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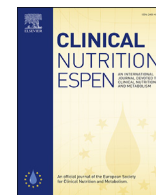

Original article

# Association between myopia and refined carbohydrate consumption: A cross-sectional study from the Constances cohort

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*Background & aims:* The effects of refined carbohydrate consumption on the prevalence of myopia have been little studied. The aim of this study is to explore the potential link between this consumption and myopia in individuals aged 40 or under in the population-based Constances cohort, in conjunction with other known risk and confounding factors.
*Methods:* The association between the probability of myopia in at least one eye and refined carbohydrate consumption was tested for 5271 participants, aged 40 or younger, in conjunction with education level, physical activity, energy intake, age, sex, fasting blood glucose, Body Mass Index (BMI), and Mediterranean diet quality. Refined carbohydrate intake was estimated by glycemic load. Myopia was assessed by the Monoyer score. Significant sex interactions led to stratified analysis by sex.
*Results:* The risk of myopia was significantly increased for men with refined carbohydrate consumption ($\boldsymbol{p} = 0.012$, Odd Ratio (OR) = 1.12, Confidence Interval (CI) = 1.02–1.22) but not for women ($\boldsymbol{p} = 0.657$, OR = 1.02, CI = 0.94–1.10). Some previously identified myopia risk factors were concurrently observed: a higher level of education increased the probability of myopia in both sexes (men $\boldsymbol{p} < 10^{-11}$, OR = 1.36, CI = 1.24–1.49; women $\boldsymbol{p} = < 10^{-4}$, OR = 1.19, CI = 1.09–1.28), while a higher level of physical activity might be protective in men ($\boldsymbol{p} = 0.08$, OR = 0.93, CI = 0.85–1.01).
*Conclusion:* This research reveals how high refined carbohydrate consumption might influence myopia and confirms recent studies on its risk factors. It also highlights significant sex differences in the prevalence and factors associated with myopia, emphasizing that modifiable risk factors, crucial for public health initiatives, may vary between men and women.
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## 1. Introduction

Myopia is a multifactorial refractive disorder characterized by blurred distance vision in eyes with a more pronounced corneal curvature and/or longer axial length than emmetropes [1]. Myopia is often considered a benign disorder, as it can be easily corrected with glasses, contact lenses or surgery. Nevertheless, high myopia is a risk factor for potentially blinding complications such as retinal detachment, subretinal neovascularization, early cataract and glaucoma [2,3].

Myopia is a truly global epidemic. Indeed, in the urbanized areas of East Asia, the prevalence of myopia in young people has risen rapidly over the last fifty years. It has risen from 5 to 20 % to over 80 % in some areas [4–9]. This phenomenon is also observed in Europe, North America and Australia, but on a smaller scale than in Asia [8,10,11].

Although a genetic basis for myopia has been shown [12], numerous epidemiological and experimental studies have demonstrated the predominant effect of environmental and lifestyle factors on its development and prevalence [6]. Myopia prevalence appears to be associated with education level,

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socioeconomic status, near work, urbanization and time spent outdoors in natural light [6–8,13,14].

Dietary habits, particularly refined carbohydrate consumption (primary sucrose, fiber-depleted gelatinous starches, high sugar corn syrup, and sugars), have emerged as potential contributors to myopia development [15]. Indeed, since the industrial revolution, but especially after the 2nd World War, refined carbohydrate consumption has risen continuously, from 5 kg/person/year in 1850 to 30–35 kg in 2017 in France, for example [16,17]. Concomitantly, the sharp increase in the prevalence of myopia observed in populations that have adopted a diet rich in refined carbohydrates [7,18] has led to the hypothesis that hyperglycemia and hyperinsulinemia play a role in the development of myopia [19–21]. For example, the Alaskan Inuit went from a 0–2 % prevalence of myopia to over 50 % in a single generation, following the Westernisation of their lifestyle, including a diet richer in refined carbohydrates [18]. Furthermore, the prevalence of myopia in diabetic patients is higher than in non-diabetics, suggesting that poor glucose metabolic control is a risk factor for myopia [22]. It has been proposed that hyperglycemia and hyperinsulinemia following repeated intake of large quantities of refined carbohydrates would affect different growth factors, leading to a disruption of ocular axial growth that could result in myopia [19,21,23]. This hypothesis has been supported by more recent evidence [23–30].

To date, the effects of refined carbohydrate consumption on the prevalence of myopia have been little studied [31–35]. The French Constances cohort, a large population-based prospective study, provides an excellent opportunity to explore the relationship between dietary factors and myopia. This study focused on a subset of participants aged 40 years or younger to minimize the confounding effects of age-related ocular changes [36,38] and to better understand the environmental and lifestyle factors influencing myopia in this age group. We sought to determine in this group the prevalence of myopia and investigated the association between refined carbohydrate consumption and myopia, while controlling for other risk/protective factors and potential confounding variables. Consumption of refined carbohydrates was estimated through the glycemic load of foods, which corresponds to their propensity to raise glycemia and therefore insulinemia. In pursuing these aims, this research seeks to improve our understanding of the potential role of dietary and lifestyle factors in the development of myopia, while offering insights that could inform the development of preventive strategies to address the increasing prevalence of myopia.

## 2. Methods

### 2.1. Study participants

The Constances cohort is a prospective cohort study of the general adult population, randomly selected among the French National Health Insurance Fund database. Recruitment took place mainly from 2012 to 2019, ending in 2021, with over 220 000 volunteers (for details see doi. org/10.13143/inserm_constances and [39–41]). Due to the partnership with the National Health Insurance Fund administered by the “Caisse nationale d'assurance maladie” (Cnam), the source population of Constances was restricted to salaried workers, professionally active or retired, thus excluding agricultural and self-employed workers which are affiliated to other health insurance funds [39,41]. Participants completed questionnaires on social and demographic characteristics, health-related behaviors and occupational conditions at baseline, and then annually. A health examination was done at baseline and every four years.

The present cross-sectional analyses were restricted to individuals included in 2015 because of a more detailed food frequency questionnaire allowing the distinction between refined and unrefined carbohydrates consumption (n = 27 263) and then, among them, to 9608 subjects not older than 40, due to the increasing risk beyond this age of capturing ocular aging in addition to the myopia event [36–38]. Participants who were not fasting prior to the health examination (n = 1024) and those being treated for diabetes (n = 26) were excluded. Also, participants not myopic or emmetropic or without a complete and coherent ocular (n = 422 and n = 814, respectively, detailed below) and dietary (n = 2051) questionnaire were excluded, leading to an analytical sample of 5271 individuals (2882 women and 2389 men). A flow chart describes the participants' selection (Fig. 1).

### 2.2. Construction of vision datasets

In order to study the presence/absence of myopia, several pieces of information from questionnaires and health examinations were used. Firstly, people were asked to answer the question "Do you currently wear glasses or contact lenses on a regular basis?" in the self-questionnaire. If they answered in the affirmative, they were asked to specify whether they had distance or near vision problems. Then, for all participants (having answered yes or no to the previous question), during the health check-up, a healthcare professional administered the Monoyer distance vision test [42] for each eye, with or without correction (wear glasses or contact lenses). The Monoyer chart is comprised of 10 rows of letters that decreased in size towards the top. The chart is placed 5 m away, and participants are asked to isolate each eye and read the letters on each row, staring from the bottom (the largest row). The visual acuity for each eye is recorded as a value ranging from 0 (failed to distinguish the largest row) to 10 (correctly discerned the smallest row). This test produces a score that determines the visual acuity for each eye. In our study, we considered that a score under or equal to 7 in at least one eye corresponded to myopia [43].

The dataset was constructed to examine the probability of myopia in at least one eye. The response variable was coded 0/1, with 0 meaning the individual was emmetropic in both eyes and 1 myopic in at least one eye. The construction of the dataset is summarized in Fig. 2. In brief, we retained individuals who answered yes to the first question as well as distance vision (Fig. 2, box b), and, among individuals who answered no to the first question, those who took the Monoyer test without correction (Fig. 2, box d, n° 2 and 3). Individuals with a Monoyer score less than or equal to 7 without correction for at least one eye (Fig. 2, box d, n° 2, and box c, n° 2), and those who took the test with correction but having distance vision problems (Fig. 2, box c, n° 1), were considered myopic. The other individuals were considered as emmetropic (Fig. 2, box c, n°3 and box d, n°3). Excluded individuals (Fig. 2, box a and box d, n°1) were used to calculate the prevalence of myopia in the group (before exclusion of individuals who did not have a complete or consistent dietary questionnaire, Fig. 1).

### 2.3. Dietary data

The "diet" section of the self-questionnaire included a food frequency questionnaire assessing the consumption of 35 food items per week. Participants were asked to indicate their usual frequency of consumption using a six-point scale: never or almost never, less than once a week, two to three times a week, four to six times a week, once a day or more, with the latter option further specifying the number of units consumed per day. The question posed was: “How frequently do you usually consume this item, regardless of preservation method, time, or place of consumption?” and no specific timeframe was mentioned. This food frequency questionnaire was designed in line with the French National Nutrition and Health

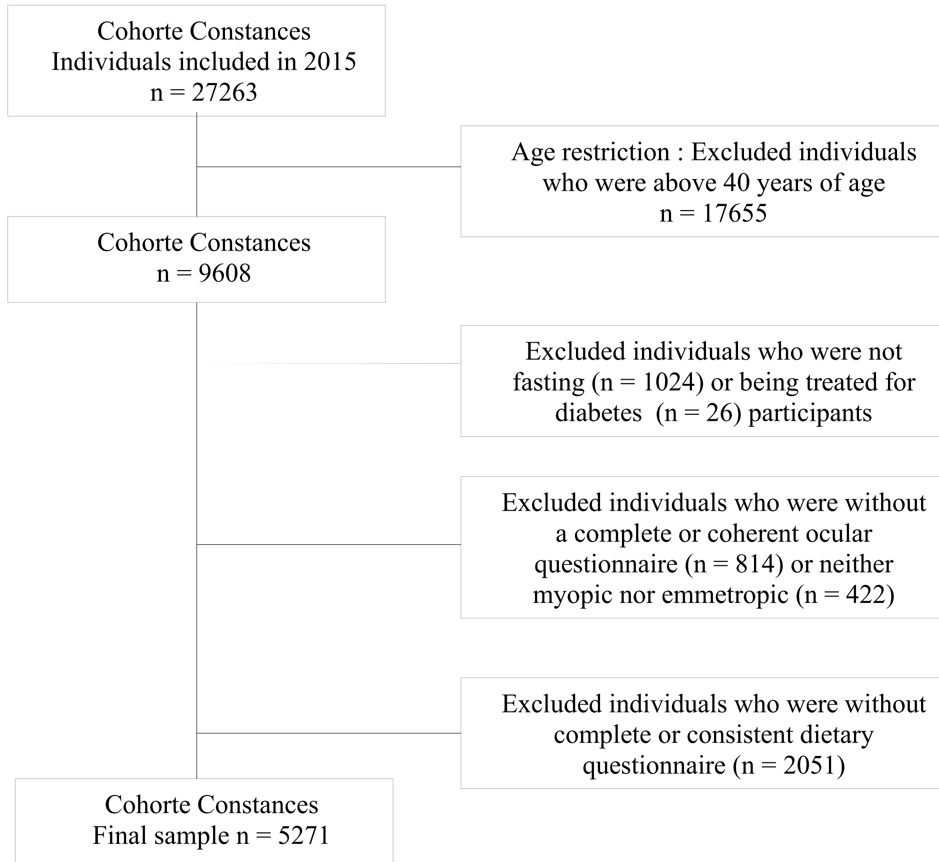


**Fig. 1.** Flowchart of population selection.

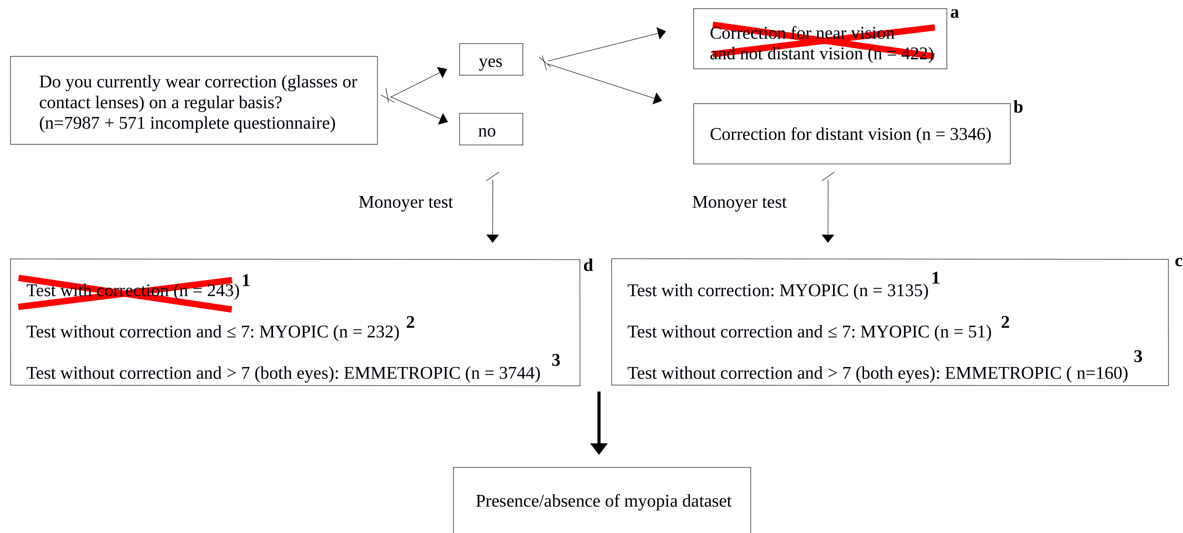


**Fig. 2.** Formation of the dataset for analyzing myopia presence/absence. Crosses denote excluded individuals. Letters and numbers in bold refer to the box quoted in the text.

Program guidelines [44,45] and has been used in previous Constances studies [46]. Reported frequencies were transformed into discrete variables as follows: 0 for never or almost never, 0.5 for less than once a week, 1 for about once a week, 2.5 for two to three times a week, 5 for four to six times a week, 7 for once a day or more and, in that case, 7 was multiplied by the number of units per day (minimum 1). Variables were expressed in servings per week.

For each food item in the food frequency questionnaire, the glycemic index (GI) was first calculated according to the International Tables of glycemic Index [47] and internet updates (http://www.glycemicindex.com), using glucose as the reference. The GI refers to the rate of glucose release by measuring the 2 h postprandial glycemia value after consumption of a food portion containing 50 g of available carbohydrates relative to 50 g of glucose

consumption. Then, for each individual and each item, Glycemic Load (GL) was calculated by multiplying the GI by the amount of available carbohydrates (g) per standard serving [48]. The GL reflects both carbohydrate quantity and quality. Compared with low-GL diets, high-GL diets elicit larger glycemic and insulinemic responses [47]. GL items are defined as “low” when the GL value is below 10 and as “high” when the value is above 20 [49]. Finally, for each individual, the glycemic load of each item was multiplied by its number of servings per week before being added together, giving an estimate of the total weekly glycemic load (GL) per individual. In the same way, energy intake in kilocalorie for each item were obtained from the Anses-Ciqual database and were calculated for each participant depending on the usual serving size. For each subject, they were summed, resulting in a total weekly energy intake estimation (EI) per individual. To measure GL independently of EI, linear model was used to produce regression of EI as a function of GL (lm function from the R lmtest package version v0.9-40 [50]). These regression residuals were then used as a new variable [51]. In this way, each subject's weekly refined residual carbohydrate consumption was described (RGL). This variable represents the glycemic load part of food that is not explained by energy intake. These methods have been applied in previous studies [52–54].

To take into account the diet quality, a Mediterranean-like diet score was calculated. An adaptation of the MedDiet score developed by [55] was used. This score is based on 11 food groups: non-refined cereals, potatoes, fruit, vegetables, legumes, fish, meat and meat products, poultry, dairy products, olive oil and alcoholic beverages. As potato consumption was not available in our study, the MedDiet score was based on the other 10 food groups. For foods presumed to be beneficial to health (non-refined cereals, fruit, vegetables, legumes, fish and olive oil), the score was constructed as follows: 0 to 5 points were awarded according to the number of servings per week, 0 points for non-consumers, 1 for ]0–1] servings, 2 points for ]1–2] servings, 3 points for ]2–3] servings, 4 points for ]3–4.5] servings and 5 points for consumption of more than 4.5 servings per week. For foods presumed to be harmful to health (meat and derivatives, poultry and dairy products), 0 to 5 points were awarded as follows: 0 for consumption of more than 4.5 portions, 1 point for ]3–4.5] portions, 2 points for ]2–3] portions, 3 points for ]1–2] portions, 4 points for ]0–1] portions and 5 points for non-consumers. For alcohol consumption, 5 points were awarded for consumption greater than 0 drinks per week and less than 3 drinks per week, 4 points for [3–4[, 3 points for [4–5[, 2 points for [5–6[, 1 point for [6–7[ and 0 for consumption greater than 7 drinks per week. For each participant, the total MedDiet score was calculated by adding the scores ranging from 0 to 5 points for each food group. Scores ranged from 0 (poor diet quality) to 50 (good diet quality). Scores ranging from 0 to 30 constitute poor dietary behavior.

### 2.4. Statistical analyses

Logistic regression was used to analyse the probability of being myopic, estimating odds ratios (ORs) and 95 % confidence intervals (Cis). The binary response variable corresponded to the presence/absence of myopia in at least one eye. The **e**xplanatory variable was subject's weekly refined residual carbohydrate consumption (RGL, quantitative). Control variables, known or likely to interact with myopia and/or refined residual carbohydrate consumption, were total weekly energy intake estimation (EI, quantitative), MedDiet score (Med, quantitative), age (quantitative), sex, fasting blood glucose (Glycemia, quantitative), body mass index (BMI, quantitative), education level (Studies, quantitative, 1 to 7) and physical activity level (PhyA, quantitative, 0 to 6). Interactions with sex were included in the model. $\boldsymbol{p} < 0.10$ was considered statistically significant for interaction terms. Given that in this model several interactions with sex were significant, the analysis was finally stratified according to sex.

All statistical analyses were performed using R software version 4.4.0 using the package lmtest v0.9-40 [50] and car [56]. All quantitative variables used in the models were centered and scaled. The significance of each term was assessed from the model including all other variables. The variance inflation factor was computed using the vif function of the R package car [57].

## 3. Results

The prevalence of myopia in at least one eye in Constances participants not older than 40 and before exclusion of individuals without a complete or consistent dietary questionnaire (n = 7897, Figs. 1 and 2) was 46 % in women and 39 % in men (43 % all, Table S1). After excluding individuals lacking complete or consistent dietary questionnaires, a total of 5271 participants were included in the analyses. The description of their characteristics and vision status are in Table 1 and Table 2, respectively. GL values were within the same range of variation as those from other studies on the French population [52,58,59].

Analyses were stratified according to sex and two logistic regressions, one for each sex, were performed. Refined carbohydrate consumption and the other control variables had different effects on the probability of myopia for men and women (Table 3, Fig. 3). Refined carbohydrate consumption significantly increased the probability of myopia in men but not in women (RGL men $\beta = 0.111$, $\boldsymbol{p} = 0.012$, OR = 1.12, CI = 1.02–1.22; RGL women $\beta = 0.017$, $\boldsymbol{p} = 0.657$, OR = 1.02, CI = 0.94–1.10, Table 3). Age significantly increased probability of myopia in women (Age, $\beta = 0.083$, $\boldsymbol{p} = 0.037$, OR = 1.09, CI = 1.00–1.18, Table 3) but this effect appeared to be driven by the last quartile of this variable (>35 years old, data not shown). In men, probability of myopia was increased but not significantly with the MedDiet score (Med $\beta = 0.079$, $\boldsymbol{p} = 0.077$, OR = 1.08, CI = 0.99–1.18, Table 3), and physical activities seemed protective but this effect was also marginally not significant (PhyA $\beta = -0.076$, $\boldsymbol{p} = 0.08$, OR = 0.93, CI = 0.85–1.01, Table 3). However, education level in both sex significantly increased probability of myopia (Studies men $\beta = 0.307$, $\boldsymbol{p} < 10^{-11}$, OR = 1.36, CI = 1.24–1.49; Studies women $\beta = 0.171$, $\boldsymbol{p} = < 10^{-4}$, OR = 1.19, CI = 1.09–1.28, Table 3). All other variables were nonsignificant. Variance inflation factors (VIFs) were <1.2, indicated that the multicollinearity between covariables was weak and not of concern [57].

## 4. Discussion

The aim of this study was to assess the impact of refined carbohydrate consumption on myopia among individuals aged 40 or younger from the French Constances cohort, a large population-based prospective study, in conjunction with other known risk and confounding factors. We found an association between myopia and this type of diet in men but not in women. The risk of myopia was increased for men with refined carbohydrate consumption. Some previously identified risk and protective factors for myopia were concurrently observed: higher levels of education were associated with an increased probability of myopia in both sexes, while higher levels of physical activity seemed to be protective in men.

### 4.1. Prevalence of myopia in Constances cohort

In this study, we examined the prevalence of myopia in the cohort participants aged 40 and under, revealing a higher

**Table 1**
Descriptive statistics of included participants' characteristics.

| | Women (n = 2882) | | | | Men (n = 2389) | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean | Sd | Range | Missing data | Mean | Sd | Range | Missing data |
| GL/week | 526.21 | 247.87 | 61.52–3428.23 | 0 | 542.08 | 259.32 | 76.59–3288.41 | 0 |
| EI/week (Kcal) | 9256 | 3597.41 | 1378–56629 | 0 | 9410 | 3666.16 | 1102–42796 | 0 |
| Med | 23.49 | 6.20 | 6–45 | 0 | 20.36 | 6.32 | 2–43 | 0 |
| Age (years) | 29.56 | 6.09 | 18.50–40 | 0 | 30.35 | 5.91 | 18.50–40 | 0 |
| Gly (mmol/l) | 4.88 | 0.42 | 3.36–13.12 | 11 (0.4 %) | 5.19 | 0.42 | 3.70–7.85 | 13 (0.5 %) |
| BMI | 22.99 | 4.25 | 15.05–53.38 | 16 (0.5 %) | 23.87 | 3.59 | 14.69–42.18 | 17 (0.7 %) |
| Studies | 5.39 | 1.34 | 1–7 | 30 (1 %) | 5.33 | 1.50 | 1–7 | 25 (1 %) |
| PhyA | 3.23 | 1.36 | 0–6 | 27 (0.9 %) | 3.31 | 1.40 | 0–6 | 20 (0.8 %) |

**Table 2**
Vision status of included participants.

| | Women | Men |
|---|---|---|
| Myopic[a] one or both eyes | 1482 | 1003 |
| Emmetropic | 1400 | 1383 |

[a] Monoyer test ≤7.

contributes to insulin resistance and subsequent compensatory hyperinsulinemia [19,67–69]. According to Cordain [19] and Galvis [23], this hyperinsulinism may promote the elongation of the eye by enhancing the activity of insulin-like growth factor-1 (IGF-1) and reducing the action of insulin-like growth factor binding protein-3 (IGFBP-3) in scleral fibroblasts.

**Table 3**
Effects of different variables on the probability of being myopic. For each variable, the estimate (β), standard error of the mean (se), $\chi^2$ statistic and corresponding p-value, Odd-ratio (OR) with 95 % confidence interval are given. Bold characters indicates significant (p < 0.05) effects.

| | Women | | | | | Men | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | β | se | $\chi^2$ | $P(>\chi^2)$ | OR (95%CI) | β | se | $\chi^2$ | $P(>\chi^2)$ | OR (95%CI) |
| Intercept | 0.056 | 0.038 | | | | −0.332 | 0.043 | | | |
| RGL | 0.017 | 0.039 | 0.197 | 0.657 | 1.017 (0.943–1.098) | 0.111 | 0.045 | 6.271 | **0.012** | 1.117 (1.023–1.220) |
| EI | 0.042 | 0.038 | 1.217 | 0.270 | 1.043 (0.967–1.125) | −0.001 | 0.044 | 0.000 | 0.985 | 0.999 (0.917–1.088) |
| Med | 0.062 | 0.040 | 2.359 | 0.125 | 1.064 (0.983–1.151) | 0.079 | 0.045 | 3.130 | 0.077 | 1.082 (0.991–1.181) |
| Age | 0.083 | 0.040 | 4.338 | **0.037** | 1.087 (1.005–1.176) | 0.045 | 0.046 | 0.974 | 0.324 | 1.046 (0.956–1.144) |
| Gly | 0.002 | 0.039 | 0.004 | 0.950 | 1.002 (0.928–1.083) | 0.036 | 0.045 | 0.652 | 0.419 | 1.037 (0.950–1.131) |
| BMI | 0.065 | 0.040 | 2.613 | 0.106 | 1.067 (0.986–1.155) | −0.021 | 0.046 | 0.216 | 0.642 | 0.979 (0.895–1.070) |
| Studies | 0.171 | 0.041 | 17.824 | $\mathbf{<10^{-4}}$ | 1.186 (1.095–1.284) | 0.307 | 0.045 | 47.146 | $\mathbf{<10^{-11}}$ | 1.360 (1.244–1.487) |
| PhyA | −0.030 | 0.039 | 0.595 | 0.441 | 0.970 (0.898–1.048) | −0.076 | 0.044 | 3.065 | 0.080 | 0.926 (0.850–1.009) |

RGL: weekly refined residual carbohydrate consumption, EI: total weekly energy intake estimation, Med: Mediterranean-like diet score, Gly: fasting blood glucose (glycemia), BMI: body mass index, Studies: education level, PhyA: physical activity level.

prevalence in women than in men (46 % and 39 %, respectively; $P(>\chi^2) < 10^{-9}$; 43 % all). Our findings are consistent with those of previous studies in Caucasian populations, supporting both the levels of prevalence observed [58] and the variation by sex [31,60]. A cross-sectional study carried out in France between January 2012 and November 2013 showed that prevalence of myopia was 52.4 % in the 20-39-year-olds (39 % for all ages) and higher in women than in men [60]. Similarly, the NHANES study conducted in the USA from 1999 to 2004 found a prevalence of 35.1 % for men and 42.3 % for women aged 20–39 [10]. It has also been shown that in Australia, women were more likely than men to develop myopia, and had greater changes in refractive measures between the ages of 20 and 28 [61]. For school-aged children, several longitudinal studies, but mainly conducted in Asian countries, have also reported a higher myopia incidence in girls [62–66].

### *4.2. Refined carbohydrates consumption and myopia*

We have shown here that refined carbohydrates consumption was not independent of myopia. Since Cordain's pioneering study in 2002 [19], there has been limited research on the potential impact of this type of diet on myopia [23,31,33–35]. The physiological mechanisms involved rely on the fact that refined carbohydrates are quickly absorbed into the bloodstream, causing a significant spike in insulin levels (hyperinsulinemia). The more refined the carbohydrate, the greater the glycemic and insulinemic responses [47]. It has been shown that chronic hyperinsulinemia

### *4.3. Sex differences in refined carbohydrate risk factors*

Interestingly, refined carbohydrate intake significantly increased the probability of myopia in men, but not in women. This result could be attributed to a quantitative difference in consumption between them, but sex had a marginally not significant influence on the refined carbohydrate consumption recorded (mean: men 542.1, women 526.2; Wilcoxon test, ***p*** = 0.07). Rather, this suggests a sex-specific metabolic or behavioral response to dietary carbohydrates that influences ocular health differently between men and women. This is in line with previous research indicating sex-specific differences in metabolic responses and dietary impacts on health outcomes [70]. Indeed, lipid and glucose metabolism are adapted to distinct sex-specific functions under the influence of sex chromosomes and hormones [71,72] and, notably, women exhibit higher overall insulin sensitivity than to men. Significant sex differences in glucose homeostasis, prediabetic conditions, and both type 1 and type 2 diabetes are also observed [73]. Men have a higher prevalence of type 2 diabetes and insulin resistance, while obesity is more common among women [72]. Consequently, the effects of hyperglycemia and hyperinsulinemia may differ between sexes. In women, higher insulin sensitivity and a lower risk of developing insulin resistance mean that growth hormones, and thus myopia, could less likely be impacted by high intake of refined carbohydrates. It is also possible that the women's food preferences changed over time and that the intake recorded here underestimated their previous refined carbohydrates

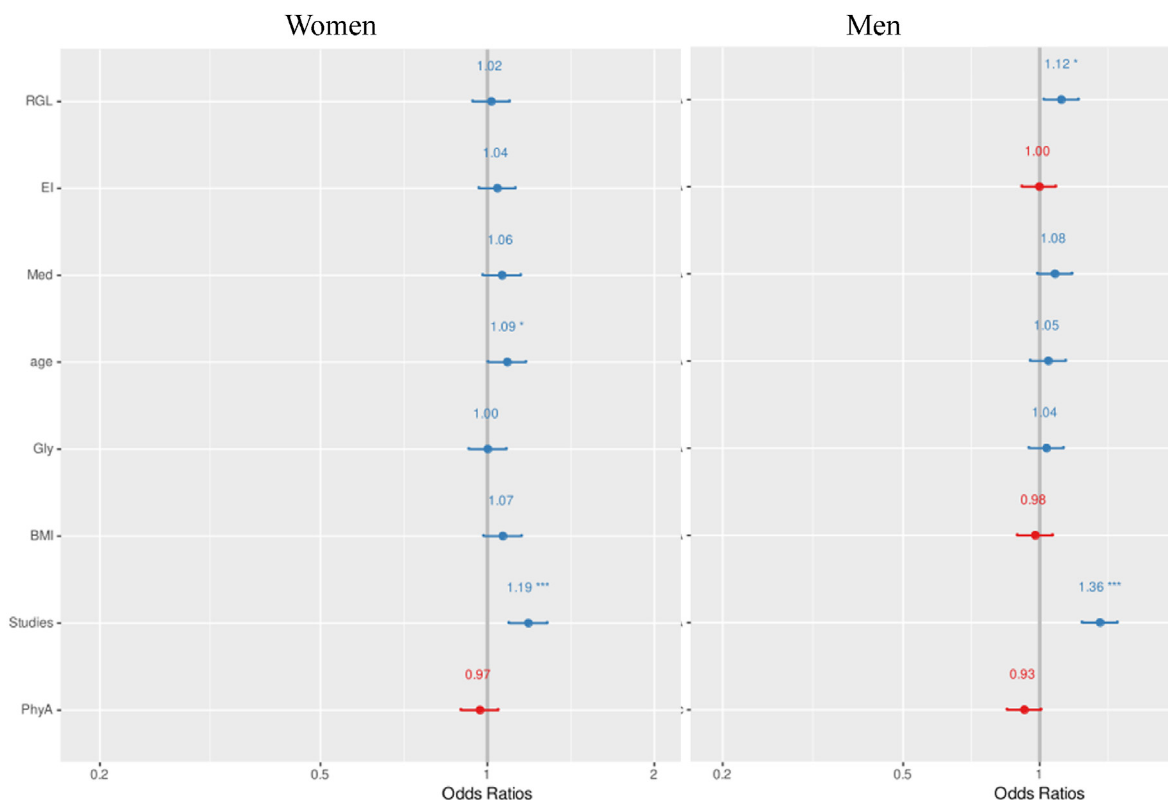


**Fig. 3.** Adjusted odd ratios and 95 % confidence intervals for the model studying the impact of risk and control variables on the probability of myopia. *p < 0.05 **p < 0.01 ***p < 0.001.

consumption at the time myopia developed. However, BMI which could be linked to their former refined carbohydrate intake was not significantly associated with myopia ($p = 0.10$, Table 3), so this would not be a clue to support this possibility.

### 4.4. Other covariables

**Education Level**. As demonstrated in numerous previous studies, education level significantly influenced myopia in both men and women, with higher levels of education associated with an increased risk of myopia. This strong association may reflect the increased near work and prolonged reading associated with higher education, supporting existing hypotheses that environmental factors related to education contribute to myopia development [6,74,75]. **Influence of Mediterranean diet.** Although the Mediterranean diet was not significantly associated with myopia in men, there was a slight negative trend suggesting a potential relationship that warrants further investigation. The Mediterranean diet, rich in fruits, vegetables, and healthy fats, has been repeatedly linked to various health benefits, including potential protective effects on vision [76,77]. However, this Mediterranean diet index does not fully differentiate carbohydrates into refined and unrefined categories, and thus perhaps insufficiently capture food quality in relation to hyperglycemia. This point merits further investigation. **Influence of physical activity.** Physical activity showed a marginal protective effect against myopia in men, although this did not reach statistical significance. Physical activity is known to have various health benefits, and some studies suggest it may help in reducing myopia progression, possibly through its effects on overall health but also and mainly through outdoor activity [8,74]. It has been shown that a 40-min increase in outdoor activity among 6-year-old children in China led to a drop in myopia incidence over the following three years [59]. The intensity of outdoor light could protect against myopia by increasing the release of retinal dopamine, which experimentally reduces eye growth [78]. **Age**. Age emerged as a significant predictor of myopia in women, but this effect was driven predominantly by those older than 35 years. Myopia typically develops and progresses most rapidly during childhood, usually stabilizing around the ages of 15–16 [79,80]. However, some studies have shown that myopia progression can continue into adulthood and particularly in women [61]. This interaction between age and sex in adulthood could be mediated by differences in biological or hormonal factors or in lifestyle habits between the sexes. This question should be explored in further studies. Anyway, this interaction age/sex underlines the importance of considering age- and sex-related factors when studying myopia, as ocular changes, biological and lifestyle factors may differ substantially throughout life and between the sexes.

### 4.5. Limitations

One of the main limitations of this study is its cross-sectional design, which limits the ability to establish causal relationships and leaves the direction of the association uncertain. Individuals with pre-existing myopia may have dietary habits differing from those without the condition. However, the large sample size of the Constances cohort provides a solid basis for the identification of significant associations, which could form the basis of future longitudinal research. Another limitation concerns self-reported dietary data, which may present recall biases and inaccuracies. As a result, the dietary exposure assessed here may not reflect previous dietary habits by failing to account for changes in food preferences over time. Additionally, given that myopia is often developed in childhood or adolescence, the current dietary intake may not be the

most relevant period for assessing its potential role in myopia onset. Nevertheless, the detailed food frequency questionnaire used is a well-established tool in nutritional epidemiology, offering reasonably reliable dietary intake assessments. Future studies should aim for prospective designs with repeated dietary assessments over time to better capture dietary exposure and its potential role in myopia development.

## 5. Conclusion

This research presents new insights into how the recent and massive consumption of refined carbohydrates might influence myopia and confirms recent studies on risk factors contributing to this visual condition. Further prospective research is needed to validate these results and clarify the mechanisms by which diet impacts myopia. Despite the specific socio-economic and occupational characteristics of the study sample, the large, randomly selected national sample provided by the Constances cohort reinforces the potential generalizability of the results to the entire French population. This study also highlights significant sex differences in the factors associated with myopia and underscores the idea that modifiable risk factors for myopia, which could be key targets for future public health initiatives, show potential variations between men and women.

## Ethical approvals

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures have been approved by the Institutional review board (IRB) of the French Institute of Health (Inserm) (Opinion n°01–011, then n°21–842), and authorized by the by the French Data Protection Authority ("Commission Nationale de l'Informatique et des Libertés", CNIL) (Authorization #910486). The biobank obtained a favorable opinion from the Committee for the protection of individuals – CPP Sud Est I (#2018-32) and an authorization from the CNIL (#DR-2-2018-137). All volunteers sign a written consent form for their participation in Constances, and, where applicable, for their participation in the biobank. All information and regulatory authorizations relating to the publication are available on the French version page 'Rights and data protection'.

## Data availability

In accordance with the Constances Charter, deidentified participant data from the Constances Cohort are available to researchers who meet the legal and ethical requirements set by the French National Commission governing data privacy laws. International researchers can access the dataset by following the procedure outlined at https://www.constances.fr/en/scientific-area/access-to-constances-2/. Additionally, all study materials, including the study protocol and data dictionary of the Constances Cohort, are freely accessible.

## Author contributions

Claire Berticat: Conceptualization, Methodology, Formal analysis, Investigation, Writing- Original draft preparation, Supervision. Elisa Venturini: Formal analysis, Investigation. Vincent Daien: Writing- Reviewing and Editing. Marcel Goldberg: Funding acquisition, Writing- Reviewing and Editing. Marie Zins: Funding acquisition, Writing- Reviewing and Editing. Michel Raymond: Writing- Reviewing and Editing.

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## Declaration of competing interest

No conflicting relationship exists for any author.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2025.03.033.

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