve eyesight twice as much in a third of the cases treated and prevent significant vision loss in more than 90% of the cases. [4,5] With dry AMD, there are very few efficient therapeutic options. So, there is a need to find preventive measures against AMD and, many studies have been developed in order to identify varying environmental factors related to the risk of developing this disease.

Smoking is the only modifiable risk factor which is certainly negative with regards to AMD. [6]

With reference to diet, many of the existing studies focus their interest only on some nutrients (isolated macro or micronutrients) or on supplements, and do not include many other factors that may be present or the interaction between nutrients in food, cooking/preparation methods, lifestyle habits or social and cultural factors. One of the most referred studies, the Age-Related Eye Disease Study (AREDS), [7] demonstrated that high doses of vitamin and antioxidant supplements may reduce the risk for progression to late onset AMD. Other researchers also state the benefits of the consumption of lutein and fatty omega-3 acids in foods. [8,9] Foods rich in carbohydrates and with a high glycemic index have also been implicated in the risk of AMD by way of the formation of advanced glycation end products, oxidative stress damage and inflammation. [10]

Until now, there have been few studies related to the consumption of food groups (meat, fruits/vegetables, among others) and the risk of early or late onset AMD, or that investigate the synergistic effect of nutrients and foods. [11] In this way, a study that would be able to relate these factors could probably infer portions and create a more balanced diet that would help prevent AMD in general. A preventive strategy, through nutritional modulation, would not only be implementable but also more attractive and efficient than taking medication, which is often expensive.

Thus, the interest in studying the effects of a standard healthy diet, such as the "Mediterranean diet", is justified so as to obtain representative and valid results on a type of nutritional pattern. This pattern still exists in Portugal, especially in rural communities. Research of this kind would allow for results and conclusions applicable not only to the Portuguese population, but also to other groups, and would provide the opportunity to identify food components that could potentially be involved in the prevention of AMD. The so-called "Mediterranean diet" currently represents the paradigm of "healthy" food and, therefore, was considered Intangible Patrimony of Humanity for some countries by UNESCO, of which Portugal has been part of since November 2013. This type of diet consists of the consumption of an abundance of products of vegetable origin (cereals, rice, dark green leafy vegetables, pulses, fresh fruit and nuts), use of olive oil as the main source of fat, moderate consumption of fish, white meat, dairy products and eggs, small quantities of red meat and the ingestion of wine with meals. Another characteristic of the Mediterranean diet is the low consumption of omega-6 fatty acids and a high consumption of omega-3. This Omega-6 and Omega-3 low ratio seems to protect against many inflammatory, oncologic and metabolic complications, [12] which could also be replicable for AMD. The Mediterranean diet is seen as a balanced diet model not only in portion size but also because it provides essential nutrients, some of which have antioxidant effects and, for this reason, are proven to protect against many diseases, such as AMD. [13-16]

The "Mediterranean diet" is a lifestyle not just a diet model, it combines local ingredients, recipes, methods of cooking, celebrations and traditions, as well as exercise, which in light of modern medicine, have been considered the model of a healthy lifestyle since 2010.

Therefore, the main objectives of this study are:

- 1. Recognize a nutritional profile and risk factors for AMD
- 2. Identify clinical instructions for the prevention of AMD through the modification of diet models and lifestyles

Secondary objectives of this study are to evaluate if:

1 - Patients suffering from AMD have poorer quality diet, which is defined here as one with low consumption of micronutrients such as zinc, antioxidants and omega-3 fatty acids, just to name a few, and the consumption of foods with a high glycemic index.

2 – Following a healthy diet, namely consuming fish, dark green leafy vegetables and fruit will have a more positive impact on the macula, which will be reflected in fewer AMD cases.

3 – Obesity, body fat distribution, smoking and lack of exercise could contribute to a greater prevalence of AMD, regardless of sex, age or diet.

MATERIAL AND METHODS

This study was designed as an extension of the observational study, transversal in sample probability "Epidemiological study of Prevalence of Age-Related Macular Degeneration AMD) in Portugal" (Protocol CC-01-2009), being conducted since 2009, in Portugal (Lousã

and Mira regions), for which some results were presented in 2012 at the 12th EURETINA Congress, at the E3 Workshop in France and at the 2014 VICT (Vision and Imaging Consortion for Translational Research) meeting held at the IBILI Auditorium.

<u>Material</u>

The study focused on the population of Lousã, namely on patients from the Health Centre and the Family Health Unit in Trevim-Sol. The number of patients from these units over 55 years old, according to the Census Bureau of NSI, is 5193. From these, 3409 were summoned to participate in this study. 1005 of these, both male and female, were selected using criteria that ensured half the patients had the disease and half did not.

These individuals were interviewed once, by a Dietician that filled in a questionnaire on lifestyle and existing chronic diseases, as well as a semi-quantitative survey on food intake frequency (Attachment I), valid for epidemiological research on the Portuguese population, [17,18] with said information pertaining to the year before the interview. A description of food habits and behaviours, such as, number of meals per day, methods of cooking/preparation and the use of different fats, was also obtained.

Both interview and exam were conducted after the filling in of an Informed Consent Form, where the objective of this study, the authorization to use the data collected and the confidentiality agreement were stated (Attachment II).

Methods

The patients were recruited during a 12-month period, from December 2012 to November 2013, using the Health Facilities file, after their family doctor explained the objectives of the study. There was also exposure through local media. Participants that signed the Informed Consent Form underwent an ophthalmological exam to ascertain whether or not the ocular pathology existed and a fundus color photograph was then taken. These photographs were

assessed by an ophthalmologic "grader" who classified them according to the existence and stage of AMD.

Survey on clinical and demographic characteristics and lifestyle and nutritional habits

The survey included 12 items to evaluate lifestyle and comorbidities, especially developed for this study. Weight and height (for Body Mass Index - BMI) and abdominal perimeter (AP) were evaluated during the interview. The existing comorbidities, including the notion of their own body weight and the practice, or not, of some form of physical exercise, were collected via patient answers. The remaining 86 items assessed the food intake frequency for groups of food in a closed section, with nine frequency categories ranging from "never to less than once a month" and "six times or more per day", and predetermined average portion size. The notes corresponding to food groups include foods according to similar nutritional composition. Food intake frequency assessment items were analysed as equivalent to daily frequency. The survey and the nutritional intake calculation were validated for the Portuguese population by researchers at Oporto University - the Faculty of Medicine and the Department of Clinical Epidemiology, Preventive Medicine and Public Health and the Institute of Public Health. [19,20] To obtain food intake, the frequency mentioned for each item was multiplied by the respective portion size model, in grams(g), and by a seasonal variation factor for foods consumed during specific seasons (0,25 was considered a 3 month seasonal average). The conversion of foods into nutrients was calculated using the Food Processor Plus computer program (ESHA Research, Salem, Oregon), with nutritional information from tables of food composition from the Department of Agriculture of the United States and adapted to Portuguese foods, whose nutrient content was added to the base original using data from the Portuguese food composition table. [19]

 $BMI \ge 30 \text{ Kg/m}^2$ was considered obesity. 80cm and 94cm for AP were considered the abdominal risk cut off for women and men, respectively.

Detection of Age-related Macular Degeneration

In the epidemiologic study all participants had a fundus color photograph taken. These photographs were then graded by an Ophthalmologist with regards to the presence of lesions related to AMD and other pathologies (Attachment III).

Statistical analysis

The strategy of data analysis in this study included the descriptive analysis and inferences using IBM SPSS Statistics Software and IBM SPSS Amos, both in version 21. Descriptive analysis, absolute frequencies, relative frequencies, averages and pattern/ standard deviations were calculated.

The study hypotheses were as follows:

Hypothesis 1: *People suffering from AMD generally have a poorer quality diet, as shown by ranking in the lower tertile for the intake of zinc, antioxidants, omega-3 fatty acids, among others, but they ranked in the upper tertile on the glycemic index / glycemic content in foods.*

Hypothesis 2: Diet quality, i.e. the better or worse adherence to the Mediterranean diet, which is the recommended standard healthy diet, could be associated with the prevalence of *AMD*.

Hypothesis 3: *The high consumption of fish, dark green leafy vegetables, fruits and pulses is beneficial for the macula, which will be reflected in the lower AMD prevalence rate.*

Hypothesis 4: *Overweight / obesity, body fat distribution, smoking and lack of exercise are significant predictors of a greater prevalence of AMD, regardless of age, sex or diet.*

Regarding the bivariate inferential statistics, we used the chi-square independence test and Mann-Whitney U test. For modeling, we used different strategies in the creation of models fitted to the data, such as the Confirmatory Factor Analysis (CFA), the technique of Structural Equation Models (SEM). The use of CFA principles is to identify the relationship between the factors and their variables, when the researcher has some knowledge on the conceptual structure of latent variables. In order to proceed with CFA, the Structural Equation Model (SEM) was used. According to Hair et al., [20] the SEM can be used for confirmation, development and assessment of new or competitive models. The SEM was used in this study with the purpose of adjusting the theoretical model to the data, so the analysis of the adjustment indices obtained is fundamental.

When the data did not follow a normal distribution, either the estimation of generalized least squares method (GLS) or the asymptotic distribution free method (ADF) was chosen, depending on what was best for the model. In other cases, the estimation was done using the maximum likelihood (ML) method.

In addition to the above described methods, classical predictor methods, such as logistic regression (dichotomous dependent variable) were also used. This regression technique is used to model the occurrence in probabilistic terms, of one of the dependent variable categories.

Ethical considerations

The protocol received a favourable opinion from the Ethics Committee for Health Facility (AIBILI) (Attachment IV).

The study was implemented and conducted according to "ICH Harmonized Tripartite Guidelines for Good Clinical Practice", with applicable local regulations (including the European Directive 2001/20/EC, Federal Regulation of the United States Code Title 21, and the Ministry of Health, Labour and Japanese Economy) and with the ethical principles represented in the Declaration of Helsinki.

Results

The various diagrams presented in this study represent different SEM regression models or Path Analysis, depending on what the data allowed for. This was the case in the high frequency of *missing values* in some variables that compromised the possibility of using the SEM. Due to this fact, even though it was possible to obtain estimates for coefficients in regression and Path Analysis cases, thus creating a model with/without latent variables, it is only possible to analyse this and not test it.

Sample characterization (descriptive statistics)

The total sample was made up of 1005 individuals who were 55-years-old or more. 121 were excluded due to the presence of other retina pathologies or technical photography problems. The final sample consisted of 884 patients (tables and results shown correspond only to some of the variables presented in this study; the remaining results are part of Attachment V, colored blue). Of these, 451 didn't have AMD, while 433 did.

As far as sociodemographic characteristics are concerned, the sample is subdivided in the following way:

			т	otal			
		Without AMD		AMD		1	otai
		n	%	n	%	n	%
Sex	Female	250	55,4%	248	57,3%	498	56%
BUX	Male	201	44,6%	185	42,7%	386	44%
Ago	< 65	146	32,4%	135	31,2%	281	32%
Age	>= 65	305	67,6%	298	68,8%	603	68%
Total	Group	451	51%	433	49%	884	100%

Table 1. Sociodemographic Characteristics

It was found that 56% of the individuals are female and 44% are male. With reference to age, 32% are under 65 and 68% are over 65.

The sample was subdivided into 2 groups – Without AMD (51%) and with AMD (49%) – in order to allow for comparison of certain characteristics between individuals in both groups. "Without AMD" lists individuals that do not show signs of macular disease and "AMD" lists those who show macular disease related to age.

Clinical characteristics are shown in table 2.

		GROUP						
		Without AMD		Without AMD		Without AMD AM		MD
		Ν	%	n	%			
Diabetes	Yes	108	23,9%	99	22,9%			
Diabetes	No	343	76,1%	334	77,1%			
	Yes	299	66,3%	306	70,7%			
Hypertension	No	152	33,7%	127	29,3%			
	Yes	250	55,4%	236	54,5%			
Dyslipidemia	No	201	44,6%	197	45,5%			
Obesity	Yes	353	78,3%	320	73,9%			
Obesity	No	98	21,7%	113	26,1%			
Exercise	Yes	147	32,6%	105	24,2%			
Exercise	No	304	67,4%	328	75,8%			
Intake of supplements	Yes	38	8,4%	37	8,5%			
(vitamins/others)	No	413	91,6%	396	91,5%			
	Smoking	25	5,5%	19	4,4%			
Smoking	Non-smoking	426	94,5%	413	95,6%			
Total	Group	451	51%	433	49%			

 Table 2. Clinical characteristics by Group

There are no significant differences between the 2 Groups with regards to Diabetes, Hypertension, Dyslipidemia, Obesity or smoking and exercise habits, although there is a difference in the level of exercise practiced among individuals without and with AMD, being that the second group leads a more sedentary lifestyle.

The following table shows the descriptive statistics of the quantitative variables studied:

			GROI	JP
		n	\overline{x}	S
	Without AMD	451	28,43	4,24
Average BMI (Kg/m ²)	AMD	433	28,33	4,37
	Total	884	28,38	4,30
	Without AMD	451	98,59	14,02
Average AP (cm)	AMD	432	98,11	14,46
	Total	883	98,36	14,23
	Without AMD	451	39,71	33,23
PYU	AMD	433	35,30	31,37
	Total	884	37,67	32,37
	Without AMD	451	4,10	,97
Number of meals/day	AMD	433	3,96	,90
	Total	884	4,03	,94

 Table 3. Descriptive statistics of quantitative data

Regarding individuals with AMD, it appears they have an average BMI (Body Mass Index) 28,33 kg/m² and an average AP (Abdominal Perimeter) of 98,11 cm. As for smoking, smokers report consuming an average of 26 cigarettes/day for the past 27 years (on average), which translates to about 35 packs per year (PYU).

With regards to individuals without AMD, they appear to have an average BMI of 28,43 kg/m² and AP of 98,59 cm. On the issue of smoking, smokers on average consume approximately 39 packs per year (PYU).

In relation to food, both those without AMD and those with AMD have an average of 4 meals a day.

Inferential Statistics

Hypothesis 1

People suffering from AMD generally have a poorer quality diet, as shown by ranking in the lower tertile for the intake of zinc, antioxidants, omega-3 fatty acids, among others, but they ranked in the upper tertile on the glycemic index / glycemic content in foods.

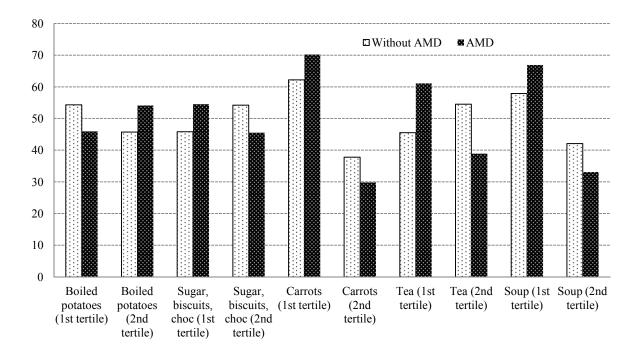
The table below shows the values for the 1st and 2nd tertiles (lower and higher consumption, respectively) of nutrients and foods. These values were tested using the chi-square test.

		GROUP			
		With	out AMD	A	MD
		n	%	n	%
Chicken or turkey ⁺	1st tertile ($\leq 17,14$)	170	50,3%	168	53,7%
	2nd tertile (\geq 34,28)	168	49,7%	145	46,3%
Sugar ⁺	1st tertile (≤88,34)	141	47,0%	153	53,1%
Sugar	2nd tertile (≥115,84)	159	53,0%	135	46,9%
Olive oil ⁺	1st tertile (≤13,50)	262	66,7%	264	70,8%
	2nd tertile (≥27,00)	131	33,3%	135	29,2%
Doiled notatoos*	1st tertile (≤34,29)	170	54,3%	133	45,9%
Boiled potatoes*	2nd tertile (≥102,86)	143	45,7%	157	54,1%
<u>Garana</u> hisarita aharahata*	1st tertile (≤6,59)	137	45,8%	144	54,5%
Sugar, biscuits, chocolates*	2nd tertile ($\geq 11,57$)	162	54,2%	120	45,5%
Carrots *	1st tertile (≤10,29)	140	62,2%	158	70,2%
Carrots	2nd tertile (≥30,86)	85	37,8%	67	29,8%
Pulses ⁺	1st tertile (≤12,01)	169	64,0%	154	65,8%
r uises	2nd tertile (≥25,71)	95	36,0%	80	34,2%
Wine ⁺	1st tertile (≤125,00)	129	83,8%	141	83,9%
W IIIC	2nd tertile (≥312,50)	25	16,2%	27	16,1%
Tea*	1st tertile (≤15,81)	40	45,5%	44	61,1%
Ita	2nd tertile (≥33,85)	48	54,5%	28	38,9%
Soup*	1st tertile (≤231,78)	150	57,9%	162	66,9%
Soup	2nd tertile (≥295,01)	109	42,1%	80	33,1%

Table 4. Values per tertile of food frequency by Group

⁺*p*>0,05

*p<0,05



Graph 1. Values per tertile of food intake frequency by Group

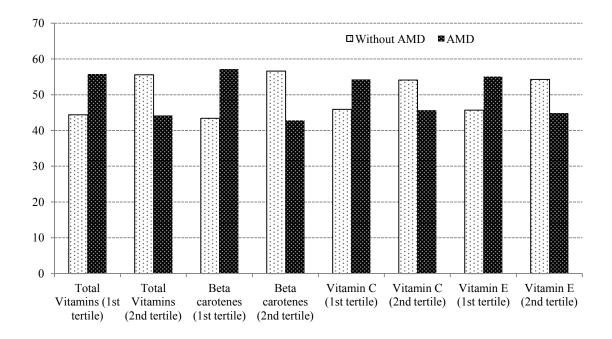
There is significant statistical evidence that "boiled potatoes", "sugar, biscuits, chocolate", "carrots", "tea", and "soup" food intake frequencies influence the presence of AMD. Participants without AMD consume significantly less "boiled potatoes", but more "sugar, biscuits, chocolate", "carrots", "tea", and "soup".

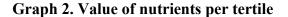
		GROUP			
		Without AMD		A	MD
		n	%	n	%
$Zinc^+$	1st tertile (≤9,11)	146	49,0%	148	51,0%
Zinc	2nd tertile (\geq 11,93)	152	51,0%	142	49,0%
Omega-3 ⁺	1st tertile (≤0,19)	152	50,0%	144	50,2%
Omega-5	2nd tertile ($\geq 0,47$)	152	50,0%	143	49,8%
Monounsaturated Fat ⁺	1st tertile (≤30,46)	149	47,6%	146	52,9%
Wonounsaturated Pat	2nd tertile (≥41,89)	164	52,4%	130	47,1%
Poli-unsaturated Fat ⁺	1st tertile (≤10,05)	140	47,6%	155	52,5%
Fon-unsaturated Fat	2nd tertile (≥12,719)	154	52,4%	140	47,5%
Fibre *	1st tertile (≤21,94)	139	45,7%	156	54,7%
ribre -	2nd tertile (≥28,99)	165	54,3%	129	45,3%

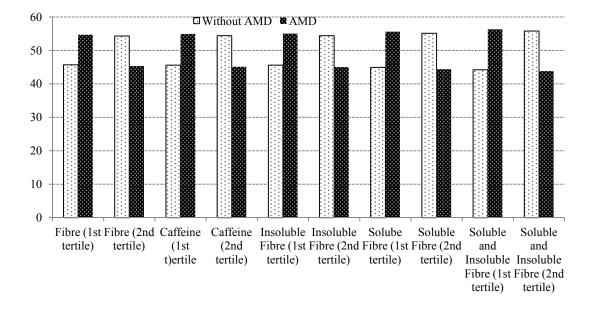
Table 5. Values per tertile of nutrients by Group

Alcohol ⁺	1st tertile (≤0,00)	194	58,3%	175	55,2%
Alconol	2nd tertile ($\geq 11,61$)	139	41,7%	142	44,8%
Alcohol $(g)^+$	\leq 30	202	78,6%	199	77,1%
Alcohol (g)	> 30	55	21,4%	59	22,9%
Caffeine *	1st tertile (≤31,77)	136	45,6%	150	54,9%
Carrenie	2nd tertile (≥78,76)	162	54,4%	123	45,1%
Total Vitamins *	1st tertile (≤1379,4)	132	44,4%	163	55,8%
Total Vitaliniis	2nd tertile (≥2066,95)	165	55,6%	129	44,2%
Beta carotenes *	1st tertile (≤865,56)	132	43,4%	163	57,2%
Deta cai otenes	2nd tertile (≥1416,37)	172	56,6%	122	42,8%
Vitamin C *	1st tertile (≤107,53)	136	45,9%	159	54,3%
v italiini C	2nd tertile (≥150,12)	160	54,1%	134	45,7%
Vitamin E *	1st tertile (≤8,62)	143	45,7%	152	55,1%
Vitamin E	2nd tertile ($\geq 11, 15$)	170	54,3%	124	44,9%
Insoluble Fibre *	1st tertile (≤14,11)	140	45,6%	155	55,0%
Insoluble Fibre	2nd tertile (≥19,06)	167	54,4%	127	45,0%
Soluble Fibre *	1st tertile (≤5,35)	136	44,9%	159	55,6%
Soluble Fibre	2nd tertile (\geq 7,29)	167	55,1%	127	44,4%
Soluble and insoluble Fibre*	1st tertile (≤9,725)	133	44,2%	162	56,3%
Soluble and insoluble Fibre	2nd tertile (≥13,20)	168	55,8%	126	43,8%
Oleic Acid ⁺	1st tertile (≤26,61)	153	48,1%	142	52,4%
Oleic Acid	2nd tertile (≥37,46)	165	51,9%	129	47,6%
Eicosanoic Acid ⁺	1st tertile (≤0,232)	154	49,7%	144	51,2%
Eleosanoie Acid	2nd tertile ($\geq 0,33$)	156	50,3%	137	48,8%
Eicosapentaenoic Acid ⁺	1st tertile (≤0,091)	150	49,3%	148	51,7%
Eleosapentachole Acid	2nd tertile (≥0,192)	154	50,7%	138	48,3%
Docosapentaenoic Acid +	1st tertile (≤0,252)	151	50,7%	145	50,2%
Docosapentacilote Acid	2nd tertile (≥0,732)	147	49,3%	144	49,8%
Docosahexaenoic Acid ⁺	1st tertile (≤0,222)	152	50,0%	145	50,5%
Docosanexactione Acid	2nd tertile ($\geq 0,444$)	152	50,0%	142	49,5%
Eicosapentaenoic, docosahexaenoic	1st tertile (≤0,421)	152	49,8%	143	50,4%
and docosapentaenoic Acids $^+$	2nd tertile (\geq 1,092)	153	50,2%	141	49,6%
Trans Fats +	1st tertile (≤0,683)	137	48,4%	159	51,8%
	2nd tertile (\geq 1,002)	146	51,6%	148	48,2%
Omega 6 ⁺	1st tertile (≤7,063)	147	49,7%	149	50,7%
	2nd tertile (≥9,264)	149	50,7%	145	49,3%
Omega 6/Omega 3 Ratio +	1st tertile (≤5,41)	154	49,7%	141	50,5%
omoga oromoga o rano -	2nd tertile ($\geq 6,68$)	156	50,3%	138	49,5%

⁺*p*>0,05 **p*<0,05







Graph 3. Value of nutrients per tertile

With respect to nutrients, the statistical significance was less than 0,05 for "Caffeine", "Fibre", "Total Vitamins", "Beta Carotenes", "Vitamin C", "Vitamin E", "Insoluble Fibre", "Soluble Fibre" and in the combination of the last two. The participants without AMD have higher levels of consumption of "Fibre", "Caffeine", Total Vitamins", "Beta Carotenes", "Vitamin C", "Vitamin E", "Insoluble Fibre", "Soluble Fibre" and both kinds of fibre than 18 the participants with AMD. The Omega 6/ Omega 3 ratio results weren't significantly different between the two groups.

Hypothesis 2

Diet quality, i.e. the better or worse adherence to the Mediterranean diet, which is the recommended standard healthy diet, could be associated with the prevalence of AMD.

To set the food patterns for each group (Without AMD and with AMD), several Exploratory Factor Analysis were conducted (EFA) with the variable related to food intake frequency and nutrients. The objective of this analysis was to determine how and to what extent the observed variables came together to "form" a small number of factors.

The confirmatory process began after EFA. Several models were tested in order to obtain the best correspondence to the data.

An unobservable variable called the Mediterranean Diet was created from the latent variables in Diagram 1.

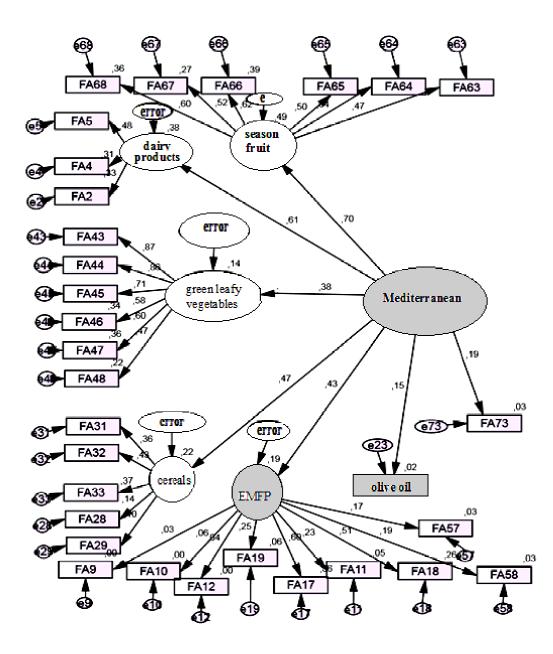


Diagram 1. Diet model of Mediterranean diet (SEM)

Key: FA2 – Half Fat Milk; FA4 – Yogurt; FA5 – Cheese; FA9 – Chicken; FA10 – Turkey and Rabbit; FA11 – Beef and Pork; FA12 – Liver; FA17 – Fatty fish, FA18 – Lean Fish; FA19 – Codfish; FA28 – Whole Wheat Bread; FA29 – Cornbread; FA31 – Rice; FA32 – Pasta; FA33 – French Fries; FA43 – White Cabbage; FA44 – Kale; FA45 – Collard Greens ; FA46 – Broccoli ; FA47 – Cauliflower; FA48 – Turnip Greens; FA57 – Pulses; FA58 – Peas; FA63 – Strawberries; FA64 – Cherries; FA65 – Peaches; FA66 – Melon; FA67 – Persimmons; FA68 – Figs; FA73 – Wine; e... - Error associated with the variable; EMFP – eggs, meat, fish, pulses.

The model established to define the pattern for the Mediterranean diet is based on the consumption of cereals, dark green leafy vegetables, fresh fruit (seasonal), olive oil, nuts, seeds, olives, dairy products, meat, fish, pulses and wine. Parsimony and absolute adjustment

measures for each of the submodels can be seen in the table right up until obtaining the final model (Diagram 1).

Cumulative effect of	Parsimony Measure	Measure of absolute adjustment
Mediterranean diet and AMD	χ^2 relative	RMSEA
Seasonal Fruit	2,924	0,053
Dairy products	3,617	0,062
Dark green leafy vegetables	3,583	0,062
Cereals	2,969	0,054
EMFP	2,825	0,052
Wine	2,774	0,051
Olive oil	2,761	0,051
Model Fit	Appropriate	Adjusted
Values of reference	Recommended Interval [1 – 5] [Hair et al., 1998] [21]	< 0,07 [Steiger, 2007] [22]

Table 6. Parsimony and adjustment Measures of a cumulative variable effect of the model

One can see that the RMSEA (Root Mean Squared Error of Approximation) value decreased as more variables were introduced into the model, making it more adjusted.

Verification of Hypothesis 2 was checked with the adjusted model variables. The following table shows the results.

	GROUP	n	Average of orders	$\bar{x}(s)$	p-value
	w/o AMD	444	438,17	120,65 (115,43)	
Dairy products	AMD	421	427,55	112,13 (92,14)	0,532
	Total	865		116,51 (104,77)	
	w/o AMD	451	451,56	27,59 (10,27)	
EMFP	AMD	433	433,06	27,06 (10,65)	0,282
(Eggs, Meat, Fish, Pulses)	Total	884		27,33 (10,46)	
	w/o AMD	446	444,34	22,11 (15,78)	
Olive oil	AMD	429	431,41	20,89 (14,31)	0,426
	Total	875		21,51 (15,08)	
	w/o AMD	451	450,85	39,36 (25,37)	
Cereals	AMD	433	433,80	36,75 (20,85)	0,321
	Total	884		38,09 (23,29)	
	w/o AMD	443	447,05	14,3 (15,1)	
Vegetables	AMD	427	423,52	12,91 (13,82)	0,167
	Total	870		13,62 (14,49)	
	w/o AMD	447	438,38	20,37 (19,5)	
Seasonal fruit	AMD	428	437,60	19,12 (14,52)	0,964
	Total	875		19,76 (17,24)	
	w/o AMD	248	251,34	221,56 (183,69)	
Wine	AMD	253	250,66	215,8 (171,42)	0,957
	Total	501		218,65 (177,44)	
	w/o AMD	441	438,17	15,01(15,52)	
Dark green leafy vegetables	AMD	426	427,55	13,83(13,84)	0,215
	Total	867			
	w/o AMD	448	451,56	19,93(14,45)	
Pulses	AMD	432	433,06	18,24(13,94)	0,101
	Total	880			
	w/o AMD	449	444,34	54,7(33,19)	
Fruit	AMD	431	431,41	51,96(29,06)	0,527
	Total	880			
	w/o AMD	451	450,85	24,3(12)	
Fish	AMD	433	433,8	23,79(11,79)	0,465
	Total	884			
Maditamaraa	w/o AMD	451	447,05	55,14(30,79)	
Mediterranean Diet	AMD	433	423,52	52,88(27,93)	0,344
Diet	Total	884			
Maditamanaan	w/o AMD	451	438,38	40,73(22,19)	
Mediterranean without wine	AMD	433	437,6	37,93(17,17)	0,037
without white	Total	884			

 Table 7. Mann-Whitney U Test in the prevalence of AMD in the Mediterranean diet

 (w/o AMD - without AMD; AMD - with AMD)

	w/o AMD	442	450,47	30,04(21,45)	
Chicken and turkey	AMD	431	434,2	29,07(18,71)	0,712
	Total	873			
	w/o AMD	448	439,59	17,66(15)	
Total meat	AMD	433	442,46	17,43(14,49)	0,867
	Total	881			

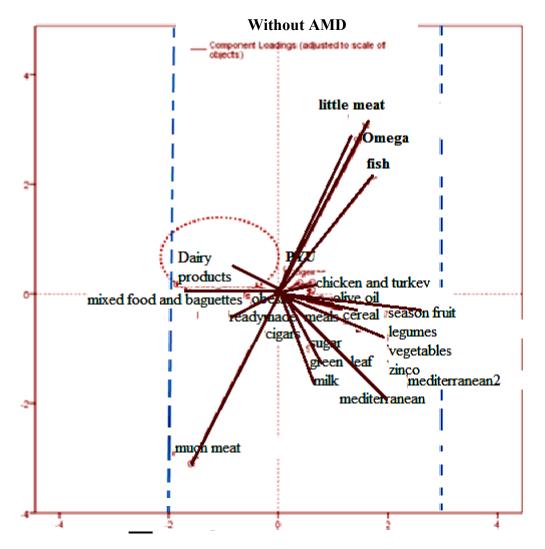
As can be seen, there are no significant differences in the type of diet in people without AMD and with AMD with the exception of the adherence to the Mediterranean diet without the consumption of wine, which is considered to be the model of a healthy diet. Indeed, people without AMD are those who follow this type of diet, if we include the consumption of wine, however, this difference ceases to exist.

The two-dimensional map that follows, resulting from Categorical Principal Components Analysis (CATPCA- optimal scaling), summarizes the present information on the original variables: chicken and turkey, zinc tertiles, sugar tertiles, omega-3 tertiles, dairy products, olive oil, cereals, vegetables, seasonal fruit, wine, dark green leafy vegetables, pulses, fruit, fish, little meat (*dummy* with values below the mean), a lot of meat (*dummy* with values above the mean), obesity, dyslipidemia, PYU, number of cigarettes, readymade food, fast food, combined foods, bread, light meals, Mediterranean diet, Mediterranean diet 2 (without wine) and AMD.

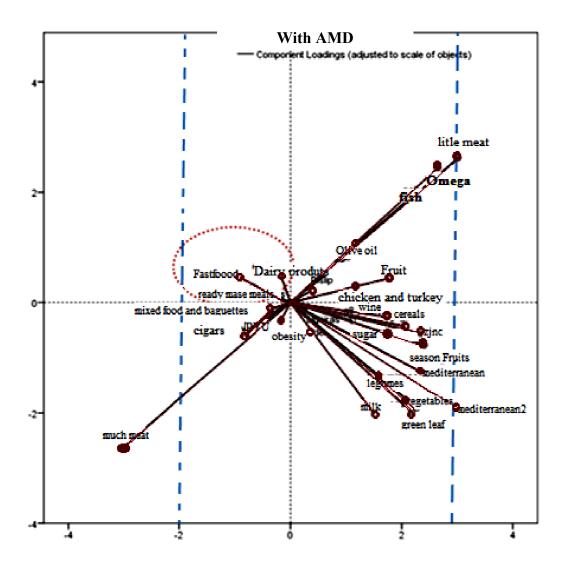
Both the summary of the model sample and the global sample (Alpha de Cronbach 0,909), as well as the two dimensions, have good internal consistency (Alpha de Cronbach, 0,824 and 0,714, for dimension 1 and 2, respectively).

We used criteria of retention components of the two factors, selecting individuals with or without AMD, in order to obtain each Graph *biplot*.

This procedure resulted in the two Graphs below where the existence of the different food pattern levels among people with and without AMD can be seen. Indeed, a diet high in fast food and readymade meals, dairy products and meat is more common in those with AMD.



Graph 4a. Two-dimensional projection of factors obtained by CATPCA (without AMD)



Graph 4b. Two-dimensional projection of factors obtained by CATPCA (with AMD)

Hypothesis 3

The high consumption of fish, dark green leafy vegetables, fruits and pulses is beneficial for the macula which will be reflected in the lower AMD prevalence rate.

Again we resorted to the structural equations model to create latent variables while always maintaining the theory and EFA as a starting point. To define the consumption of food in the hypothesis, several EFA with variables related to the consumption of fish, dark green leafy

vegetables, fruits and pulses were conducted. The confirmatory process began after EFA. Several models were tested until the most adjusted to the data was obtained (Diagram 2).

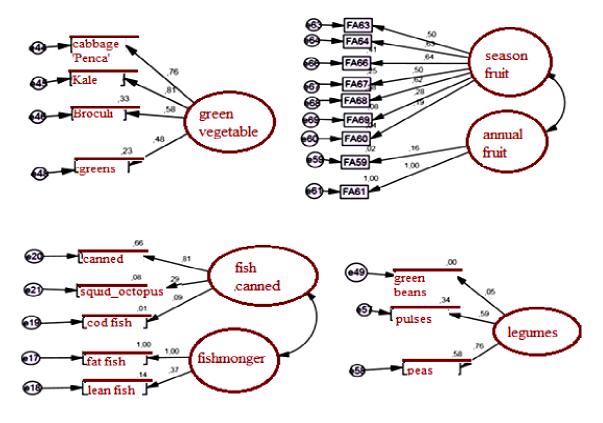


Diagram 2. SEM of latent variables related to the consumption of fish, dark green leafy vegetables, fruits and pulses

Key: FA59 – Apples and pears; FA60 – Oranges; FA61 – Bananas; FA63 – Strawberries; FA64 – Cherries; FA66 – Melon; FA67 – Persimmons; FA68 – Figs; FA69 – Grapes; e... – error related to the variable

The following table shows estimates of parsimony and absolute adjustment for each model.

Table 8. SEM estimates on the consumption of fish, dark green leafy green vegetables, fruits and pulses

Latent Variables	Parsimony measure	Absolute adjustment measure
	χ^2 relative	RMSEA
Dark green leafy veg.	7,536	0,098
Pulses	*	0,145
Fruit	2,371	0,045
Fish	2,667	0,050
Fit Model	Recommended Interval [1-5]	Adjusted < 0,07
Reference Values	[Hair et al., 1998] [21]	[Steiger, 2007] [22]
*	1	

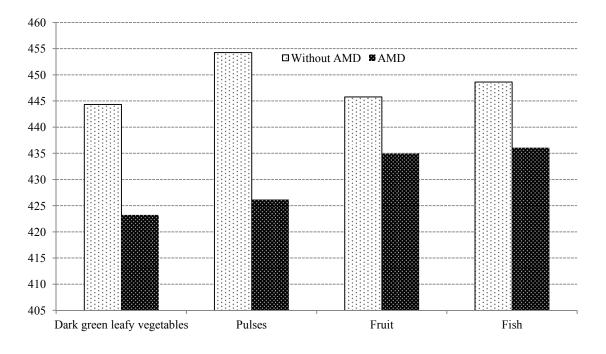
*The model showed zero degrees of freedom, so, the model can be estimated but not evaluated..

Hypothesis verification under analysis can be done after the modelling process.

	GROUP	Ν	Average of	$\bar{x}(s)$	p-value
			orders		
Dark green leafy vegetables	w/o AMD	441	444,37	15,01 (15,52)	
	AMD	426	423,27	13,83 (13,84)	0,215
vegetables	Total	867		14,43 (14,72)	
Pulses	w/o AMD	448	454,28	19,93 (14,45)	
	AMD	432	426,20	18,24 (13,94)	0,101
	Total	880		19,1 (14,22)	
Fruit	w/o AMD	449	445,81	54,7 (33,19)	
	AMD	431	434,97	51,96 (29,06)	0,527
	Total	880		53,36 (31,25)	
Fish	w/o AMD	451	448,64	24,3 (12)	
	AMD	433	436,10	23,79 (11,79)	0,465
	Total	884		24,05 (11,89)	

 Table 9. Mann-Whitney U test for AMD prevalence by food type consumed

 (w/o AMD - without AMD; AMD - with AMD)



Graph 5. AMD prevalence by food type

There are differences that are not statistically significant for the prevalence of AMD for the consumption of fish, dark green leafy vegetables, fruit and pulses.

Hypothesis 4

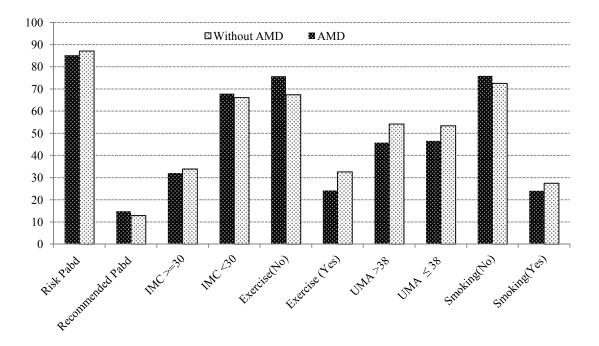
Being overweight / obesity, body fat distribution, smoking and lack of exercise are significant predictors of a greater prevalence of AMD, regardless of age, sex or diet.

Verification of this hypothesis started with the exploratory study of the association between the variables concerned, obesity (BMI), abdominal perimeter (AP), smoking and exercise habits. The chi square test was used for this. Results can be seen in the table.

		Without AMD		AMD		
		n	%	n	%	
Smoking ¹	Yes (includes ex-smokers)	124	27,5%	104	24,1%	
Shloking	No	327	72,5%	328	75,9%	
PYU^2	\leq 38 PYU	70	53,4%	61	46,6%	
FIU	>38 PYU	rs) 124 27,5% 104 327 72,5% 328 70 53,4% 61 45 54,2% 38 147 32,6% 105 304 67,4% 328 298 66,1% 294 153 33,9% 139 58 12,9% 64	45,8%			
EXERCISE ³	Yes	147	32,6%	105	24,2%	
EAEKCISE	No	304	67,4%	27,5%10472,5%32853,4%6154,2%3832,6%10567,4%32866,1%29433,9%13912,9%6487,1%368	75,8%	
$BMI^4 (Kg/m^2)$	<30	298	66,1%	294	67,9%	
Divit (Kg/iii)	>=30	153	33,9%	139	32,1%	
AP ⁵	Recommended	58	12,9%	64	14,8%	
	Risk	393	87,1%	368	85,2%	
${}^{1}p=0.246 \chi^{2}_{(1)}=1.348; {}^{2}p=0.911 \chi^{2}_{(1)}=0.012;$ ${}^{3}n=0.006 \chi^{2}_{-}=7.548; {}^{4}n=0.565 \chi^{2}_{-}=0.222; {}^{-5}n=0.400 \chi^{2}_{-}=0.708$						

Table 10. BMI, AP, smoking and exercise versus AMD

 $^{3}p=0,006 \chi^{2}{}_{(1)}=7,548; \ ^{4}p=0,565 \chi^{2}{}_{(1)}=0,332; \ ^{5}p=0,400 \chi^{2}{}_{(1)}=0,708$



Graph 6. BMI, AP, smoking and exercise versus AMD

Despite the independent variables not showing evidence associated to AMD, with the exception of the "exercise" variable, all others were included in the logistic model. However, these did not estimate the risk prediction of AMD. Continuing with the hypothesis study, we proceeded with a new regression analysis for dependent binary data (Logit), where the dependent variable was selected for AMD (dichotomy) and the independent variable was "Exercise". The method selected for this analysis was the Enter method since it only requires one independent variable.

lst Step			В	S.E.	Wald	df	Sig.	Exp(B)
Constant -,336 ,128 6,934 1 ,008 ,71	1 at Stop	EXERCISE (1)	,412	,151	7,506	1	,006	1,511
	ist step	Constant	-,336	,128	6,934	1	,008	,714

a. Variable(s) entered on step 1: EXERCISE.

We can observe that the probability of someone who does not exercise suffer from AMD is 51.1% compared to those who do, with a pseudo-R² (Nagelkerke) of 1.1%.

Discussion

To the best of our knowledge, this is the first study in Portugal that seeks to correlate eating habits and lifestyles with the prevalence of AMD, emphasizing the model of the Mediterranean lifestyle.

Food and lifestyles have been implicated in the ageing and development process of chronic degenerative diseases, especially when studying their pathogenesis based on cell hyperoxidation, in common inflammatory processes and in relation to extracellular matrix changes. It is common knowledge that genetic and epigenetic factors are very important in the onset of AMD and that they also interfere in the ageing process. Diet and other lifestyle factors exert their influence through epigenetics and interfere with the oxidative metabolism, inflammation and cellular degeneration, thereby conditioning ageing, cellular damage, and other related pathologies. Pathological alterations specifically regarding AMD were observed, not only at a photoreceptor and at the pigmented epithelium level (which are highly metabolically active and, therefore, more sensitive to oxidative stress and the accumulation of metabolic toxins like lipofuscin), but also at the Bruch's membrane and choroid level. [23] Thus, diet, especially the antioxidant nutrients present in it and the environment have become increasingly valued as a modifiable factor for AMD. [24-27]

The sample collected in our study is not representative of the Portuguese population and, therefore, the results cannot be extrapolated. It is a very homogeneous sample, particularly in regards to geographical location (only the population of Lousã), age group (55 years old or more) and, eventually, in eating habits and lifestyle, which may reflect common influences on all the population studied.

Due to the age (most individuals are more than 65 years old) and the selection process, the frequency of chronic pathologies related to ageing, particularly AMD, is very high. In fact,

these findings can be explained by the sample selection: the sample consisted of people from Lousã who participated in the epidemiological study of AMD, and we tried to select an equal number of people with and without AMD.

There are studies which report a very different prevalence of AMD. In a meta-analysis that included 25,000 individuals the prevalence rate was between 12 and 16%. [28] In any case, the objective of this study was not to calculate the prevalence of this disease in this population, but rather to access the risk factors present.

In our sample, the intake of supplements was reduced (8.4% in individuals without AMD and 8.5% in those with AMD), so it is not believed to be a confounding factor. Diabetes Mellitus, Dyslipidemia and Hypertension are also not confounding factors because although the frequency of these pathologies was elevated in both groups, it did not vary between them.

Our study confirmed that individuals suffering from AMD have a poorer diet in terms of quality when compared to those that do not suffer from the disease.

Certain foods such as soup, carrots and tea are consumed in smaller quantities by those suffering from AMD. These foods contain high levels of antioxidants, carotenoids, lutein, vitamins C and E and polyphenols (especially flavonoids and xanthines from tea). The Rotterdam Study also showed a reduction in the risk of AMD in individuals who consumed high levels of carotenes and vitamin C. [29] Other studies on dietary supplements of these and other micronutrients [30-32] did not prove this benefit, perhaps because supplements have a different absortion, metabolization and bioavailability than when they are naturally found in food. On the other hand, the Mediterranean diet composition that comprises a set of enhancing and synergistic nutrients with antioxidant properties, [33] emerged as having a lower AMD prevalence, corroborating the theory that nutrients in nature are more beneficial than those from supplements.

The importance of vitamins C and E is still controversial [34-36] but, in this study, it was proven that both have some influence on the development of the disease, since there was a significant difference on their intake in both groups studied, with a higher consumption occurring in individuals not suffering from AMD.

With regard to caffeine, there are significant differences between both groups, although there are studies where this difference is not apparent. [37] This fact is interesting, if one considers coffee as the main vehicle for caffeine. The content of xanthine in coffee, which is a potent antioxidant, should be considered, given the link between this micronutrient and the prevention of AMD. [38] Of course, coffee contains various phenolic acids among which are chlorogenic acids, which are also antioxidants, and probably important in the prevention of AMD.

When evaluating the nutrients separately, it was found that individuals without AMD ingest higher quantities of significant nutrients on the Mediterranean diet. In addition to those already mentioned, they also consume those found in pulses, fish and eggs, which provide fibre, vegetable protein, antioxidant vitamins and minerals, fatty omega-3 acids, lutein and zeaxanthin, which are known protectors of AMD, [9,11] although some of them, on their own, have shown no statistically significant differences between the two groups as is the example of the Omega 6/Omega 3 ratio.

Olive oil, one of the foods consumed in great quantities in Portugal and on the Mediterranean diet, is also consumed in great quantities by individuals in our sample, hence the lack of significant difference between the two groups. Nevertheless, it should be noted that its consumption is globally higher in individuals without AMD (53% in the higher tertile to 46.9% in those with AMD). Although not statistically significant due to the homogeneity of the sample, the difference could be clinically significant, and again interfere with the higher

consumption of, for example, Vitamin E and monounsaturated fats found in individuals without AMD.

It should be noted, though, that nutrient serum levels are unknown in individuals in the sample. This could help in interpreting the results because, given the frequency of chronic diseases, some of our patients may have an oxidative consumption of these nutrients due to the existence of other pathologies that affect them, like Diabetes Mellitus or other vascular diseases. Patients may also have a food consumption that enhances oxidative stress that leads to other chronic diseases.

A contradictory finding was the intake of sweets and chocolate in the group of people without AMD because there are studies that have shown a positive association between the intake of food with high a glycemic index and the development of AMD. [39] The glycemic index was not evaluated in our group but it is possible to speculate that, given the high adherence to the Mediterranean diet by this population, the glycemic index in this group is less than that in other populations studied to date. The higher dietary fiber consumption in the group without AMD is enough to condition lower glycemic levels. The type of sweets and time of their ingestion is also unknown, which can modify the way these simple carbohydrates are absorbed and metabolized and consequent level of blood glucose. It should be noted that the variable "sugar", analyzed separately, did not reveal any significant difference between groups, which is in agreement with the indication that it is not the total intake of carbohydrates that matters but rather the type of carbohydrate. [40] The consumption of sweets and chocolates was also not significantly different. In both groups evaluated, the frequency of diabetes was 23%, so the serum levels of glucose did not affect the glycemic index of the foods.

One cannot fail to highlight the trend, although not statistically significant, is that, in general, the consumption of healthier foods / nutrients, such as white meat, fatty omega-3 acids,

monounsaturates and polyunsaturates is more evident in individuals without AMD, as was proven in several studies. [9,14,24,41] Oleic, eicosanoic, eicosapentaenoic, and docosahexaenoic acids also stand out.

Again, the analysis in context with all of the nutrients is important. We should not rely on the evaluation of isolated nutrients but rather on the evaluation of all of them, integrated in food and their interactions. [8,14]

It is known that the composition of food varies seasonally, but this factor was not analyzed in the sample because it was not considered a confounding factor, given the geographical homogeneity and because some studies [13] found no significant differences in consumption. In other less homogenous studies, however, this factor should be considered because seasonality is one of the Mediterranean diet characteristics.

By grouping foods, it was possible to define a dietary pattern for this population and it was concluded that the pattern was within the Mediterranean diet characteristics in relation to fruit, dairy products, vegetables, cereals, eggs, meat and fish, wine and olive oil. Although, individuals without AMD are those with the highest consumption of these foods, the biggest difference between the groups with regards to this pattern, is the consumption of wine. Those without AMD follow a diet that is "more" Mediterranean when the variable "wine" is removed. The fact that wine consumption and other alcoholic beverages is, after all, quite high in this population, could be a confounding factor for this pattern. The argument could be in the type of alcoholic beverage, or, in this case, in the quantity ingested. Wine, with its resveratrol content could function as an AMD protector, due to the fact that it is an antioxidant. On the other hand, alcohol is a neurotoxin with oxidative stress and neoangiogenesis potential. It damages the brain and could also damage the retina. In this population, where the consumption of alcohol is similar in both groups, but always lower in the group without AMD, it is impossible to draw any firm conclusions, which is consistent

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with other studies that also found no difference with regards to alcohol. [42] In the Beaver Dam Eye Study [43] individuals with a history of heavy alcohol consumption developed more exudative AMD, which may indicate that dose and type of beverage may have an effect. However, in the Melbourne study, [44] researchers found that even mild to moderate alcohol consumption had a negative influence on the risk of AMD and wine consumption had no apparent benefit, as was the case in our sample.

In grouping the predominant dietary factors in either group (with or without AMD), it was possible to verify that readymade meals and fast food were related to AMD. These foods lose their antioxidant components to industrial processing and contain trans fats, and, together with unprotected oxidative damage, may contribute to retina damage.

Failure to find different dietary patterns in the different groups could be related to the homogeneity of the previously cited sample, unlike in some studies that state that patients with AMD consume less fish, pulses, fowl meat and consume more red meat, for example. [41] Even so, although there were no significant differences, people who ate less fish, dark leafy green vegetables, fruits and pulses are those who have AMD, which supports the information from other studies. [11]

In the hypothesis tested for overweight / obesity, body fat distribution, smoking and exercise, the latter stood out overwhelmingly, corresponding to an increase of 51.1% in the probability that those who do not exercise will develop AMD. There are many comparative studies that support exercise as a significant factor in preventing the onset of AMD. [11,45,46]

As for the type and intensity of exercise, this was not characterized, but it can be said that almost no one from the entire sample practiced anaerobic exercise, and mostly, there was a slight to moderate level of physical activity, with no apparent difference between individuals and within each group. Nevertheless, there are studies that show that intense physical exercise reduces the risk of AMD. [45] Our study only proved the benefit of moderate physical exercise.

In contrast to other studies [11,24,47-50], obesity and smoking demonstrated no quantifiable relationship with the appearance and development of AMD. Both groups showed a noticeable distribution of body fat (very high AP), without a significant difference between them, but, on average, higher in those with AMD. Since abdominal fat is a pro-oxidant condition, one would actually expect to find that patients (with AMD) have an increased AP, without being necessarily obese, as in other studies. [51,52] With regards to smoking habits, no conclusions are expected since smoking habits were similar in both groups.

Although it was not one of the objectives of this study, and, therefore, not proven, it is still worth mentioning that chronic disease, ageing and degenerative diseases are the result of a number of factors and lifestyle habits, as some researchers claim. [11] It is possible that the existing controversy on the subject is due to the difficulties in "measuring" and accurately quantifying these dietary factors and lifestyle habits.

In this sense it is also necessary to note that many people have difficulty in maintaining adequate dietary intakes, particularly of antioxidant nutrients, which may be a predisposing or worsening factor for AMD or for ageing and chronic diseases. Taking supplements may be appropriate for these individuals. For patients with AMD (even at an early stage), with or without nutritional deficiencies, the intake of supplements may also be a prudent measure. [53, 54]

The therapeutic effect of supplements seems to raise no doubts. When talking about prevention in healthy individuals without nutritional deficiencies, however, the intake of supplements is still controversial. According to some researchers, excessive doses of certain nutrients may have deleterious effects [55] and this may happen with the addition of

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supplements in individuals with adequate levels of the same. Nevertheless, this concept is something that needs to be confirmed.

Therefore, preventive and/or therapeutic measures are still unclear. Could the solution be the intake of supplements or could diet play a major role in it? Is the Mediterranean diet the answer? Or could it rather be the combination of several factors: diet, exercise, body fat distribution, body weight and giving up smoking, the ultimate solution when all together, thus contextualizing what is called "*a healthy lifestyle*"?

Surely, in the light of the different studies on the matter and our own results, interest in the Mediterranean diet and exercise should be reinforced as preventive factors against chronic pathologies and AMD in particular, especially when recent data suggests that alterations caused by oxidative damage could play an important role in the formation of *drusens* [56]. This implies that antioxidants that are present in the Mediterranean diet and are formed over a lifestyle of healthy habits may already have a preventive effect in the onset of this disease.

There is the need to increase and diversify our sample, and, eventually, conduct an intervention study in order to improve the understanding of these issues.

There are also some limitations in this study worth mentioning. The fact that the sample was too homogenous in terms of eating and lifestyle habits may be a conditioning factor in not obtaining significant result differences. It is true that all individuals participating in this study live in Lousã and, therefore, have a similar social and cultural structure. It is a rural area where many have home gardens and cultures without industrial intervention. On the other hand, the fact that the investigation was conducted at one time and not as a follow-up study of the participants and their evolution, may have an influence on the results.

Conclusions

In the group studied, one can conclude that the nutritional profile acts as protection against AMD and is associated to the elevated consumption of foods such as carrots, tea, biscuits, chocolate and soup, as well as exercise. One can also conclude that in this study and population, nutrients, such as fiber, caffeine, vitamin C, carotenes and vitamin E, play a greater part in the protection against AMD.

The dietary pattern model followed by the group/population studied is that of the "Mediterranean diet" and the factor "wine" has an influence on the disease. Individuals without AMD follow a diet with solid Mediterranean characteristics.

Exercise seems to serve as a protection factor against AMD.

In this group, obesity, distribution of body fat and smoking habits are not statistically associated to the disease.

The future goal of this study is to extend it to other areas of the Central Region or, perhaps, across the whole country, so as to allow for direct comparison between rural and urban areas, as well as coastal and interior areas, determining diet patterns and comparing them.

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ATTACHMENTS

Attachment I - Questionnaire

Inquérito - estilos de vida e hábitos alimentares

Data do Inquérito: ___/ / ___ Iniciais: |__| Número de Participante:|_| |_| |_|

Parte A – Estilos de vida

1.Sexo: Feminino 🗆 Masculino 🗖			
2.Data nascimento://			
3.Profissão: 4	.Escolaridade:		
5.Peso: Kg Altura: m	Perímetro abdominal:	2	cm
6.Patologias Diagnosticadas:			
		Sim	Não
Diabetes Mellitus			
Hipertensão arterial			
Dislipidémia (hipercolesterolemia, hipertri	gliceridemia, etc)		
Obesidade/Excesso de peso			
Outra patologia. Qual?			
 Futebol Basquetebol Natação Mais do que uma modalidade Outras. Qual? Quantas horas por semana? 			
8. Toma algum suplemento de vitaminas e/ou mi	nerais ou outro suplem	ento alim	entar?
Sim □ Não□ Se sim: Qual e qual o motivo?			
Nº Comprimidos/dia o	u dose diária:		
9. Fuma? Sim 🗆 Nunca fumou 🗆 Deixou	de fumar 🗆		
Número de cigarros /dia em média (1 charuto=2 cigarros; 1 cachimbo=4 cigarros)	Número de anos que fi	umou	
10. Normalmente quantas refeições faz por dia?			
11. Toma o pequeno almoço diariamente? Sin	m 🗆 Não 🗆		
12. No quotidiano, qual (quais) o (s) tipo (s) de al	limentação predominan	te (s)?	
 Refeição tradicional (sopa, prato, sob Fast food (hambúrgueres, pizzas, cao Alimentos pré confeccionados (rissóis Pratos combinados, baguetes Refeições ligeiras (saladas, sopas, etc Outro tipo. Qual? 	horros, etc) , refeições congeladas, etc)	Sim Sim Sim Sim Sim Sim Sim	Não Não Não Não Não



Por favor, antes de iniciar o questionário leia as instruções da página anterior.

Pense durante o último ano quantas vezes por dia, semana ou mês, em média, consumiu cada um dos alimentos referidos. Na coluna referente à quantidade deverá assinalar se sua porção é igual, menor ou maior do que a referida como porção média. Para os alimentos consumidos só em determinadas épocas do ano, anote a frequência com que o alimento é consumido nessa época e assinale com uma cruz (x) na última coluna (Sazonal).

		Frequência alimentar									Quantid	ade		8
I. P. LÁCTEOS	Nunca	1-3	1	2-4	5-6	1	2-3	4-5	6 +	Porção	A su	a porção	ó é:	a z
	ou <1 mês	por mês	por sem	por sem	por sem	por dia	por dia	por dia	por dia	Média	Menor	Igual	Maior	0 n a
1. Leite gordo	0	0	0	0	0	0	0	0	0	1 chávena = 250 ml	0	0	0	
2. Leite meio-gordo	0	0	0	0	0	0	0	0	0	1 chávena = 250 ml	0	0	0	
3. Leite magro	0	0	0	0	0	0	0	0	0	1 chávena = 250 ml	0	0	0	
4. logurte	0	0	0	0	0	0	0	0	0	Um =125g	0	0	0	
5.Queijo (de qualquer tipo incluin do queijo fresco e requeijão) 6. Sobremesas lácteas:	0	0	0	0	0	0	0	0	0	1 fatia = 30g	0	0	0	
 Sobremesas lacteas: pudim, aletria e leite creme, etc 	0	0	0	0	0	0	0	0	0	Um ou 1 prato sobreme sa	0	0	0	
7. Gelados	0	0	0	0	0	0	0	0	0	Um ou 2 bolas	0	0	0	
			1	Frequên	cia alin 5-6	nentar 1	2-3	4-5	6+	Porcão	Quantid	ade la porção	. A.	a a z
II. OVOS, CARNES E PEIXES	Nunca ou <1 mês	1-3 por mês	por sem	por sem	por sem	por dia	por dia	por dia	por dia	Média	Menor	lgual	Maior	0 11 21
8.Ovos	0	0	0	0	0	0	0	0	0	Um	0	0	0	
9.Frango	0	0	0	0	0	0	0	0	0	1 porção ou 2 peças=150g	0	0	0	
10.Peru, coelho	0	0	0	0	0	0	0	0	0	1 porção ou 2 peças=150g	0	0	0	
11.Carne vaca, porco,cabrito	0	0	0	0	0	0	0	0	0	1 porção =120g	0	0	0	
12. Figado de vaca, porco, frango	0	0	0	0	0	0	0	0	0	1 porção = 120g	0	0	0	
13 Língua, mão de vaca, tripas, chispe, coração, rim	0	0	0	0	0	0	0	0	0	1 porção =100g	0	0	0	
14.Fiambre, chouriço, salpição, presunto, etc	0	0	0	0	0	0	0	0	0	2 fatias ou 3 rodelas =20g	0	0	0	
15. Salsichas	0	0	0	0	0	0	0	0	0	3 médias	0	0	0	
16. Toucinho, bacon	0	0	0	0	0	0	0	0	0	2 fatias=50g	0	0	0	回
 Peixe gordo: sardinha, cavala, carapau, salmão, 	0	0	0	0	0	0	0	0	0	1 porção =125g	0	0	0	
 Peixe magro: pescada, faneca, dourada, etc 	0	0	0	0	0	0	0	0	0	1 porção =125g	0	0	0	
19.Bacalhau	0	0	0	0	0	0	0	0	0	1 porção =125g	0	0	0	
20.Peixe conserva: atum, sardin has,etc	0	0	0	0	0	0	0	0	0	1 lata	0	0	0	
21.Lulas, polvo	0	0	0	0	0	0	0	0	0	1 porção =100g	0	0	0	
22.Camarão, amêijoas, mexilhão, etc	0	0	0	0	0	0	0	0	0	1 prato sobremesa =100g	0	0	0	
			Fi	requênc	ia alime	entar					Quantid			8 8
III. Óleos e Gorduras	Nunca ou <1	1-3 por	1 por	2-4 por	5-6 por	1 por	2-3 por	4-5 por	6+ por	Porção Média	Asu	la porção	oé:	
	mês	mês	sem	sem	sem	dia	dia	dia	dia	1.00	Menor	Igual	Maior	i
23. Azeite 24. Óleos: girassol, milho,	0	0	0	0	0	0	0	0	0	1 colher sopa 1 colher sopa	0	0	0	
soja 25. Margarina	0	ŏ	0	ŏ	ŏ	õ	õ	õ	0	1 colher chá	ŏ	õ	õ	
26. Manteiga	0	0	0	0	0	0	0	0	0	1 colher chá	0	0	0	



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			Fr	equênc		ntar					Quantid			2 8 8
IV.PÃO, CEREAIS E	Nunca ou <1	1-3 por	1 por	2-4 por	5-6 por	1 por	2-3 por	4-5 por	6 + por	Porção Média		a porção		2 0 1
SIMILARES	mês	mês	sem	sem	sem	dia	dia	dia	dia	Media	Menor	Igual	Maior	a I
27. Pão branco ou tostas	0	0	0	0	0	0	0	0	0	Um ou 2 tostas = 40g	0	0	0	
28. Pão (ou tostas), integral,centeio, mistura	0	0	0	0	0	0	0	0	0	Um ou 2 tostas= 50g	0	0	0	
29. Broa, broa de avintes	0	0	0	0	0	0	0	0	0	1 fatia = 80g	0	0	0	
30. Flocos cereais (muesli, corn-flakes, chocapic,etc.)	0	0	0	0	0	0	0	0	0	1 chávena =40g	0	0	0	
31. Arroz	0	0	0	0	0	0	0	0	0	1½ prato = 1 00g	0	0	0	
 Massas: esparguete, macarrão, etc. 	0	0	0	0	0	0	0	0	0	1⁄2 prato = 100g	0	0	0	
33. Batatas fritas caseiras	0	0	0	0	0	0	0	0	0	1/2 prato = 100g	0	0	0	
34. Batatas fritas de pacote	0	0	0	0	0	0	0	0	0	pequeno =30g	0	0	0	
35. Batatas cozidas, assadas, estufadas e puré	0	0	0	0	0	0	0	0	0	2 batatas médias =160 g	0	0	0	
			Fi	requênc		entar					Quantid	ade		8 8
V.DOCES E PASTÉIS	Nunca ou <1 mês	1-3 por mês	1 por sem	2-4 por sem	5-6 por sem	1 por dia	2-3 por dia	4-5 por dia	6 + por dia	=30g O O 2 batatas médias O O =160 g O O Porção Média A sua porção é: Menor Igual Maior 3 bolachas O O 3 bolachas O O 3 bolachas O O 1 fatia = 80g O O 3 quadrados; O O 1 colher sopa O O 1 colher sobremesa; O O 1 colher sopt O O 1 colher sopt O O 1 pacote O O				x o n a -
36. Bolachas tipo maria, água e sal ou integrais	0	0	0	0	0	0	0	0	0	3 bolachas	0	0	0	
37. Outras bolachas ou biscoitos	0	0	0	0	0	0	0	0	0	3 bolachas	0	0	0	
38. Croissant, pasteis, bolicao, doughnut ou bolos	0	0	0	0	0	0	0	0	0		0	0	0	
39. Chocolate (tablete ou	0	0	0	0	0	0	0	0	0	3 quadrados;	0	0	0	
em pó) 40. Snacks de chocolate (Mars, Twix, Kit Kat, etc.)	0	0	0	0	0	0	0	0	0		0	0	0	
41. Marmelada, compota, geleia, mel	0	0	0	0	0	0	0	0	0		0	0	0	
42. Açúcar	0	0	0	0	0	0	0	0	0	sobremesa;	0	0	0	
			F	requên	cia alim	entar	<u> </u>	<u> </u>		- p	Quantid	ade		8 8
VI. HORTALIÇAS E	Nunca	1-3	1	2-4	5-6	1	2-3	4-5	6+	Porção		la porção	ó é:	2
LEGUMES	ou <1 mês	por mês	por sem	por sem	por sem	por dia	por dia	por dia	por dia	Média	Menor	Igual	Maior	n 3
43. Couve branca, couve lombarda	0	0	0	0	0	0	0	0	0	1/2 chávena =75g	0	0	0	
44. Penca, Tronchuda	0	0	0	0	0	0	0	0	0	1/2 chávena = 65g	0	0	0	
45. Couve galega	0	0	0	0	0	0	0	0	0	1/2 chávena =65g	0	0	0	
46. Brócolos	0	0	0	0	0	0	0	0	0	1½ chávena =85g	0	0	0	
47. Couve-flor, Couve-bruxelas	0	0	0	0	0	0	0	0	0	1/2 chávena =65g	0	0	0	
48. Grelos, Nabiças, Espinafres	0	0	0	0	0	0	0	0	0	1/2 chávena =72g	0	0	0	
49. Feijão verde	0	0	0	0	0	0	0	0	0	1⁄2 chávena =65g	0	0	0	
50. Alface, Agrião	0	0	0	0	0	0	0	0	0	1/2 chávena =15g	0	0	0	
51. Cebola	0	0	0	0	0	0	0	0	0	1/2 média=40g	0	0	0	
52. Cenoura	0	0	0	0	0	0	0	0	0	1 média=80g	0	0	0	
53. Nabo	0	0	0	0	0	0	0	0	0	1 médio=78g	0	0	0	
54. Tomate fresco 55. Pimento	0	00	0	0	0	0	0	0	0	1/2 médio=63g 1/2 médio=68g	00	00	00	同
55. Pimento 56. Pepino	0	0	0	0	0	0	0	0	0	1/4 médio=68g	0	00	00	
57. Leguminosas: feijão,	0	0	0	0	0	0	0	0	0	1 chávena	0	0	0	
grão de bico														
58. Ervilha grão, Fava	0	0	0	0	0	0	0	0	0	1/2 chávena	0	0	0	

ID 0

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			Fr	equênc	ia alime	ntar					Quantid	a de		a a z
VII. FRUTOS	Nunca	1-3	1	2-4	5-6	1	2-3	4-5	6+	Porção Média		a porção	-	a
	ou <1 mês	por mês	por sem	por sem	por sem	por dia	por dia	por dia	por dia	weula	Menor	Igual	Maior	п а 1
59. Maça, pêra	0	0	0	0	0	0	0	0	0	uma média	0	0	0	
60. Laranja, Tangerinas	0	0	0	0	0	0	0	0	0	1 média; 2 médias	0	0	0	
61. Banana	0	0	0	0	0	0	0	0	0	uma média	0	0	0	
62. Kiwi	0	0	0	0	0	0	0	0	0	um médio	0	0	0	
63. Morangos	0	0	0	0	0	0	0	0	0	1 chávena	0	0	0	
64. Cerejas	0	0	0	0	0	0	0	0	0	1 cháven a	0	0	0	
65. Pêssego, Ameixa	0	0	0	0	0	0	0	0	0	1 médio; 3 médios	0	0	0	
66. Melão, Melancia	0	0	0	0	0	0	0	0	0	1 fatia média = 150g	0	0	0	
67. Diospiro	0	0	0	0	0	0	0	0	0	1 médio	0	0	0	
68. Figo fresco, Nêsperas, Damascos	0	0	0	0	0	0	0	0	0	3 médios	0	0	0	
69. Uvas frescas	0	0	0	0	0	0	0	0	0	1 cacho médio	0	0	0	
70. Frutos conserva pêssego, ananás	0	0	0	0	0	0	0	0	0	2 metades ou rod elas	0	0	0	
71. Amêndoas, avelās, nozes, amendoins, pistachio, etc.	0	0	0	0	0	0	0	0	0	1/2 chávena (descascado)	0	0	0	
72. Azeitonas	0	0	0	0	0	0	0	0	0	6 un idades	0	0	0	
			F	requênc	ia alime	ntar					Quantid	ade		8
VIII. BEBIDAS E	Nunca	1-3	1	2-4	5-6	1	2-3	4-5	6 +	Porção	A su	a porção	bé:	8 2 0
MISCELANEAS	ou <1 mês	por mês	por sem	por sem	por sem	por dia	por dia	por dia	por dia	Média	Menor	Igual	Maior	п а 1
73. Vinho	0	0	0	0	0	0	0	0	0	1 copo=125ml	0	0	0	
74. Cerveja	0	0	0	0	0	0	0	0	0	1 garrafa ou 1 lata=330 ml	0	0	0	
 Bebidas brancas: whisky, aguardente, brandy, etc 	0	0	0	0	0	0	0	0	0	1 cálice = 40 ml	0	0	0	
 Coca-cola, pepsi-cola ou outras colas 	0	0	0	0	0	0	0	0	0	1 garrafa ou 1 lata =330 ml	0	0	0	
77. Ice-tea	0	0	0	~	0	~	-	-	-	1 garrafa ou	0	0	0	
78.Outros refrigerantes,	_		0	0	0	0	0	0	0	1 lata=330 ml	0	<u> </u>		
sumos de fruta ou néctares	0	0	0	0	0	0	0	0	0	1 lata=330 ml 1 garrafa ou 1 copo = 250 ml	0	0	0	
sumos de fruta ou néctares embalados 79.Café (incluindo pingo, meia de leite e outras										1 garrafa ou 1 copo	-	-		
sumos de fruta ou néctares embalados 79. Café (incluindo pingo, meia de leite e outras bebidas com café) 80. Chá preto e verde	0	0	0	0	0	0	0	0	0	1 garrafa ou 1 copo = 250 ml 1 cháven a	0	0	0	
sumos de fruta ou néctares embalados 79. Café (incluindo pingo, meia de leite e outras bebidas com café)	0 0	0	0	0	0	0	0 0	0	0 0	1 garrafa ou 1 copo = 250 mi 1 cháven a ca fé	0	0	0	
sumos de fruta ou néctares embalados 79. Café (incluindo pingo, meia de leite e outras bebidas com café) 80. Chá preto e verde 81. Croquetes, rissóis,	0 0 0	0 0 0	000	0	0 0	0 0 0	0 0 0	000	0 0 0	1 garrafa ou 1 copo = 250 ml 1 cháven a café 1 cháven a	0	0	0 0 0	
sumos de fruta ou néctares embalados 79. Café (incluindo pingo, meia de leite e outras bebidas com café) 80. Chá preto e verde 81. Croquetes, rissóis, bolinhos de bacalhau, etc. 82. Maionese 83. Molho de tomate,	0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	1 garrafa ou 1 copo = 250 mi 1 chávena café 1 chávena 3 unidades 1 colher sobremesa 1 colher	0 0 0	0 0 0	0 0 0 0	
sumos de fruta ou néctares embalados 79. Café (incluindo pingo, meia de leite e outras bebidas com café) 80. Chá preto e verde 81. Croquetes, rissóis, bolinhos de bacalhau, etc. 82. Maionese	0 0 0 0	0 0 0 0 0	0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0	1 garrafa ou 1 copo = 250 ml 1 chávena ca fé 1 chávena 3 unidades 1 colher sobremesa 1 colher sopa Meia	0 0 0 0	0 0 0 0 0	0 0 0 0 0	
sumos de fruta ou néctares embalados 79. Café (incluindo pingo, meia de leite e outras bebidas com café) 80. Chá preto e verde 81. Croquetes, rissóis, bolinhos de bacalhau, etc. 82. Maionese 83. Molho de tomate, ketchup	0 0 0 0 0 0	0 0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0 0	1 garrafa ou 1 copo = 250 ml 1 chávena café 1 chávena 3 unidades 1 colher sobremesa 1 colher sopa	0 0 0 0 0 0	0 0 0 0 0	0 0 0 0 0 0	

Existe algum alimento ou bebida que eu não tenha mencionado e que tenha consumido pelo menos 1 vez por semana mesmo em pequenas quantidades, ou numa época em particular. Por ex: frutos tropicais, sumos de fruta natural, bebidas espirituosas, café de mistura, alheiras, farinheiras, frutos secos (figo, ameixa, damasco), produtos dietéticos, rebuçados, etc.

			F	⁻ re quên	cia alim	nentar				Quantidade	8 8
Outros Alimentos	Nunca ou <1 mês	1-3 por mês	1 por sem	2-4 por sem	5-6 por sem	1 por dia	2-3 por dia	4-5 por dia	6 + por dia	Porção Média	z n a
	0	0	0	0	0	0	0	0	0		
	0	0	0	0	0	0	0	0	0		
	0	0	0	0	0	0	0	0	0		



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Unidade de Epidemiologia Nutricional Serviço de Higiene e Epidemiologia - FMUP

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Attachment II – Informed Consent Form

FOLHA DE INFORMAÇÃO AO PARTICIPANTE/ CONSENTIMENTO INFORMADO

TÍTULO DO ENSAIO CLÍNICO:

QUESTIONÁRIO SOBRE O ESTILO DE VIDA E HÁBITOS ALIMENTARES DA POPULAÇÃO PORTUGUESA COM 55 ANOS OU SUPERIOR.

PROTOCOLO Nº.	4C-2012-04
PROMOTOR IDCT	Prof. Rufino Silva - AIBILI
INVESTIGADOR COORDENADOR	Prof. Rufino Silva
<u>CENTRO DE ENSAIO</u>	[Nome do Centro de saúde / Unidade de Saúde Familar]
INVESTIGADOR PRINCIPAL	Prof. Rufino Silva
MORADA	AIBILI – Associação para Investigação Biomédica e Inovação em Luz e Imagem
CONTACTO TELEFÓNICO	239 480 105
FAX	239 480 117

NOME DO DOENTE

(IMPRESSO)

É convidado(a) a responder ao "Questionário sobre estilo de vida e hábitos alimentares" porque participou no "Estudo epidemiológico da prevalência de maculopatia relacionada com a idade em Portugal".

Um membro da equipa irá esclarecer qualquer dúvida que tenha sobre o termo de consentimento e também alguma palavra ou informação que possa não entender.

Caso queira participar, ser-lhe-á solicitado que assine e date este formulário. Após a sua assinatura e do elemento da equipa, ser-lhe-á entregue uma cópia. Caso não queira participar, não haverá qualquer penalização.

1. INFORMAÇÃO GERAL E OBJECTIVOS DO ENSAIO CLÍNICO

A realização deste Questionário, que irá decorrer neste Centro de Ensaio: ______, procura verificar a influência do estilo de vida e hábitos alimentares no desenvolvimento da Degenerescência Macular Relacionada com a Idade.

A Degenerescência Macular relacionada com a Idade é considerada uma das principais causas da perda de visão acima dos 55 anos e consiste na degenerescência da área central da retina (mácula), conduzindo a uma diminuição acentuada e irreversível da visão.

Este Questionário foi aprovado pela Comissão de Ética Independente da AIBILI de modo a garantir a proteção dos seus direitos e garantir prova pública dessa proteção.

2. PROCEDIMENTOS E CONDUÇÃO DO ENSAIO CLÍNICO

Ser-lhe-ão colocadas questões sobre o seu estilo de vida (por exemplo, se pratica desporto, quantas refeições faz por dia, se é fumador, etc.) e sobre os seus hábitos alimentares. Demorará cerca de 15 minutos a responder ao Questionário. Prevê-se que 4000 pessoas respondam a este Questionário.

3. RISCOS E POTENCIAIS INCONVENIENTES PARA O DOENTE

A sua participação neste ensaio não acarreta qualquer risco ou inconveniente, uma vez que consiste apenas em responder a um Questionário.

4. POTENCIAIS BENEFÍCIOS

A informação que será recolhida irá contribuir para perceber a influência do estilo de vida e hábitos alimentares no desenvolvimento Degenerescência Macular Relacionada com a Idade, o que permitirá uma melhor prevenção desta doença.

5. PARTICIPAÇÃO/ ABANDONO VOLUNTÁRIO

Pode abandonar a sua participação a qualquer momento, isto é, pode parar de responder ao Questionário a qualquer momento ou retirar o seu Consentimento para que as suas respostas não sejam usadas.

6. CONFIDENCIALIDADE

Os seus registos manter-se-ão confidenciais e anonimizados de acordo com os regulamentos e leis aplicáveis. Se os resultados deste Estudo forem publicados a sua identidade manter-se-á confidencial.

7. COMPENSAÇÃO

Este é um Estudo da iniciativa do Investigador e por isso não haverá qualquer compensação financeira para os Investigadores nem para os participantes.

8. CONTACTOS

Contacto para qualquer informação sobre o ensaio clínico e os seus direitos:

Comissão de Ética da AIBILI

Prof. Francisco Corte Real Gonçalves

Azinhaga de Santa Comba, Celas

3000-548 Coimbra

Tel: 239 480 100

Contacto do centro clínico em caso de alguma ocorrência relacionada com este Estudo:

Investigador Coordenador: Dr. Rufino Silva

Contacto Telefónico: 239 480 105

NÃO ASSINE ESTE FORMULÁRIO DE CONSENTIMENTO INFORMADO A MENOS QUE TENHA TIDO A OPORTUNIDADE DE PERGUNTAR E TER RECEBIDO RESPOSTAS SATISFATÓRIAS A TODAS AS SUAS PERGUNTAS.

CONSENTIMENTO INFORMADO

- 1. Declaro ter lido este formulário e aceito de forma voluntária responder ao Questionário.
- 2. Fui devidamente informado(a) da natureza do Questionário e do que é esperado da minha parte.
- 3. Tive a oportunidade de fazer perguntas sobre o Questionário e percebi as respostas e as informações que me foram dadas.
- 4. Aceito que utilizem a informação relativa à minha história médica no estrito respeito do segredo médico e anonimato. Os meus dados serão mantidos estritamente confidenciais. Eu autorizo a consulta dos meus dados apenas por pessoas designadas pelo Promotor e por representantes das Autoridades Reguladoras.
- 5. Autorizo o uso dos resultados do Questionário e, em particular, aceito que esses resultados sejam divulgados.
- 6. Aceito que os dados gerados durante o Questionário sejam informatizados pelo Promotor ou por si designado.

Eu posso exercer o meu direito de rectificação e/ ou oposição.

Fui informado que o Estudo pode ser interrompido por decisão do Investigador, do Promotor ou das Autoridades Reguladoras.

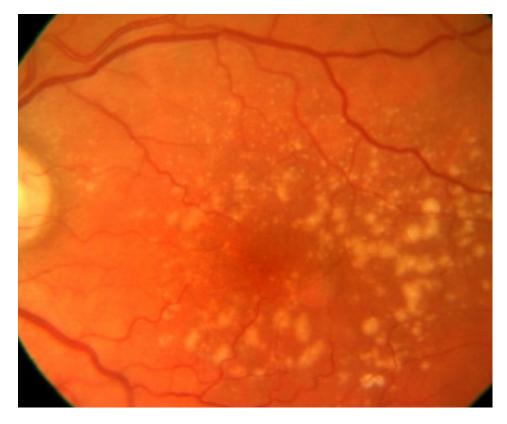
Nome do Participante

Assinatura : _____ Data: ____/___/____

Eu confirmo que expliquei ao participante acima mencionado a natureza, o objetivo e os potenciais riscos do ensaio clínico acima mencionado.

Nome do Entrevistador:			
Assinatura:	Data:	_/	_/

Attachment III – Fundus Color Photography



Soft and coalescent drusens are visible (patient with AMD)

Attachment IV - Opinion of the AIBILI Ethics Committee on Health



Exmo. Senhor Prof. Doutor Rufino Silva AIBILI Azinhaga de Santa Comba, Celas 3000-548 Coimbra

COMISSÃO DE ÉTICA - 2012/11/06

S/ referência: 021/2012/AIBILI/4C, de 2012/10/23

Assunto: CE 184 - "Life style and food habits questionnaire in the Portuguese population aged 55 or more" - Protocol nº: 4C-2012-04

Parecer favorável

Exmo. Senhor,

Tenho a honra de comunicar a V. Exa. que, na sua 114^a reunião de 6 de Novembro de 2012, a Comissão de Ética, após analisada a seguinte documentação: "Modelo Específico da Comissão de Ética" - Mod.CEv6, de 2012/10/23; Nome e Morada do Promotor, de 2012/10/23; Nome e Morada do Investigador Principal, de 2012/10/23; Curriculum Vitae do Investigador Principal; "Clinical Protocol nº 4C-2012-04" – Ref^a Imp. 16-2-2/0, Protocol Version #0 de 2012-10-22; "Folha de Informação ao Participante / Consentimento Informado" – Ref^a Imp 16-2-4-P/0, Versão do CI 0 de 2012-10-22 e "Inquérito – estilos de vida e hábitos alimentares" – Ref^a Inquérito Versão 0 de 2012/10/23, submetida através do v/ oficio mencionado em epígrafe, emitiu parecer favorável ao estudo observacional em questão, estando salvaguardados os princípios do consentimento informado e da confidencialidade.

Com os melhores cumprimentos,

O Presidente da Comissão de Ética

(Francisco Corte-Real Gonçalves)

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Attachment V – Complete complementary tables

Т	able 1. Sociodemogra	aphic	Characte	cs			
			Grou		т	otal	
		With	out AMD	A	MD	1	otai
		n	%	n	%	n	%
Sex	Female	250	55,4%	248	57,3%	498	56%
Sex	Male	201	44,6%	185	42,7%	386	44%
A 90	< 65	146	32,4%	135	31,2%	281	32%
Age	>= 65	305	67,6%	298	68,8%	603	68%
Job	Employed	44	9,8%	42	9,7%	86	10%
100	Unemployed	407	90,2%	391	90,3%	798	90%
	W/ education	47	10,4%	59	13,6%	106	12%
Academic studies	Basic education	361	80,0%	339	78,3%	700	79%
Academic studies	Secondary education	24	5,3%	19	4,4%	43	5%
	University	19	4,2%	16	3,7%	35	4%
Total	Group	451	51%	433	49%	884	100%

Table 1. Sociodemographic Characteristics

Table 1. Sociodemographic Characteristics by Group and Gender

				Gro	up		
		V	Vithout AMD			AMD	
		Female	Male	Total	Female	Male	Total
	n	250	201	451	248	185	433
Weight	\overline{x}	70,33	81,55	75,33	70,00	81,96	75,11
	S	12,78	11,73	13,51	11,63	13,00	13,58
	n	250	201	451	248	185	433
Height	\overline{x}	1,57	1,69	1,62	1,58	1,69	1,63
	S	0,05	0,06	0,08	0,06	0,06	0,08
	n	250	201	451	248	185	433
BMI	\bar{x}	28,32	28,56	28,43	28,04	28,72	28,33
	S	4,53	3,86	4,24	4,50	4,18	4,37
	n	250	201	451	248	185	433
AP	\overline{x}	94,65	103,50	98,59	93,32	104,50	98,1
	S	11,57	15,22	14,02	14,03	12,46	14,46
	n	250	201	451	248	185	433
Number of cigarretes	\overline{x}	24,54	27,61	26,87	24,55	26,25	25,70
	S	10,84	19,42	17,75	17,25	18,89	18,30
	n	250	201	451	248	185	433
Smoking years	\bar{x}	29,55	28,23	28,55	27,33	26,59	26,81
	S	14,01	15,95	15,46	15,16	15,70	15,48
	n	250	201	451	248	185	433
PYU	\overline{x}	37,41	38,62	38,32	32,81	34,76	34,19
	S	24,20	35,49	33,00	28,30	31,95	30,80
	n	250	201	451	248	185	433
Number of meals/day	\overline{x}	4,24	3,92	4,10	4,06	3,83	3,96
	S	1,02	,89	,97	,90	,89	,90

					G	roup			
			Witho	ut AMD			AN	٨D	
		F	emale	1	Male	F	emale	l	Male
		n	%	n	%	n	%	n	%
Dishetes	Yes	49	19,6%	59	29,4%	49	19,8%	50	27,0%
Diabetes	No	201	80,4%	142	70,6%	199	80,2%	135	73,0%
Umortongion	Yes	169	67,6%	130	64,7%	167	67,3%	139	75,1%
Hypertension	No	81	32,4%	71	35,3%	81	32,7%	46	24,9%
Dialinidamia	Yes	147	58,8%	103	51,2%	142	57,3%	94	50,8%
Dislipidemia	No	103	41,2%	98	48,8%	106	42,7%	91	49,2%
Obsister	Yes	195	78,0%	158	78,6%	182	73,4%	138	74,6%
Obesity	No	55	22,0%	43	21,4%	66	26,6%	47	25,4%
Exercise	Yes	82	32,8%	65	32,3%	65	26,2%	40	21,6%
Exercise	No	168	67,2%	136	67,7%	183	73,8%	145	78,4%
Sumplemente	Yes	26	10,4%	12	6,0%	26	10,5%	11	5,9%
Supplements	No	224	89,6%	189	94,0%	222	89,5%	174	94,1%
	Smokes	30	12,0%	94	46,8%	30	12,1%	74	40,2%
Smoker	Doesn't smoke	220	88,0%	107	53,2%	218	87,9%	110	59,8%
Total	Group/sex	250	28,28%	201	22,74%	248	28,05%	185	20,93%

Table 2. Clinical Characteristics by Group and Gender

Table 3. Descriptive statistics of quantitative data

			Group	
		n	x	S
	W/ AMD	451	75,33	13,51
Weight	AMD	433	75,11	13,58
	Total	884	75,22	13,54
	W/ AMD	451	1,62	,08
Height	AMD	433	1,63	,08
	Total	884	1,62	,08
	W/ AMD	451	28,43	4,24
BMI	AMD	433	28,33	4,37
	Total	884	28,38	4,30
	W/ AMD	451	98,59	14,02
AP	AMD	432	98,11	14,46
	Total	883	98,36	14,23
	W/ AMD	451	26,87	17,75
Number of cigarretes	AMD	433	25,76	18,36
	Total	884	26,36	18,00
	W/ AMD	451	28,55	15,46
Smoking years	AMD	433	26,81	15,48
	Total	884	27,74	15,46
	W/ AMD	451	39,71	33,23
PYU	AMD	433	35,30	31,37
	Total	884	37,67	32,37
	W/ AMD	451	4,10	,97
Number of meals/day	AMD	433	3,96	,90
	Total	884	4,03	,94

			Grou	лb	
		With	out AMD	A	MD
		n	%	n	%
Chicken or turkey ⁺ (FA9 +	1st tertile($\leq 17, 14$)	170	50,3%	168	53,7%
FA10)	2nd tertile(≥34,28)	168	49,7%	145	46,3%
Sugar ⁺	1st tertile(≤88,34)	141	47,0%	153	53,1%
Sugar	2nd tertile(≥115,84)	159	53,0%	135	46,9%
Meat ⁺	1st tertile($\leq 8,94$)	152	51,7%	138	48,1%
(FA11 a FA16)	2nd tertile(≥19,44)	142	48,3%	149	51,9%
Oily fish ⁺ (FA17)	1st tertile($\leq 14,28$)	237	90,5%	242	91,7%
	2nd tertile(≥42,86)	25	9,5%	22	8,3%
White fish ⁺ (FA18)	1st tertile($\leq 14,28$)	225	88,2%	228	90,5%
	2nd tertile(\geq 42,86)	30	11,8%	24	9,5%
Cod fish	1st tertile($\leq 17, 14$)	204	52,3%	190	47,7%
(FA19) ⁺	2nd tertile(\geq 51,43)	186	47,7%	184	49,2%
White fish and cod fish	1st tertile($\leq 19,28$)	149	48,7%	142	51,4%
$(FA18 e FA19)^+$	2nd tertile(\geq 32,86)	157	51,3%	134	48,6%
Olive oil (FA23) ⁺	1st tertile(≤13,5)	262	66,7%	264	70,8%
01170 011 (17125)	2nd tertile(≥27)	131	33,3%	135	29,2%
Bread, broa and cereal	1st tertile(≤50)	161	52,1%	139	48,6%
$(FA27 a FA30)^+$	2nd tertile(≥88,27)	148	47,9%	147	51,4%
French fries (FA33 e FA34)	1st tertile($\leq 4,34$)	101	59,4%	92	52,9%
+	2nd tertile(\geq 7,14)	69	40,6%	82	47,1%
Boiled potatoes (FA35)*	1st tertile(≤34,29)	170	54,3%	133	45,9%
	2nd tertile($\geq 102,86$)	143	45,7%	157	54,1%
Sugar, biscuits and	1st tertile(≤6,59)	137	45,8%	144	54,5%
chocolates (FA36 a FA42)*	2nd tertile($\geq 11,57$)	162	54,2%	120	45,5%
Cabbage (FA43, FA44,	1st tertile($\leq 3, 21$)	135	47,7%	125	53,4%
• • • • • • • • • • • • • • • • • • •		1.40	50.00/		
FA45) ⁺	2nd tertile(\geq 8,29)	148	52,3%	109	46,6%
FA45) ⁺ Broccoli and cauliflower	2nd tertile(≥8,29) 1st tertile(≤5,04)	101	46,5%	109 112	46,6% 51,4%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺	2nd tertile(\geq 8,29) 1st tertile(\leq 5,04) 2nd tertile(\geq 9,29)	101 116	46,5% 53,5%	109 112 106	46,6% 51,4% 48,6%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48,	$2nd tertile(\geq 8,29)$ $1st tertile(\leq 5,04)$ $2nd tertile(\geq 9,29)$ $1st tertile(\leq 7,35)$	101 116 139	46,5% 53,5% 47,3%	109 112 106 141	46,6% 51,4% 48,6% 50,9%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺	2nd tertile(\geq 8,29) 1st tertile(\leq 5,04) 2nd tertile(\geq 9,29) 1st tertile(\leq 7,35) 2nd tertile(\geq 12,96)	101 116 139 155	46,5% 53,5% 47,3% 52,7%	109 112 106 141 136	46,6% 51,4% 48,6% 50,9% 49,1%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48,	2nd tertile($\geq 8, 29$)1st tertile($\leq 5, 04$)2nd tertile($\geq 9, 29$)1st tertile($\leq 7, 35$)2nd tertile($\geq 12, 96$)1st tertile($\leq 10, 29$)	101 116 139 155 140	46,5% 53,5% 47,3% 52,7% 62,2%	109 112 106 141 136 158	46,6% 51,4% 48,6% 50,9% 49,1% 70,2%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48, FA49, FA50) ⁺ Carrots (FA52)*	2nd tertile($\geq 8, 29$)1st tertile($\leq 5, 04$)2nd tertile($\geq 9, 29$)1st tertile($\leq 7, 35$)2nd tertile($\geq 12, 96$)1st tertile($\leq 10, 29$)2nd tertile($\geq 30, 86$)	101 116 139 155 140 85	46,5% 53,5% 47,3% 52,7% 62,2% 37,8%	109 112 106 141 136 158 67	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48, FA49, FA50) ⁺ Carrots (FA52)* Tomatoes	2nd tertile($\geq 8, 29$)1st tertile($\leq 5, 04$)2nd tertile($\geq 9, 29$)1st tertile($\geq 7, 35$)2nd tertile($\geq 12, 96$)1st tertile($\leq 10, 29$)2nd tertile($\geq 30, 86$)1st tertile($\leq 12, 38$)	101 116 139 155 140 85 155	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7%	109 112 106 141 136 158 67 151	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48, FA49, FA50) ⁺ Carrots (FA52)*	2nd tertile($\geq 8, 29$)1st tertile($\leq 5, 04$)2nd tertile($\geq 9, 29$)1st tertile($\leq 7, 35$)2nd tertile($\geq 12, 96$)1st tertile($\leq 10, 29$)2nd tertile($\geq 30, 86$)1st tertile($\leq 12, 38$)2nd tertile($\geq 24, 75$)	101 116 139 155 140 85 155 139	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3%	109 112 106 141 136 158 67 151 133	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48, FA49, FA50) ⁺ Carrots (FA52)* Tomatoes	$2nd tertile(\geq 8,29)$ $1st tertile(\leq 5,04)$ $2nd tertile(\geq 9,29)$ $1st tertile(\geq 7,35)$ $2nd tertile(\geq 12,96)$ $1st tertile(\geq 10,29)$ $2nd tertile(\geq 30,86)$ $1st tertile(\leq 12,38)$ $2nd tertile(\geq 24,75)$ $1st tertile(\leq 12,01)$	101 116 139 155 140 85 155 139 169	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0%	109 112 106 141 136 158 67 151 133 154	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48, FA49, FA50) ⁺ Carrots (FA52)* Tomatoes (FA54) ⁺	2nd tertile($\geq 8, 29$)1st tertile($\leq 5, 04$)2nd tertile($\geq 9, 29$)1st tertile($\leq 7, 35$)2nd tertile($\geq 12, 96$)1st tertile($\leq 10, 29$)2nd tertile($\geq 30, 86$)1st tertile($\leq 12, 38$)2nd tertile($\geq 24, 75$)1st tertile($\leq 12, 01$)2nd tertile($\geq 25, 71$)	101 116 139 155 140 85 155 139 169 95	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0% 36,0%	109 112 106 141 136 158 67 151 133 154 80	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8% 34,2%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48, FA49, FA50) ⁺ Carrots (FA52)* Tomatoes (FA54) ⁺ Pulses (FA57) ⁺	$2nd tertile(\geq 8,29)$ $1st tertile(\leq 5,04)$ $2nd tertile(\geq 9,29)$ $1st tertile(\geq 7,35)$ $2nd tertile(\geq 12,96)$ $1st tertile(\geq 10,29)$ $2nd tertile(\geq 30,86)$ $1st tertile(\leq 12,38)$ $2nd tertile(\geq 24,75)$ $1st tertile(\leq 12,01)$ $2nd tertile(\geq 25,71)$ $1st tertile(\leq 5,51)$	101 116 139 155 140 85 155 139 169 95 152	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0% 36,0% 56,1%	109 112 106 141 136 158 67 151 133 154 80 122	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8% 34,2% 49,2%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48, FA49, FA50) ⁺ Carrots (FA52)* Tomatoes (FA54) ⁺	2nd tertile($\geq 8, 29$)1st tertile($\leq 5, 04$)2nd tertile($\geq 9, 29$)1st tertile($\geq 12, 96$)1st tertile($\geq 10, 29$)2nd tertile($\geq 10, 29$)2nd tertile($\geq 30, 86$)1st tertile($\leq 12, 38$)2nd tertile($\geq 24, 75$)1st tertile($\leq 12, 01$)2nd tertile($\geq 25, 71$)1st tertile($\leq 5, 51$)2nd tertile($\geq 11, 79$)	101 116 139 155 140 85 155 139 169 95 152 119	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0% 36,0% 56,1% 43,9%	109 112 106 141 136 158 67 151 133 154 80 122 126	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8% 34,2% 49,2% 50,8%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48, FA49, FA50) ⁺ Carrots (FA52)* Tomatoes (FA54) ⁺ Pulses (FA57) ⁺	$2nd tertile(\geq 8,29)$ $1st tertile(\leq 5,04)$ $2nd tertile(\geq 9,29)$ $1st tertile(\geq 12,96)$ $1st tertile(\geq 10,29)$ $2nd tertile(\geq 10,29)$ $2nd tertile(\geq 30,86)$ $1st tertile(\geq 12,38)$ $2nd tertile(\geq 24,75)$ $1st tertile(\geq 12,01)$ $2nd tertile(\geq 12,01)$ $2nd tertile(\geq 5,51)$ $2nd tertile(\geq 11,79)$ $1st tertile(\leq 18,19)$	101 116 139 155 140 85 155 139 169 95 152 119 144	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0% 36,0% 56,1% 43,9% 48,0%	109 112 106 141 136 158 67 151 133 154 80 122 126 148	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8% 34,2% 49,2% 50,8% 51,9%
FA45)*Broccoli and cauliflower (FA46, FA47)*Greens and lettuce (FA48, FA49, FA50)*Carrots (FA52)*Tomatoes (FA54)*Pulses (FA57)*Peas (FA57)*Peas (FA58)*Fruits (FA60 a F69)*	$2nd tertile(\geq 8,29)$ $1st tertile(\leq 5,04)$ $2nd tertile(\geq 9,29)$ $1st tertile(\geq 12,96)$ $1st tertile(\geq 10,29)$ $2nd tertile(\geq 30,86)$ $1st tertile(\geq 12,38)$ $2nd tertile(\geq 12,38)$ $2nd tertile(\geq 12,01)$ $1st tertile(\leq 12,01)$ $2nd tertile(\geq 5,51)$ $2nd tertile(\geq 11,79)$ $1st tertile(\geq 18,19)$ $2nd tertile(\geq 28,22)$	101 116 139 155 140 85 155 139 169 95 152 119 144	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0% 36,0% 56,1% 43,9% 48,0% 52,0%	109 112 106 141 136 158 67 151 133 154 80 122 126 148 137	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8% 34,2% 49,2% 50,8% 51,9% 48,1%
FA45) ⁺ Broccoli and cauliflower (FA46, FA47) ⁺ Greens and lettuce (FA48, FA49, FA50) ⁺ Carrots (FA52)* Tomatoes (FA54) ⁺ Pulses (FA57) ⁺ Peas (FA58) ⁺	$2nd tertile(\geq 8,29)$ $1st tertile(\leq 5,04)$ $2nd tertile(\geq 9,29)$ $1st tertile(\geq 12,96)$ $1st tertile(\geq 10,29)$ $2nd tertile(\geq 10,29)$ $2nd tertile(\geq 12,38)$ $2nd tertile(\geq 12,38)$ $2nd tertile(\geq 24,75)$ $1st tertile(\geq 12,01)$ $2nd tertile(\geq 25,71)$ $1st tertile(\geq 5,51)$ $2nd tertile(\geq 11,79)$ $1st tertile(\leq 18,19)$ $2nd tertile(\geq 125)$	101 116 139 155 140 85 155 139 169 95 152 119 144 156 129	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0% 36,0% 56,1% 43,9% 48,0% 52,0% 83,8%	109 112 106 141 136 158 67 151 133 154 80 122 126 148 137 141	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8% 34,2% 49,2% 50,8% 51,9% 48,1% 83,9%
FA45)*Broccoli and cauliflower (FA46, FA47)*Greens and lettuce (FA48, FA49, FA50)*Carrots (FA52)*Tomatoes (FA54)*Pulses (FA57)*Peas (FA58)*Fruits (FA60 a F69)*Wine (FA73)*	$2nd tertile(\geq 8,29)$ $1st tertile(\leq 5,04)$ $2nd tertile(\geq 9,29)$ $1st tertile(\geq 12,96)$ $1st tertile(\geq 10,29)$ $2nd tertile(\geq 10,29)$ $2nd tertile(\geq 30,86)$ $1st tertile(\geq 12,38)$ $2nd tertile(\geq 24,75)$ $1st tertile(\geq 12,01)$ $2nd tertile(\geq 12,01)$ $2nd tertile(\geq 5,51)$ $2nd tertile(\geq 11,79)$ $1st tertile(\leq 18,19)$ $2nd tertile(\geq 12,22)$ $1st tertile(\geq 12,5)$ $2nd tertile(\geq 312,5)$	101 116 139 155 140 85 155 139 169 95 152 119 144 156 129 25	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0% 36,0% 56,1% 43,9% 48,0% 52,0% 83,8% 16,2%	109 112 106 141 136 158 67 151 133 154 80 122 126 148 137 141 27	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8% 34,2% 49,2% 50,8% 51,9% 48,1% 83,9% 16,1%
FA45)*Broccoli and cauliflower (FA46, FA47)*Greens and lettuce (FA48, FA49, FA50)*Carrots (FA52)*Tomatoes (FA54)*Pulses (FA57)*Peas (FA57)*Peas (FA58)*Fruits (FA60 a F69)*	$2nd tertile(\geq 8,29)$ $1st tertile(\leq 5,04)$ $2nd tertile(\geq 9,29)$ $1st tertile(\geq 12,96)$ $1st tertile(\geq 10,29)$ $2nd tertile(\geq 30,86)$ $1st tertile(\geq 12,38)$ $2nd tertile(\geq 12,38)$ $2nd tertile(\geq 12,01)$ $2nd tertile(\geq 12,01)$ $2nd tertile(\geq 5,51)$ $2nd tertile(\geq 5,51)$ $2nd tertile(\geq 11,79)$ $1st tertile(\geq 18,19)$ $2nd tertile(\geq 18,19)$ $2nd tertile(\geq 125)$ $2nd tertile(\geq 312,5)$ $1st tertile(\leq 22,01)$	101 116 139 155 140 85 155 139 169 95 152 119 144 156 129 25 24	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0% 36,0% 56,1% 43,9% 48,0% 52,0% 83,8% 16,2% 52,2%	109 112 106 141 136 158 67 151 133 154 80 122 126 148 137 141 27 30	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8% 34,2% 49,2% 50,8% 51,9% 48,1% 83,9% 16,1% 71,4%
FA45)*Broccoli and cauliflower (FA46, FA47)*Greens and lettuce (FA48, FA49, FA50)*Carrots (FA52)*Tomatoes (FA54)*Pulses (FA57)*Peas (FA58)*Fruits (FA60 a F69)*Wine (FA73)*	$2nd tertile(\geq 8,29)$ $1st tertile(\leq 5,04)$ $2nd tertile(\geq 9,29)$ $1st tertile(\geq 12,96)$ $1st tertile(\geq 10,29)$ $2nd tertile(\geq 10,29)$ $2nd tertile(\geq 30,86)$ $1st tertile(\geq 12,38)$ $2nd tertile(\geq 24,75)$ $1st tertile(\geq 12,01)$ $2nd tertile(\geq 12,01)$ $2nd tertile(\geq 5,51)$ $2nd tertile(\geq 11,79)$ $1st tertile(\leq 18,19)$ $2nd tertile(\geq 12,22)$ $1st tertile(\geq 12,5)$ $2nd tertile(\geq 312,5)$	101 116 139 155 140 85 155 139 169 95 152 119 144 156 129 25	46,5% 53,5% 47,3% 52,7% 62,2% 37,8% 52,7% 47,3% 64,0% 36,0% 56,1% 43,9% 48,0% 52,0% 83,8% 16,2%	109 112 106 141 136 158 67 151 133 154 80 122 126 148 137 141 27	46,6% 51,4% 48,6% 50,9% 49,1% 70,2% 29,8% 53,2% 46,8% 65,8% 34,2% 49,2% 50,8% 51,9% 48,1% 83,9% 16,1%

Table 4. Values per tertile of food frequ	ency by Group
	Group

	2nd tertile(\geq 15,72)	17	39,5%	16	34,0%
Soda, ice-tea and coke	1st tertile(≤23,56)	47	58,7%	46	52,3%
$(FA76, FA77, FA78)^+$	2nd tertile(≥111,87)	33	41,3%	42	47,7%
Coffee (FA79) ⁺	1st tertile(≤45)	185	88,1%	192	92,3%
Collee (FA79)	2nd tertile(\geq 112,51)	25	11,9%	16	7,7%
Tea	1st tertile(≤15,81)	40	45,5%	44	61,1%
Tea (FA80)*	$\frac{1 \text{ st tertile}(\leq 15, 81)}{2 \text{ nd tertile}(\geq 33, 85)}$	40 48	45,5% 54,5%	44 28	61,1% 38,9%
		-	,		,
(FA80)*	2nd tertile(\geq 33,85)	48	54,5%	28	38,9%

 Tabela 5. Values per tertile of nutrients by Group
 Group

		Group				
		Without AMD		AMD		
		n	%	n	%	
7 • +	1st tertile(≤9,11)	146	49,0%	148	51,0%	
Zinc^+	2nd tertile(≥11,93)	152	51,0%	142	49,0%	
	1st tertile(≤0,19)	152	50,0%	144	50,2%	
Omega-3 (N87, N88, N89)	2nd tertile($\geq 0,47$)	152	50,0%	143	49,8%	
$Colorise^+(N11)$	1st tertile(≤1880,43)	147	48,4%	148	51,9%	
Calories ⁺ (N1)	2nd tertile(≥2367,29)	157	51,6%	137	48,1%	
$Coloring (M1)^+$	\geq 2000	263	58,3%	242	55,9%	
Calories $(N1)^+$	< 2000	188	41,7%	191	44,1%	
$T_{ada} = \frac{1}{2} \left(\sum_{i=1}^{n} \sum_{j=1}^{n} \sum_{i=1}^{n} \sum_{i=1}^{n} \sum_{i=1}^{n} \sum_{j=1}^{n} \sum_{i=1}^{n} \sum_{j=1}^{n} \sum_{i=1}$	1st tertile(≤64,894)	143	48,3%	152	51,9%	
Total fat $(N4)^+$	2nd tertile(≥82,48)	153	51,7%	141	48,1%	
Saturated fat (N5) ⁺	1st tertile($\leq 17,02$)	136	46,9%	159	53,2%	
Saturated fat (NS)	2nd tertile(≥22,28)	154	53,1%	140	46,8%	
More compacture to d for $(NIC)^+$	1st tertile(≤30,46)	149	47,6%	146	52,9%	
Monounsaturated fat $(N6)^+$	2nd tertile(≥41,89)	164	52,4%	130	47,1%	
Doliver actions to d fat $(N7)^+$	1st tertile(≤10,05)	140	47,6%	155	52,5%	
Poliunsaturated fat $(N7)^+$	2nd tertile(≥12,719)	154	52,4%	140	47,5%	
$C_{alactorel}$ (NI2) ⁺	1st tertile(≤223,57)	147	50,3%	148	49,8%	
Colesterol (N8) ⁺	2nd tertile(≥301,29)	145	49,7%	149	50,2%	
Fibre (NO)*	1st tertile(≤21,94)	139	45,7%	156	54,7%	
Fibre (N9)*	2nd tertile(≥28,99)	165	54,3%	129	45,3%	
Complex carbon hidrates (N10) ⁺	1st tertile(≤55,22)	140	47,5%	155	52,7%	
Complex carbon mutates (N10)	2nd tertile(≥74,581)	155	52,5%	139	47,3%	
Alcohol (N12) ⁺	1st tertile(≤0)	194	58,3%	175	55,2%	
Alcohol (N12)	2nd tertile(≥11,61)	139	41,7%	142	44,8%	
Álcohol (g) (N12) ⁺	≤ 30	202	78,6%	199	77,1%	
Alcohol (g) (N12)	> 30	55	21,4%	59	22,9%	
C_{α}	1st tertile(≤31,77)	136	45,6%	150	54,9%	
Caffeine (N13)*	2nd tertile(≥78,76)	162	54,4%	123	45,1%	
Total withoming (N14)*	1st tertile(≤1379,4)	132	44,4%	163	55,8%	
Total vitamins (N14)*	2nd tertile(≥2066,95)	165	55,6%	129	44,2%	
Retinol (N15) ⁺	1st tertile(≤236,35)	151	50,0%	144	50,2%	
Keunor (IN13)	2nd tertile(≥690,64)	151	50,0%	135	49,8%	
Data aspetance (NIIA)*	1st tertile(≤865,56)	132	43,4%	163	57,2%	
Beta carotenes (N16)*	2nd tertile(≥1416,37)	172	56,6%	122	42,8%	

	1 + (-1) = (-1	140	40.50/	150	51.00/
Thiamine (N17) ⁺	$\frac{1 \text{ st tertile}(\leq 1,379)}{2 \text{ nd tertile}(\geq 1,792)}$	146 155	48,5% 51,5%	150 139	51,9% 48,1%
Riboflavin (N18) ⁺	1st tertile($\leq 1,607$)	139 157	47,0%	156 135	53,2%
	2nd tertile($\geq 2,123$)		53,0%		46,8%
Niacin (N19) ⁺	1st tertile($\leq 17,532$)	148	48,7%	147	51,6%
	2nd tertile($\geq 23,05$)	156	51,3%	138	48,4%
Vitamin B6 (N21) ⁺	$1 \text{ st tertile}(\leq 1,865)$	147	47,9%	148	52,5%
	2nd tertile($\geq 2,45$)	160	52,1%	134	47,5%
Vitamin B12 (N22) ⁺	$1 \text{ st tertile}(\leq 7,06)$	152	51,4%	143	48,8%
	2nd tertile(\geq 10,23)	144	48,6%	150	51,2%
Folate (N23) ⁺	1 st tertile($\leq 235,031$)	153	49,0%	142	51,3%
	2nd tertile(\geq 321,90)	159	51,0%	135	48,7%
Vitamin C (N25)*	1st tertile(≤107,53)	136	45,9%	159	54,3%
	2nd tertile($\geq 150, 12$)	160	54,1%	134	45,7%
Vitamin D (N26) ⁺	1st tertile(≤2,984)	148	49,7%	147	50,5%
	2nd tertile(\geq 4,88)	150	50,3%	144	49,5%
Vitamin E (N27)*	1st tertile(≤8,62)	143	45,7%	152	55,1%
	2nd tertile($\geq 11, 15$)	170	54,3%	124	44,9%
Calcium (N29) ⁺	1st tertile(≤714,03)	138	47,4%	157	52,7%
Culotum (1(2))	2nd tertile(≥1020,24)	153	52,6%	141	47,3%
Magnesium (N32) ⁺	1st tertile(≤297,81)	138	46,6%	157	53,6%
Winghestulli (192)	2nd tertile(≥381,8)	158	53,4%	136	46,4%
Phosphorus (N34) ⁺	1st tertile(≤1160,85)	142	47,8%	153	52,4%
Thosphorus (1134)	2nd tertile(≥1483,76)	155	52,2%	139	47,6%
Selenium (N36) ⁺	1st tertile(≤79,26)	139	47,3%	156	52,9%
Scientum (1450)	2nd tertile(≥107,53)	155	52,7%	139	47,1%
Sodium (N37) ⁺	1st tertile(≤1785,86)	142	48,1%	153	52,0%
Sourum (1457)	2nd tertile(≥2375,87)	153	51,9%	141	48,0%
Biotin (N41) ⁺	1st tertile($\leq 6,2$)	148	48,8%	147	51,4%
Biotili (1141)	2nd tertile($\geq 9,52$)	155	51,2%	139	48,6%
Incoluble fibre (142)*	1st tertile(≤14,11)	140	45,6%	155	55,0%
Insoluble fibre (N48)*	2nd tertile(≥19,06)	167	54,4%	127	45,0%
Soluble fibre (NI40)*	1st tertile(≤5,35)	136	44,9%	159	55,6%
Soluble fibre (N49)*	2nd tertile(\geq 7,29)	167	55,1%	127	44,4%
Soluble and insoluble fibre	1st tertile(≤9,725)	133	44,2%	162	56,3%
(N48, N49)*	2nd tertile(\geq 13,20)	168	55,8%	126	43,8%
$\mathbf{L}_{\mathbf{r}}$	1st tertile(≤3,323)	149	48,9%	146	51,4%
Isoleucine (N57) ⁺	2nd tertile(\geq 4,28)	156	51,1%	138	48,6%
$\mathbf{L}_{\text{ansign}} (\mathbf{M}_{\mathbf{F}} 0)^+$	1st tertile($\leq 5,545$)	145	48,7%	150	51,7%
Leucine (N58) ⁺	2nd tertile(≥7,093)	153	51,3%	140	48,3%
	1st tertile(≤1,694)	148	49,0%	147	51,2%
Methionine (N60) ⁺	2nd tertile($\geq 2,176$)	154	51,0%	140	48,8%
\mathbf{M}_{1}	1st tertile(≤4,208)	151	50,2%	144	50,0%
Valine (N67) ⁺	2nd tertile($\geq 5,385$)	150	49,8%	144	50,0%
Isoleucine, Leucine e Valine	1st tertile(≤4,33)	148	48,8%	147	51,4%
	2nd tertile($\geq 5,6$)	155	51,2%	139	48,6%
(N57, N58, N67) ⁺	$2\pi \alpha \text{ tertile}(\leq 3.0)$		1 2 2 2 2		
(N57, N58, N67) ⁺		144	49,8%	154	52,2%
(N57, N58, N67) ⁺ Arachidonic acid (N76, N86) ⁺	$\frac{211}{1 \text{ st tertile}(\leq 0,058)}$ $211 \text{ tertile}(\leq 0,058)$ $211 \text{ tertile}(\geq 0,081)$		49,8% 50,2%	154 141	52,2% 47,8%

	2nd tertile(≥37,46)	165	51,9%	129	47,6%
Eicosanoic Acid (N81) ⁺	1st tertile(≤0,232)	154	49,7%	144	51,2%
Elcosalioic Acid (1881)	2nd tertile($\geq 0,33$)	156	50,3%	137	48,8%
	1st tertile(≤3,896)	143	49,0%	150	50,8%
Linoleic Acid (N83, N84) ⁺	2nd tertile(≥5,033)	149	51,0%	145	49,2%
Eicosapentaenoic Acid (N87) ⁺	1st tertile(≤0,091)	150	49,3%	148	51,7%
Elcosapentaenoic Acid (N87)	2nd tertile(≥0,192)	154	50,7%	138	48,3%
\mathbf{D} $(\mathbf{A}, \mathbf{A}) = \mathbf{A} + \mathbf{A} +$	1st tertile(≤0,252)	151	50,7%	145	50,2%
Docosapentaenoic Acid (N88) ⁺	2nd tertile(≥0,732)	147	49,3%	144	49,8%
Docosahexaenoic Acid (N89) ⁺	1st tertile(≤0,222)	152	50,0%	145	50,5%
Docosanexaenoic Acid (1889)	2nd tertile($\geq 0,444$)	152	50,0%	142	49,5%
Eicosapentaenoic, docosahexa-enoic and	1st tertile(≤0,421)	152	49,8%	143	50,4%
docosapentaenoic ac.s (N87, N88, N89) ⁺	2nd tertile(\geq 1,092)	153	50,2%	141	49,6%
Trans Ests $(NI00)^+$	1st tertile(≤0,683)	137	48,4%	159	51,8%
Trans Fats $(N90)^+$	2nd tertile(\geq 1,002)	146	51,6%	148	48,2%
	1st tertile(≤7,063)	147	49,7%	149	50,7%
Omega 6 (N92) ⁺	2nd tertile(≥9,264)	149	50,7%	145	49,3%
Omaga 6/Omaga 2 Patia +	1st tertile(≤5,41)	154	49,7%	141	50,5%
Omega 6/Omega 3 Ratio ⁺	2nd tertile($\geq 6,68$)	156	50,3%	138	49,5%

Attachment VI – List of nutrients and units of measurement

Lista de nutrientes e respectivas unidades

Nome variável	Descrição (unidades/dia)
CALORIES	Energia (kcal)
PROTEIN	Proteínas (g)
CARBOHYDRA	Hidratos de carbono (g)
FATTOTAL	Total de gordura (g)
SATURATEDF	Gordura Saturada (g)
MONOFAT	Gordura monoinsaturada (g)
POLYFAT	Gordura polinsaturada (g)
CHOLESTERO	Colesterol (mg)
DIETARYFIB	Fibra Alimentar (g)
COMPLEXCAR	Hidratos de carbono complexos (g)
SUGARS	Açucares (g)
ALCOHOL	Álcool (g)
CAFFEINE	Cafeína (mg)
TOTALVITA	Total de vitamina A (RE)
ARETINOL	Retinol (RE)
ACAROTENOI	Carotenoides a (RE)
THIAMINB1	Tiamina B1 (mg)
RIBOFLAVIN	Riboflavina B2 (mg)
NIACINB3	Niacina B3 (mg)
NIACINEQUI	Equivalentes de Niacina (mg)
VITAMINB6	Vitamina B6 (mg)
VITAMINB12	Vitamina B12 (mcg)
FOLATE	Folato (mcg)
PANTOTHENI	Ácido Pantoténico (mg)
VITAMINC	Vitamina C (mg)
VITAMIND	Vitamina D (mcg)
VITEALPHAE	Vitamina E (mg)
VITAMINK	Vitamina K (mcg)
CALCIUM	Cálcio (mg)
COPPER	Cobre (mg)
IRON	Ferro (mg)
MAGNESIUM	Magnésio (mg)
MANGANESE	Manganésio (mcg)
PHOSPHORUS	Fósforo (mg)
POTASSIUM	Potássio (mg)
SELENIUM	Selénio (mg)
SODIUM1	Sódio intrínseco (mg)
SODIUM2	Estimativa sódio intrínseco + adicionado confecção (mg)
ZINC	Zinco (mg)
WATER	Água (%)
BIOTIN	Biotina (mcg)
BORON	Boro (mg)
CHLORIDE	Cloro (mg)
CHROMIUM	Crómio (mcg)
FLUORIDE	Flúor
IODINE	lodo (mcg)
MOLYBDENUM	Molibdénio (mcg)

INSOLFIBER	Fibra insolúvel (g)
SOLUBLEFIB	Fibra solúvel (g)
ALANINE	Alanina (g)
ARGININE	Arginina (g)
ASPARTATE	Aspartato (g)
CYSTINE	Cistina (g)
GLUTAMATE	Glutamato (g)
GLYCINE	Glicina (g)
HISTIDINE	Histidina (g)
ISOLEUCINE	Isoleucina (g)
LEUCINE	Leucina (g)
LYSINE	Lisina (g)
METHIONINE	Metionina (g)
PHENYLALAN	Fenilalanina (g)
PROLINE	Prolina (g)
SERINE	Serina (g)
THREONINE	Treonina (g)
TRYPTOPHAN	Triptofano (g)
TYROSINE	Tirosina (g)
VALINE	Valina (g)
N40BUTRIC	Ácido Bútirico (g)
N60CAPRIOC	Ácido Caproico (g)
N80CAPRYLI	Ácido Caprilico (g)
N100CAPRIC	Ácido Caprico (g)
N120LAURIC	Ácido Laurico (g)
N140MYRIST	Ácido Miristico (g)
N160PALMIT	Ácido Palmitico (g)
N180STEARI	Ácido Estearico (g)
N200ARACHI	Ácido Araquidico (g)
N220BEHENA	Behenate (g)
N141MYRIST	Ácido Miristoleico (g)
N161PALMIT	Ácido Palmitol (g)
N1810LEIC	Ácido Oleico (g)
N201EICOSE	Ácido Eicosanoico (g)
N221ERUCIC	Ácido Erucico (g)
N182LINOLE	Ácido Linoleico (g)
N183LINOLE	Ácido Linolenico (g)
N184STEARI	Ácido Estearidonico (g)
N204ARACHI	Ácido Araquidónico (g)
N205EPA	Ácido Ecosopentanóico (g)
N225DPA	Ácido docosopentanóico (g)
N226DHA	Ácido docosohexanóico (g)
TRANSFA	Ácidos gordos Trans (g)
OMEGA3FA	Ácidos gordos ómega 3 (g)
OMEGA6FA	Ácidos gordos ómega 6 (g)
ASH	Cinza (g)
GRAMWEIGHT	Quantidade total de alimentos
ORAMITEIOITI	secondado total de annentos