Analysis using national databases reveals a positive association between dietary polyunsaturated fatty acids with TV watching and diabetes in European females

Jason Pither¹, Amy Botta¹, Chittaranjan Maity², Sanjoy Ghosh¹*

¹ Department of Biology, IK Barber School of Arts and Sciences, University of British Columbia-Okanagan, Kelowna, Canada, ² Department of Biochemistry, KPC Medical College, Kolkata, West Bengal, India

* sanjoy.ghosh@ubc.ca

Abstract

In recent years, dietary polyunsaturated fatty acids (PUFA) have increased in parallel to sedentary behavior and diabetes across the world. To test any putative association between dietary PUFA and sedentary behavior or diabetes in females, we obtained country-specific, cross-sectional data on sedentary activity and diabetes prevalence from European Cardiovascular Statistics 2012. Age and gender-specific, nutritional data from each country were obtained from nutritional surveys as well. Socioeconomic (GDP), physical environment (urbanization index) and climatic confounders were accounted for each country. Upon analysis, we found a strong, positive association between sedentary lifestyle in 11-yr old girls (> = 2 hours of TV/weekday) and dietary PUFA across 21 European countries. Further, a weak association of dietary PUFA and a strong relationship of per-capita GDP was established with elevated fasting blood glucose [(> = 7.0 mmol/L; or on medication] among 25+ year old adult females across 23 countries in Europe. In summary, we present novel ecological evidence that dietary PUFA is strongly associated with sedentary behavior among pre-teen girls and weakly associated with diabetes among adult women across Europe. In the latter group, per-capita GDP was a significant predictor for diabetes as well. Therefore, we recommend that prospective randomized controlled trials (RCTs) be implemented to evaluate if ubiquitous presence of dietary PUFA and low socioeconomic status are possible confounders when intervening to treat/prevent sedentary lifestyle or diabetes in female subjects in Western nations.

Introduction

Observational studies have suggested that an improper diet and sedentary behaviour are independent risk factors for chronic diseases like obesity, diabetes and cardiovascular diseases [1, 2]. However, the inter-relationship between diet and physical activity, if any remains unclear. Traditionally, spontaneous physical activity is recognized to be a function of either total caloric intake or the overall macronutrient composition of the diet [3]. However, whether the chemical type of macronutrients alter physical activity remains unknown.
We reported recently that in Canada, increases in dietary fat between the 1970’s and 2000’s are attributable to increased consumption of monounsaturated (MUFA) and polyunsaturated fatty acids (PUFA) but not saturated fatty acids (SFA) [4]. Indeed, to protect against cardiovascular diseases, SFA has been deliberately removed from our food supply in favour of MUFA and PUFA [5–7]. In a recent worldwide survey of dietary fat intakes between 1990 and 2010, both North America and parts of Europe demonstrate a higher intake of PUFA whereas saturated fat intakes remained similar [7]. In this time frame, USA demonstrated a 318% increase of its diabetic population from 6.5 million to 20.7 million patients [8] and European diabetes rates also increased [9, 10]. The incidence of diabetes in the Western population was indeed paralleled by also a rise in sedentary behavior. North American children and youth spend between 40–60% of their waking hours in sedentary pastimes like TV watching, video games etc. [11, 12]. In a recent European study, a third of the children across eight nations in the IDE-FICS (Identification and prevention of dietary- and lifestyle-induced health effects in children and infants) survey, demonstrated increased sedentary behavior which correlated the most with increased TV watching as an indicator [13]. Is it possible that sedentary behaviour is caused by dietary unsaturated fats? Indeed, 4–8 yr old children in USA and Canada increasingly consume a diet rich in unsaturated fats [14, 15]. Most recently, we also showed that even sources of saturated fats like butter which are preferred at a younger age in the Western world, now have increasing n-6 PUFA [16]. Therefore, we hypothesized a possible biological link between unsaturated fat diets and rising sedentary behaviour and diabetes.

With its genetically concordant yet nutritionally diverse population [17], the European region provides a more suitable setting to test for such associations. In Europe, populations demonstrate varied PUFA and MUFA intakes. Mediterranean countries such as Greece, Italy and Spain have higher MUFA intakes through olive oil [18], whereas n-6 PUFA consumption in Central and Eastern European countries are the highest [19]. Nevertheless, even in the European context, the relationship between dietary MUFA, PUFA and metabolic outcomes such as diabetes, remains unclear. For example: (i) in a mixed sex population in England, administration of MUFA or PUFA rich diet for 24 days did not influence insulin sensitivity in type 2 diabetic subjects [20], whereas (ii) a study from Spain involving insulin-resistant females reported the opposite finding [21]. Furthermore, in earlier studies, (iii) high n-6 PUFA was positively associated with insulin resistance in the Israeli population [22], whereas (iv) MUFA was shown to improve insulin sensitivity in Spanish women [23]. In contrast, (v) in a recent study, 6-week MUFA diet in a healthy Portugese population did not demonstrate any changes in biomarkers of diabetes [24].

Controlling for confounders like urbanization, per-capita GDP or climatic variables which alter physical activity levels in humans, we show that sedentary behaviour in pre-teen girls in Europe is significantly associated with PUFA intakes. With respect to adult European women, despite PUFA intakes demonstrating an association, per-capita GDP emerged as the only significant predictor for elevated blood glucose. We suggest that more attention be paid to dietary PUFA and socioeconomic status as potential confounders, when planning lifestyle interventions to treat/correct sedentary behaviour and diabetes, at least in female subjects.

**Methods**

**Sedentary behaviour, PUFA intakes and weight gain in European children**

While the biological effects of MUFA is gender-neutral, a clear sex difference exists with the metabolic effects of PUFA *in vivo*. PUFA desaturation and bioconversion to carcinogenic eicosanoids as well as its oxidative modification is higher in females [25]. Consistent with this
notion, reports have linked countries with high PUFA intakes like Israel and the USA, with a high rate of female cancers [26, 27]. In basic research, we also demonstrated significant loss of spontaneous activity and elevated insulin resistance in mice fed PUFA diets irrespective of either total food intake or body weight [4]. Therefore, we focussed our analysis to the female sex, taking advantage of published data concerning European females from across Europe.

TV watching (screen time) is a prime, universal indicator for sedentary behaviour in pre-teens and adolescents [28, 29], especially in Europe [13]. Among adolescents, sedentary behaviour and screen time increases with age [30]. According to a recent analysis of 161 studies, there was an increase of 30 mins of sedentary behavior with each increasing year among adolescents [31]. Because we wanted to see biological effects of diet and not age, we evaluated TV watching data on the youngest females (i.e. 11 years) reported in the European Cardiovascular Statistics 2012 database (https://www.escardio.org/static_file/Escardio/Press-media/press-releases/2013/EU-cardiovascular-disease-statistics-2012.pdf).

A pre-teen age group has the added advantage of being shielded from a well-known effect of advancing age on loss of physical activity among older adolescents or adults [32]. Moreover as girls also rapidly lower their physical activity levels as they age, biological differences due to dietary variations could be lost in girls in a higher age group, even as early as 13 years [33].

Data about national sedentary behaviour patterns (Table 6.5 in [34]) and prevalence of overweight/obesity (Table 10.3 in [34]) among 11 yr old female children were obtained from the most recent version of European Cardiovascular Statistics 2012 [34]. We used 2009/10 data for TV watching, except for Bulgaria and Italy, for which 2009/10 values were missing, but 2005/06 values were provided. For these two countries, we predicted 2009/10 values based on a highly significant model-II regression relating 2009/10 values to 2005/06 values for the other 19 countries; the regression R-square was 0.80, and had slope and intercept estimates of 0.929 (95% confidence limits: 0.73, 1.17) and 0.325, respectively.

Estimates of sex-specific PUFA and MUFA intakes were obtained from a comprehensive report of nutritional intakes in European children [35]. The report assessed both macro and micronutrient analysis as obtained from both local and national surveys and opinions among experts across Europe. The surveys included in the study had to be a) published, b) based on individual dietary intakes, c) with adequate information available to evaluate its accuracy, d) obtained after 1987, e) with a narrow age window to provide age and sex-specific data, f) of a sample size of at least 25, representative of the national population. MUFA and PUFA intake data in female children was obtained from twenty-one such surveys across various ages across Europe (page S175 and S176 for MUFA and PUFA data respectively in [35]). Sedentary behavior, prevalence of overweight/obesity and nutritional data for female children across Europe are also summarized in Table 1.

Diabetes, PUFA intakes and weight gain in European women

Insulin resistance can be undetected for years before it turns into overt diabetes. Thus, to gain insights regarding the incidence of diabetes from epidemiological data, we used data about the prevalence of elevated blood glucose in adult females (25+ yrs old). Similar to pre-teen female data, data about prevalence of elevated glucose across Europe (page 113, Table 11.2 in [34]), and prevalence of female obesity (page 104, Table 10.1 in [34]) were obtained from the European Cardiovascular Statistics 2012. Estimates of sex-specific adult intakes of total fat, MUFA or PUFA [page 232, Table 1 in [36]] in adults were obtained from a recent report providing dietary FA intakes among individuals above 18 years of age across the world [36]. Sample size of respondents from each country on MUFA or PUFA intakes were also obtained from the same table. Data describing the mean dietary fat composition, incidence of obesity and elevated
blood glucose (≥ 7.0 mmol/L or on medication) of women from specific European countries are presented in Table 2.

Socioeconomic and geographical confounds

The relationship between dietary fats and physical activity in humans is potentially confounded by socioeconomic [37], built environment (such as urbanization [38]) and climatic (e.g. sunlight hours, mean temperature [39]) factors. Moreover, restricting analyses to a single population may encompass little variation, thereby limiting power of such analysis. As an example, in North America, where intake of PUFA is extensive [36], the lack of a control population consuming less PUFA may hide a specific effect of PUFA on physical activity. In contrast, Europe provides a suitable system for conducting analysis of such relationships because: (i) European populations are among the most genetically homogenous in the world [17]; (ii) detailed and extensive data about diet and disease are available for many European countries (see below); (iii) dietary PUFA and MUFA intakes vary considerably among European countries, and (iv) so too do socioeconomic indicators and climate. Level of urbanization and associated physical environments, which can deter or encourage physical activity through access to parks, open spaces and use of non-motorized transport was included as a confounding variable

Table 1. Prevalence of sedentary behaviour among 11 yr old girls with mean intakes of MUFA and PUFA in this age group across Europe.

| Country          | % of female children who watch >2 hrs of TV per day‡ | % of 11yr old female children overweight and obese‡ | Mean MUFA Intake (% E) † | Mean PUFA Intake (% E) † |
|------------------|------------------------------------------------------|--------------------------------------------------|--------------------------|--------------------------|
| Austria          | 37                                                   | 16.7                                             | 13                       | 5.5                      |
| Belgium          | 47.5*                                                | 26.7                                             | 14.5                     | 6.7                      |
| Bulgaria         | 75.6**                                               | 17.9                                             | 10.5                     | 11.6                     |
| Czech Republic   | 56                                                   | 16.8                                             | -                        | 5.8                      |
| Denmark          | 58                                                   | 15.3                                             | 10.5                     | 4.6                      |
| Estonia          | 68                                                   | 7                                                | 12.5                     | 6.5                      |
| Finland          | 58                                                   | 13                                               | 13.7                     | 6                        |
| France           | 42                                                   | 14.9                                             | -                        | 4.4                      |
| Germany          | 43                                                   | 17.7                                             | 12.8                     | 6                        |
| Greece           | 64                                                   | 16                                               | 16.9                     | 6.6                      |
| Hungary          | 48                                                   | 25.9                                             | 9.6                      | 2.9                      |
| Israel           | 48                                                   | -                                                | 5.05                     | 12                       |
| Italy            | 72.8**                                               | 35.9                                             | 12.2                     | 5.6                      |
| Netherlands      | 42                                                   | 17.9                                             | 12.2                     | 6.4                      |
| Norway           | 64                                                   | 14.7                                             | 10.7                     | 5.6                      |
| Poland           | 42                                                   | 12.4                                             | 13.5                     | 9.5                      |
| Slovakia         | 61                                                   | 16.2                                             | 9.4                      | 7.5                      |
| Slovenia         | 60                                                   | 24.4                                             | 9.6                      | 6.4                      |
| Spain            | 69                                                   | 22.9                                             | 16                       | 4.6                      |
| Sweden           | 66                                                   | 19.5                                             | 11                       | 4.6                      |
| United Kingdom   | 55                                                   | 26.1                                             | 11.5                     | 5.2                      |

‡ Data from Nichols et al; European Cardiovascular Disease Statistics 2012., Table 6.5 and 10.3.
† Data from Lambert et.al.; British Journal of Nutrition (2004), 92, Suppl. 2, S147–S211; Tables in pages S175 and S176. E; energy.
- indicates that no value was available for these parameters in these countries.
* represents average of “Belgium (Flemmish) and Belgium (French)”.
** these values were predicted based on a regression of 2009/10 values on 2005/06 values using the other 19 countries (see methods).

https://doi.org/10.1371/journal.pone.0173084.t001
in our analyses. We did so using the urbanization index of the countries, as published by the United Nations World Urbanization Prospectus 2011 Revision, which describes the percentage of the total population living in urban areas. Average physical activity has been associated with the average affluence of a nation [37]. To account for this confounder, per capita GDP data were obtained from the 2011 World Bank data in US dollars.

Physical activity has also been associated with a variety of climate and weather-related variables [40]. Wikipedia, which reports data from country-specific meteorological organizations, was the source for the following climate variables, corresponding to countries’ capital cities: their latitudes, average annual sunshine hours, the average July daily maximum temperatures, and mean annual temperature, which is now depicted in S1 Fig. Data for each European country are summarized in Table 3.

Statistical analyses

Data regarding children and women were analyzed separately. All analyses were conducted using R package [41]. We used a Bonferroni adjustment when conducting multiple tests. Pairwise associations between all variables were visually assessed using scatterplots, and were statistically evaluated using Spearman (rank) correlation. For each response variable of interest,

| Country       | % of women with elevated blood glucose* † | % of obese women † | Mean MUFA Intake (% E) ‡ | Mean PUFA Intake (% E) ‡ | Sample size for nutritional data‡ |
|---------------|------------------------------------------|------------------|--------------------------|--------------------------|----------------------------------|
| Austria       | 4.6                                      | 20.8             | 12.5                     | 8                        | 2123                             |
| Belgium       | 6.4                                      | 10.2             | 13.8                     | 6.8                      | 3245                             |
| Bulgaria      | 8.9                                      | 19.2             | 9.9                      | 11.3                     | 860                              |
| Czech Republic| 9.1                                      | 22.3             | 13                       | 7                        | 7913                             |
| Denmark       | 5.9                                      | 11.8             | 12                       | 5                        | 3151                             |
| Finland       | 6.3                                      | 13.5             | 12.4                     | 6.2                      | 1594                             |
| France        | 4.3                                      | 17.6             | 11.8                     | 3.9                      | 1089                             |
| Germany       | 6.3                                      | 21.1             | 12.8                     | 6.5                      | 1000                             |
| Greece        | 7.9                                      | 25.6             | 22.3                     | 6.6                      | 20942                            |
| Hungary       | 8.5                                      | 18.2             | 11.3                     | 8.9                      | 3077                             |
| Israel        | 8.7                                      | 25.7             | 11                       | 8                        | 3242                             |
| Italy         | 5.4                                      | 9.1              | 12.8                     | 4.8                      | 1461                             |
| Ireland       | 5.6                                      | 21.3             | 12                       | 7                        | 1097                             |
| Netherlands   | 4.1                                      | 10.1             | 12                       | 6.8                      | 2106                             |
| Norway        | 7.7                                      | 21               | 10.8                     | 5.4                      | 2672                             |
| Poland        | 6.9                                      | 23.8             | 15.4                     | 5.2                      | 2893                             |
| Portugal      | 5.7                                      | 13.4             | 12.4                     | 4.9                      | 489                              |
| Russia        | 10.7                                     | 21.6             | 16                       | 9                        | 9098                             |
| Slovakia      | 9.2                                      | 5.9              | 11.9                     | 8.7                      | 4018                             |
| Slovenia      | 8.8                                      | 13.8             | 13                       | 3.9                      | 2183                             |
| Spain         | 8.8                                      | 21.4             | 15.9                     | 5.6                      | 10208                            |
| Sweden        | 6                                        | 11               | 12.5                     | 4.7                      | 1217                             |
| UK            | 5.7                                      | 26               | 11.7                     | 5.9                      | 434                              |

* Age standardized prevalence estimate of raised fasting blood glucose (≥ 7.0 mmol/L or on medication) (%).
† Data from Nichols et al; European Cardiovascular Disease Statistics 2012., Table 10.1 and 11.2.
‡ Data from Harika et al.; Ann Nutr Metab 63, 229–238, 2013; Table 1; E; energy.

https://doi.org/10.1371/journal.pone.0173084.t002
we conducted multiple regressions, each time including per-capita GDP, climate variables, and urbanization index as confounders, and MUFA and PUFA as predictors of interest [42].

With N between 21 and 23 countries (depending on analysis), we (i) used latitude as a single proxy for climate variables, as it was strongly correlated with each of mean annual temperature, maximum July temperature, and annual hours of sunlight (S1 Fig), and (ii) excluded MUFA as a predictor variable as initial Spearman’s correlation analyses revealed no associations with any of the other variables of interest. This strategy further served to increase sample size and thus power, because some countries were missing MUFA data (Table 1).

For the analyses of adult data, the dietary report provides sample sizes associated with estimates of MUFA and PUFA intakes [36]. As these sample sizes varied considerably among countries (from 434 in the UK to 20942 in Greece), we conducted weighted regressions, with log-transformed sample sizes providing the weighting factor. Regression assumptions were assessed via standard residual diagnostics.

Results

Sedentary behaviour among European 11-year-old girls is associated with dietary PUFA

Sedentary behaviour among European 11-year-old girls was significantly positively associated with reported mean PUFA intake for the specific country (\( P < 0.005; \) Fig 1). Mean MUFA

| Country | Per-capita GDP (USD) | Urbanization Index | Latitude in °N | Annual sunlight hours | Maximum July temperature (in °C) | Mean annual temperature (in °C) |
|---------|----------------------|--------------------|----------------|-----------------------|----------------------------------|-------------------------------|
| Austria | 51131                | 67.7               | 48             | 1804                  | 25.6                             | 10.2                          |
| Belgium | 47802                | 97.5               | 51             | 1546                  | 23                               | 10.5                          |
| Bulgaria | 7589                | 73.1               | 42             | 2300                  | 28                               | 11.4                          |
| Czech R. | 21656               | 73.4               | 50             | 1668                  | 23.3                             | 7.9                           |
| Denmark | 61304                | 86.9               | 56             | 1539                  | 20.4                             | 8                             |
| Estonia | 17177                | 69.5               | 59             | 1738                  | 19                               | 5                             |
| Finland | 50788                | 83.7               | 60             | 1819                  | 22                               | 5.6                           |
| France  | 43811                | 85.8               | 49             | 1662                  | 25                               | 12.4                          |
| Germany | 45868                | 73.9               | 53             | 1626                  | 24                               | 9.6                           |
| Greece  | 25962                | 61.4               | 38             | 2848                  | 33.4                             | 18.5                          |
| Hungary | 13983                | 69.5               | 48             | 1988                  | 26.6                             | 10.5                          |
| Israel  | 51948                | 91.9               | 31             | 3397                  | 29                               | 17.5                          |
| Italy   | 33275                | 68.4               | 42             | 2473                  | 30.3                             | 15.2                          |
| Ireland | 38365                | 62.2               | 53             | 1453                  | 20.2                             | 11                            |
| Netherlands | 53537            | 83.2               | 52             | 1662                  | 22                               | 10.2                          |
| Norway  | 100575               | 79.4               | 60             | 1668                  | 21.5                             | 5.7                           |
| Poland  | 13776                | 60.9               | 52             | 1571                  | 23.8                             | 8.2                           |
| Portugal | 23195               | 61.1               | 38             | 2806                  | 27.9                             | 17.5                          |
| Russia  | 13324                | 73.8               | 55             | 1731                  | 24.3                             | 5.8                           |
| Slovakia | 18066               | 54.7               | 48             | 2038                  | 27.5                             | 10.5                          |
| Slovenia | 24965               | 49.9               | 46             | 1798                  | 26.5                             | 10.2                          |
| Spain   | 31973                | 77.4               | 40             | 2769                  | 31.2                             | 14.6                          |
| Sweden  | 59594                | 85.2               | 59             | 1821                  | 21.9                             | 6.6                           |
| U.K. *  | 40975                | 79.6               | 52             | 1480                  | 23.2                             | 11.5                          |

*U.K.: United Kingdom.

GDP: World Bank data in US dollars as of 2011.

Urbanization: United Nations World Urbanization Prospectus 2011 Revision.

https://doi.org/10.1371/journal.pone.0173084.t003
intake was not correlated with any variables. Prevalence of overweight/obesity among European 11-year-old girls was negatively associated with the latitude of the country’s capital city at the unadjusted alpha level (Spearman \( \rho = -0.45 \), \( N = 20; P = 0.045 \)), but not with any other variables (Fig 1).

After accounting for confounders, mean PUFA intake was found to be a highly significant predictor of sedentary behaviour among European 11-year-old girls (Fig 2A; Table 4). On average, for every percentage increase in PUFA, and holding all other variables constant, there was a predicted increase of 3.95% in the prevalence of sedentary behaviour (90% confidence

---

**Fig 1.** Scatterplot matrix depicting bivariate relationships between all response and independent variables for 11 yr old female children across 21 European countries. For descriptions of variable names and raw data, please see Table 1. Numbers in the upper diagonal represent Spearman rank correlation coefficients (\( * P \leq 0.10; ** P \leq 0.05; *** \) significant at Bonferroni-adjusted alpha, i.e. \( P \leq 0.1 / 21 \approx 0.005 \)). Lines in lower diagonal panels represent locally weighted smoothers. Histograms of each variable are included in the diagonal.

https://doi.org/10.1371/journal.pone.0173084.g001
In a least-squares regression that includes only mean PUFA intake as a predictor (thus not accounting for potential confounders), a remarkable 50% of the variation in sedentary behaviour is accounted for (Fig 2B; regression intercept and slope: 30.71 and 3.93, respectively; $F_{1,19} = 21.35, P = 0.002$).

In our model of prevalence of overweight among European 11-year-old girls, latitude of the capital city of a country was a significant negative predictor ($P = 0.02$), though the overall multiple regression was not significant (Table 4): On average, for every degree increase in latitude of the capital city, and holding all other variables constant, there was a predicted decrease of 0.63% in the prevalence of overweight (90% confidence limits: $–1.20, –0.21$). Such effects of latitude were predicted earlier on physical activity among school age children and adolescents [40].

### Table 4. Results of multiple least-squares regression for 11-year old European girls.

Shown are partial coefficients with 90% confidence intervals (999 permutations). The coefficients can be interpreted as the amount by which the response variable changes when the given predictor (independent) variable increases by one unit, holding all other predictor variables constant. Bold confidence intervals indicate those that exclude zero.

| Response variable | Independent variable | Partial coefficient | 90% confidence interval |
|-------------------|----------------------|---------------------|------------------------|
| **A. % of 11yr old female population that watches 2 hours or more of TV on weekdays** | (intercept) | 10.73 | $–26.47, 44.49$ |
| | Per-capita GDP (thousands) (US$) | $–0.21$ | $–0.33, 0.13$ |
| | Urbanization | 0.17 | $–0.09, 0.67$ |
| | Latitude of capital city | 0.30 | $–0.31, 0.71$ |
| | PUFA (%E) | 3.95 | $2.25, 5.53$ |
| **B. % of population as overweight including obesity** | (intercept) | 48.67 | $21.58, 84.73$ |
| | Per-capita GDP (thousands) (US$) | 0.02 | $–0.12, 0.13$ |
| | Urbanization | 0.10 | $–0.18, 0.33$ |
| | Latitude of capital city | $–0.63$ | $–1.19, –0.21$ |
| | PUFA (%E) | $–1.04$ | $–2.25, 0.56$ |

Adjusted R-square = 0.52 $F_{4,16} = 6.41$, $P = 0.003$

Adjusted R-square = 0.21 $F_{4,15} = 2.26$, $P = 0.111$
Blood glucose in adult European females and dietary PUFA

Among 25+ year old women, we found that raised fasting blood glucose (≥ 7.0 mmol/L) or on medication was positively associated with adult PUFA intakes (Fig 3; Spearman rho = 0.44; N = 23; P = 0.037), but this association was not significant at our Bonferroni-adjusted alpha level of ≈ 0.005. Nevertheless, given our limited sample size (N = 23 countries), we consider this finding noteworthy. Prevalence of obesity among 25+ year old European women was not significantly associated with any of the covariates (Fig 3).

Fig 3. Scatterplot matrix depicting bivariate relationships between all response and independent variables for 25+ years female women across 23 European countries. For descriptions of variable names and raw data, please see Table 2. Numbers in the upper diagonal represent Spearman rank correlation coefficients (* P ≤ 0.10; ** P ≤ 0.05; *** significant at Bonferroni-adjusted alpha, i.e. P ≤ 0.1 ÷ 21 ≈ 0.005). Lines in lower diagonal panels represent locally weighted smoothers. Histograms of each variable are included in the diagonal.
In the multiple regression analyses, residual diagnostics revealed Norway to be a strong outlier (due to its extremely high per capita GDP; Table 3), so it was excluded from subsequent analyses. Conclusions were qualitatively identical with it included. Per-capita GDP was a significant negative predictor of raised fasting blood glucose ($>7.0\text{ mmol/L}$) or on medication in adult women. On average, for every $1000 (USD) increase in per-capita GDP, and holding all other variables constant, there was a predicted decrease of $0.08\%$ in the prevalence of raised glucose (90% confidence limits: $–0.120, –0.009$) (Table 5). Lastly, as observed in our analyses of children data, none of the variables tested were significant predictors of obesity among women (Table 5).

### Discussion

Over the last 40 years, a synergistic effect of improper diet and lack of physical activity has been blamed for the rapid rise in various chronic diseases like obesity, diabetes and cancer [1]. A high fat diet and sedentary behaviour is considered obesogenic and detrimental. However, the literature remains divided over their inter-relationship. Contrary to common belief, higher caloric intake either does not influence or induces higher spontaneous activity in rodents [43]. In lean humans, excess energy provision is also balanced by increased spontaneous activity and thermogenesis, at least in the short-term [3]. It is increasingly recognized that a low carbohydrate diet (i.e. high in fat) has either no effect on type 2 diabetes in women or is actually beneficial [44–46]. Therefore, rather than total fat, the fat composition of a diet may be vital in influencing sedentary behaviour and diabetes in women.

Besides PUFA and MUFA intakes, in our analyses, we incorporated data from European countries with varied climate (Italy vs. Norway), urbanization (Slovenia vs. England), per-capita GDP (Bulgaria vs. Germany) and geography (Austria vs. Spain). We first demonstrate that sedentary behaviour among 11 year old European female children is significantly positively associated with mean PUFA intakes, after controlling for the significant negative effect of per-capita GDP. Although the underlying biological causes are not clear, there is considerable evidence of clinical depression in women with a high n-6 PUFA diet [47]. Interestingly, depression in teen females is strongly associated with 2 or more hours of TV watching behavior as well [48]. Most recently, we demonstrated that a high n-6 PUFA but not MUFA rich diet,
promotes loss of spontaneous activity and insulin resistance in mice [4]. Most interestingly, it has been demonstrated that muscle phospholipid n-6 PUFA content increases with a sedentary profile even in healthy humans [49].

Although sedentary activity data was available, data on diabetes in 11 year was unavailable as insulin or blood glucose values are not usually measured in this age group. As sedentary behavior can be a factor in causing diabetes, we evaluated the incidence of elevated blood glucose in 25+yr old adult females from across Europe. In Spearman’s rank correlation analysis, we found evidence of a positive association between the prevalence of elevated glucose in adult females with reported adult PUFA intakes (Fig 2), but given the limited sample size, this association was not significant at our stringent Bonferroni-adjusted alpha level (0.005). Following multiple regression analysis, per-capita GDP emerged as the sole significant predictor of the incidence of elevated glucose in adult females. Socioeconomic status can be a strong predictor of diabetes, and this relationship is stronger for women than in men [50–52]. The probable causes identified involve chronic stress, smoking, poor housing conditions, lack of exercise and education, all of which are related to worsening metabolic profiles. It is also known that low socioeconomic status encourages consumption of cheaper vegetable oils containing high PUFA [53]. In contrast, a direct relationship between breast milk MUFA and higher socioeconomic status is also known [54].

Interestingly, in both young girls and adult women, neither sedentary behaviour nor elevated blood glucose could be associated with the incidence of overweight/obesity in the population. Despite common perceptions, the relationship between sedentary behavior and obesity is not straightforward in children and adolescents as extensively reviewed earlier [28, 55]. The link between media time and BMI is weak at best in this particular age group. With regards to our analysis, an age of 11 years can also be an insufficient time biologically to accumulate body fat in pre-teen females, even in those with an increased screen time. With respect to adult 25+yr old females, there is extensive under-reporting of obesity in self-report surveys which could have prevented detection of an association [56]. Moreover, with respect to diabetes, it has been known for quite some time that the relationship of adiposity to insulin resistance is confounded in the female sex during reproductive years due to the protective effects of sex hormones [57]. Unfortunately, we feel that the same hormones that prevent against insulin resistance due to general adiposity, often leads to detrimental effects of PUFA specifically by enhancing its bioconversion [25].

PUFA subtypes like n-3 or n-6 PUFAs were not discriminated in our study due to the lack of such differentiations in our databases. At least in the US and most Western nations, both n-3 and n-6 PUFA appear to have increased in recent years with increasing use of vegetable oils like soybean (n-6 and n-3 PUFA at 10 and 50% of total fatty acids) and canola (n-6 and n-3 PUFA at 9 and 21% of total fatty acids) [6, 7]. In a 2015 study, dietary n-3 PUFA was identified as a causative factor for lowering physical activity during class time in iron-deficient South African school children aged 6–11 years, which could not be reversed following iron supplementation [58]. A recent meta-analysis reports that n-3 PUFA supplementation might be related to lowering of aggression in humans which deters spontaneous activity as well [59].

In parallel, dietary n-6 PUFA has been linked to a loss of physical activity in an aged Italian cohort [60]. Regarding diabetes, an example at the population level is illustrated by India. In 2000, there were 31.7 million diabetic cases in India which doubled to more than 62 million individuals within a decade [61]. However, in a national study on the prevalence of diabetes between 1972–1975 involving 35,000 Indians above 14 years of age, diabetes prevalence was only 1.5–2.1% of the population surveyed [62]. Currently, in cities like Kolkata, India, 11.6% of the population suffers from diabetes [61]. It has been speculated for a long time that the rising incidence of diabetes in India is linked to a 'switch' to unsaturated vegetable oils from
traditional tropical, saturated oils [63, 64]. In a recent survey involving 27,012 South Indians who traditionally used palm and coconut oils (rich in saturated fats, 9% PUFA) as the chief cooking medium, introduction of sunflower oil (~70% PUFA) was identified as the major cause for developing metabolic syndrome including insulin resistance and hyperlipidemia [65].

**Study limitations**

As with any ecological study, associations established using population-level data do not necessarily reflect any causality. In a perfect world, prospective, individual level data from the same year would be obtainable from the entire European cohort in both nutritional intake and sedentary behaviour patterns, which would lead to definitive answers to our question. However, rarely do any one nutritional or behavioral survey cross national boundaries, much less in the same or similar years. The objective of this cross-sectional study was to find associations between PUFA or MUFA intakes and rising sedentary behaviour or diabetes in European populations. To avoid any potential bias on our part, we used a single published database of nutrient intake both for adult [36] and children [35]. These are the most up to date, comprehensive nationwide databases available for these age groups available currently. We also used a single database i.e. the European Cardiovascular Statistics database 2012 [22] for sedentary behaviour and blood glucose data.

Overall, this study provides evidence for a positive ecological association between excess dietary PUFA intake across Europe with sedentary behaviour among female children and marginal associations with elevated blood glucose in adult females. A negative association between PUFA intake and per-capita GDP in adult females was also established in this analysis. Considering all confounders, lower per-capita GDP emerged as the strongest predictor for diabetes in adult females. In light of such results, we call for prospective RCTs evaluating a possible link of dietary PUFA and socioeconomic status on inducing sedentary behaviour and insulin resistance in female subjects.

**Supporting information**

S1 Fig. Climactic relationships across Europe. Scatterplot matrix depicting bivariate relationships between the latitude of the European capital cities, mean annual temperature (MAT), maximum July temperature (July_maxtemp), and total sunlight hours (Sunlight) across European countries. Numbers in the upper diagonal represent Spearman rank correlation coefficients (* P ≤ 0.10; ** P ≤ 0.05; *** significant at Bonferroni-adjusted alpha, i.e. P ≤ 0.1 / 6 ≈ 0.017). Lines in lower diagonal panels represent locally weighted smoothers. Histograms of each variable are included in the diagonal.

**Author Contributions**

Conceptualization: SG.

Data curation: JP.

Formal analysis: JP AB.

Funding acquisition: SG.

Investigation: JP AB.

Methodology: SG JP.
Project administration: SG.
Resources: SG.
Software: JP.
Supervision: SG.
Validation: CRM.
Visualization: CRM SG JP.
Writing – original draft: SG JP AB.
Writing – review & editing: SG JP CRM AB.

References
1. Waxman A. Why a Global Strategy on Diet, Physical Activity and Health? In: Simopoulos A, editor. Nutrition and Fitness: Mental Health, Aging, and the Implementation of a Healthy Diet and Physical Activity Lifestyle 95. Basel: Karger; 2005. p. 182–6.
2. Physical activity and good nutrition: essential elements to prevent chronic diseases and obesity 2003. Nutr Clin Care. 2003; 6(3):135–8. Epub 2004/02/26. PMID: 14579458
3. Westerterp KR. Physical activity, food intake, and body weight regulation: insights from doubly labeled water studies. Nutr Rev. 2010; 68(3):148–54. Epub 2010/04/14. https://doi.org/10.1111/j.1753-4887.2010.00270.x PMID: 20384845
4. Wong CK, Botta A, Pitler J, Dai C, Gibson WT, Ghosh S. A high-fat diet rich in corn oil reduces spontaneous locomotor activity and induces insulin resistance in mice. J Nutr Biochem. 2015; 26(4):319–26. Epub 2015/01/04. https://doi.org/10.1016/j.jnutbio.2014.11.004 PMID: 25555452
5. German JB, Dillard CJ. Saturated fats: what dietary intake? Am J Clin Nutr. 2004; 80(3):550–9. Epub 2004/08/24. PMID: 15321792
6. Blasbalg TL, Hibbeln JR, Ramsden CE, Majchrzak SF, Rawlings RR. Changes in consumption of omega-3 and omega-6 fatty acids in the United States during the 20th century. Am J Clin Nutr. 2011; 93 (5):950–62. Epub 2011/03/04. https://doi.org/10.3945/ajcn.110.006643 PMID: 21367944
7. Micha R, Khatibzadeh S, Shi P, Fahimi S, Lim S, Andrews KG, et al. Global, regional, and national consumption levels of dietary fats and oils in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys. BMJ. 2014; 348:g2272. Epub 2014/04/17. PubMed Central PMCID: PMC3967052. https://doi.org/10.1136/bmj.g2272 PMID: 24736206
8. Gregg EW, Li Y, Wang J, Burrows NR, Ali MK, Rolka D, et al. Changes in diabetes-related complications in the United States, 1990–2010. N Engl J Med. 2014; 370(16):1514–23. Epub 2014/04/18. https://doi.org/10.1056/NEJMoa1310799 PMID: 24738668
9. Andersson T, Ahlbom A, Magnusson C, Carlsson S. Prevalence and incidence of diabetes in Stockholm County 1990–2010. PLoS One. 2014; 9(8):e104033. Epub 2014/08/15. PubMed Central PMCID: PMC4134405. https://doi.org/10.1371/journal.pone.0104033 PMID: 25121976
10. Tamayo T, Rosenbauer J, Wild SH, Spijkerman AM, Baan C, Forouhi NG, et al. Diabetes in Europe: an update. Diabetes Res Clin Pract. 2014; 103(2):206–17. Epub 2013/12/05. https://doi.org/10.1016/j.diabres.2013.11.007 PMID: 24300019
11. Saunders TJ, Chaput JP, Tremblay MS. Sedentary Behaviour as an Emerging Risk Factor for Cardio-metabolic Diseases in Children and Youth. Can J Diabetes. 2014; 38(1):53–61. Epub 2014/02/04. https://doi.org/10.1016/j.jcjd.2013.08.266 PMID: 24485214
12. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999–2000. JAMA. 2002; 288(14):1728–32. Epub 2002/10/09. PMID: 12365956
13. Santalaistra-Pasiaas AM, Mouratidou T, Verbestel V, Bammann K, Molnar D, Sieri S, et al. Physical activity and sedentary behaviour in European children: the IDEFICS study. Public Health Nutr. 2014; 17 (10):2295–306. Epub 2013/10/10. https://doi.org/10.1017/S1366820213002486 PMID: 24103326
14. Keim SA, Brunam AM. Dietary intake of polyunsaturated fatty acids and fish among US children 12–60 months of age. Matern Child Nutr. 2013. Epub 2013/09/17.
15. Madden SM, Garlach CF, Holub BJ. Direct diet quantification indicates low intakes of (n-3) fatty acids in children 4 to 8 years old. J Nutr. 2009; 139(3):528–32. https://doi.org/10.3945/jn.108.100628 PMID: 19158221
16. Botta A, Ghosh S. Exploring the impact of n-6 PUFA-rich oilseed production on commercial butter compositions worldwide. Journal of Agricultural and Food Chemistry. 2016;(in press).

17. Rosenberg NA, Pritchard JK, Weber JL, Cann HM, Kidd KK, Zhivotovsky LA, et al. Genetic structure of human populations. Science. 2002; 298(5602):2381–5. Epub 2002/12/21. https://doi.org/10.1126/science.1078311 PMID: 12493913

18. Kris-Etherton PM, Committee fTN. Monounsaturated Fatty Acids and Risk of Cardiovascular Disease. Circulation. 1999; 100(11):1253–8. PMID: 10484550

19. Hozyasz K. Alternative n-3 PUFA Sources in Central European Diet before Westernization—Case Report from Poland. J Food Res. 2013; 2(2):29–35. Epub 2013.

20. Brynes AE, Edwards CM, Jadhav A, Ghatel MA, Bloom SR, Frost GS. Diet-induced change in fatty acid composition of plasma triacylglycerols is not associated with change in glucagon-like peptide 1 or insulin sensitivity in people with type 2 diabetes. Am J Clin Nutr. 2000; 72(5):1111–8. Epub 2000/11/04. PMID: 11063437

21. Paniaqua JA, de la Sacristana AG, Sanchez E, Romero I, Vidal-Puig A, Berral FJ, et al. A MUFA-rich diet improves posprandial glucose, and GLP-1 responses in insulin-resistant subjects. J Am Coll Nutr. 2007; 26(5):434–44. Epub 2007/10/05. PMID: 17914131

22. Yam D, Eliraz A, Berry EM. Diet and disease—the Israeli paradox: possible dangers of a high omega-6 polyunsaturated fatty acid diet. Isr J Med Sci. 1996; 32(11):1134–43. PMID: 8960090

23. Soriguier F, Esteva I, Rojo-Martinez G, Ruiz de Adana MS, Dobarganes MC, Garcia-Almeida JM, et al. Oleic acid from cooking oils is associated with lower insulin resistance in the general population (Pizarra study). Eur J Endocrinol. 2004; 150(1):33–9. Epub 2004/01/10. PMID: 14713277

24. Silva S, Bronze MR, Figueira ME, Siwy J, Mischak H, Combet E, et al. Impact of a 6-wk olive oil supplementation in healthy adults on urinary proteomic biomarkers of coronary artery disease, chronic kidney disease, and diabetes (types 1 and 2): a randomized, parallel, controlled, double-blind study. Am J Clin Nutr. 2015; in press.

25. Alessandri JM, Extier A, Al-Gubory KH, Langelier B, Baudry C, LePoupon C, et al. Ovariectomy and 17beta-estradiol alter transcription of lipid metabolism genes and proportions of neo-formed n-3 and n-6 long-chain polyunsaturated fatty acids differently in brain and liver. J Nutr Biochem. 2011; 22(9):820–7. Epub 2010/12/07. https://doi.org/10.1016/j.nutbio.2010.07.005 PMID: 21129945

26. Shapiro N. Women’s higher risk with N-6 PUFA vs. men’s relative advantage: an “N-6 gender nutrition paradox” hypothesis. Isr Med Assoc J. 2012; 14(7):435–41. Epub 2012/09/08. PMID: 22953621

27. Shapiro N. Israeli ‘cancer shift’ over heart disease mortality may be led by greater risk in women with high intake of n-6 fatty acids. Eur J Cancer Prev. 2007; 16(5):486–94. Epub 2007/12/18. https://doi.org/10.1097/CEJ.0b013e3280145b6d PMID: 17923822

28. Rey-Lopez JP, Vicente-Rodriguez G, Biosca M, Moreno LA. Sedentary behaviour and obesity development in children and adolescents. Nutr Metab Cardiovasc Dis. 2008; 18(3):242–51. Epub 2007/12/18. https://doi.org/10.1016/j.numecd.2007.07.008 PMID: 18083016

29. Tremblay MS, Wills J. Is the Canadian childhood obesity epidemic related to physical inactivity? Int J Obes Relat Metab Disord. 2003; 27(9):1100–5. https://doi.org/10.1038/sj.ijo.0802376 PMID: 12917717

30. Trang NH, Hong TK, van der Ploeg HP, Hardy LL, Kelly PJ, Dibley MJ. Longitudinal sedentary behavior changes in adolescents in Ho Chi Minh City. Am J Prev Med. 2013; 44(3):223–30. https://doi.org/10.1016/j.amepre.2012.10.021 PMID: 23415118

31. Tanaka C, Reilly JJ, Huang WY. Longitudinal changes in objectively measured sedentary behaviour and their relationship with adiposity in children and adolescents: systematic review and evidence appraisal. Obes Rev. 2014; 15(10):791–803. Epub 2014/06/06. https://doi.org/10.1111/obr.12195 PMID: 24899125

32. Telama R, Yang X. Decline of physical activity from youth to young adulthood in Finland. Med Sci Sports Exerc. 2000; 32(9):1617–22. Epub 2000/09/20. PMID: 10994914

33. Nader PR, Bradley RH, Houts RM, McRitchie SL, O’Brien M. Moderate-to-vigorous physical activity from ages 9 to 15 years. JAMA. 2008; 300(3):295–305. Epub 2008/07/18. https://doi.org/10.1001/jama.300.3.295 PMID: 18632544

34. Nichols M, Townsend N, Scarborough P, Rayner M. European Cardiovascular Disease Statistics 4th edition 2012: EuroHeart II. Eur Heart J. 2013; 34(39):3007. Epub 2013/10/16.

35. Lambert J, Agostoni C, Elmadfa I, Hulshof K, Krause E, Livingstone B, et al. Dietary intake and nutritional status of children and adolescents in Europe. Br J Nutr. 2004; 92 Suppl 2:S147–211. Epub 2004/11/04.

36. Harika RK, Eliander A, Alseema M, Osendarp SJ, Zock PL. Intake of Fatty acids in general populations worldwide does not meet dietary recommendations to prevent coronary heart disease: a systematic...
40. Kolle E, Steene-Johannessen J, Andersen LB, Andersen SA. Seasonal variation in objectively assessed physical activity among children and adolescents in Norway: a cross-sectional study. Int J Behav Nutr Phys Act. 2009; 6:36. Epub 2009/07/01. PubMed Central PMCID: PMC2711042. https://doi.org/10.1186/1479-5868-6-36 PMID: 19563650

41. Team. RC. R: A language and environment for statistical computing. 2014. Available from: http://www.r-project.org/.

42. McNamee R. Regression modelling and other methods to control confounding. Occup Environ Med. 2005; 62(7):500–6, 472. Epub 2005/06/18. PubMed Central PMCID: PMC1741049. https://doi.org/10.1136/oem.2002.001115 PMID: 15961628

43. Kim JH, Park Y, Kim D. Dietary influences on nonexercise physical activity and energy expenditure in C57BL/6J mice. J Food Sci. 2012; 77(2):H63–8. Epub 2012/01/10. https://doi.org/10.1111/j.1750-3841.2011.02522.x PMID: 22225400

44. Halton TL, Liu S, Manson JE, Hu FB. Low-carbohydrate-diet score and risk of type 2 diabetes in women. Am J Clin Nutr. 2008; 87(2):339–46. Epub 2008/02/09. PubMed Central PMCID: PMC2760285. PMID: 18225623

45. Halton TL, Willett WC, Liu S, Manson JE, Albert CM, Rexrode K, et al. Low-carbohydrate-diet score and the risk of coronary heart disease in women. N Engl J Med. 2006; 355(19):1991–2002. Epub 2006/11/10. https://doi.org/10.1056/NEJMoa055317 PMID: 17093250

46. Feinman RD, Pogozelski WK, Astrup A, Bernstein RK, Fine EJ, Westman EC, et al. Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. Nutrition. 2014. Epub 2014/10/08.

47. Conklin SM, Manuck SB, Yao JK, Flory JD, Hibbeln JR, Muldoon MF. High omega-6 and low omega-3 fatty acids are associated with depressive symptoms and neurotoxicity. Psychosom Med. 2007; 69(9):932–4. Epub 2007/11/10. https://doi.org/10.1097/PSY.0b013e31815aaa42 PMID: 17991818

48. Primack BA, Swanier B, Georgiopoulou AM, Land SR, Fine MJ. Association between media use in adolescence and depression in young adulthood: a longitudinal study. Arch Gen Psychiatry. 2009; 66(2):181–8. Epub 2009/02/04. PubMed Central PMCID: PMC3004674. https://doi.org/10.1001/archgenpsychiatry.2008.532 PMID: 19188540

49. Helge JW, Wu BJ, Willer M, Daugaard JR, Storlien LH, Kiens B. Training affects muscle phospholipid fatty acid composition in humans. J Appl Physiol (1985). 2001; 90(2):670–7. Epub 2001/02/13. PMID: 11160068

50. Agardh E, Allebeck P, Hallqvist J, Moradi T, Sidoruchk A. Type 2 diabetes incidence and socio-economic position: a systematic review and meta-analysis. Int J Epidemiol. 2011; 40(3):804–18. Epub 2011/02/22. https://doi.org/10.1093/ije/dyr029 PMID: 21335614

51. Dancia-Panaiteacu S, Dancia-Panaiteacu M, Bryant T, Daiki I, Pilkington B, Raphael D. Diabetes prevalence and income: Results of the Canadian Community Health Survey. Health Policy. 2011; 99(2):116–23. Epub 2010/08/21. https://doi.org/10.1016/j.healthpol.2010.07.018 PMID: 20724018

52. Stringhini S, Tabak AG, Akbaraly TN, Sabia S, Shipley MJ, Marmot MG, et al. Contribution of modifiable risk factors to social inequalities in type 2 diabetes: prospective Whitehall II cohort study. BMJ. 2012; 345:e5452. Epub 2012/08/24. PubMed Central PMCID: PMC3424226. https://doi.org/10.1136/bmj.e5452 PMID: 22915665

53. Briand A, Dewey KG, Reinhart GA. Fatty acid status in early life in low-income countries—overview of the situation, policy and research priorities. Matern Child Nutr. 2011; 7 Suppl 2:141–8. Epub 2011/03/05.

54. Pita ML, Morales J, Sanchez-Pozo A, Martinez-Valverde JA, Gil A. Influence of the mother's weight and socioeconomic status on the fatty acid composition of human milk. Ann Nutr Metab. 1985; 29(6):366–73. Epub 1985/01/01. PMID: 4062247
55. Marshall SJ, Biddle SJ, Gorely T, Cameron N, Murdey I. Relationships between media use, body fatness and physical activity in children and youth: a meta-analysis. Int J Obes Relat Metab Disord. 2004; 28(10):1238–46. Epub 2004/08/18. https://doi.org/10.1038/sj.ijo.0802706 PMID: 15314635

56. Obarzanek E, Schreiber GB, Crawford PB, Goldman SR, Barrier PM, Frederick MM, et al. Energy intake and physical activity in relation to indexes of body fat: the National Heart, Lung, and Blood Institute Growth and Health Study. Am J Clin Nutr. 1994; 60(1):15–22. Epub 1994/07/01. PMID: 8017331

57. Karpe F, Dickmann JR, Frayn KN. Fatty acids, obesity, and insulin resistance: time for a reevaluation. Diabetes. 2011; 60(10):2441–9. PubMed Central PMCID: PMCPMC3178283. https://doi.org/10.2337/db11-0425 PMID: 21948998

58. Smuts CM, Greeff J, Kvalsvig J, Zimmermann MB, Baumgartner J. Long-chain n-3 PUFA supplementation decreases physical activity during class time in iron-deficient South African school children. Br J Nutr. 2015; 113(2):212–24. Epub 2014/12/05. https://doi.org/10.1017/S0007114514003493 PMID: 25471216

59. Gajos JM, Beaver KM. The effect of omega-3 fatty acids on aggression: A meta-analysis. Neurosci Biobehav Rev. 2016; 69:147–58. Epub 2016/07/28. https://doi.org/10.1016/j.neubiorev.2016.07.017 PMID: 27450580

60. Abbatecola AM, Cherubini A, Guralnik JM, Andres Lacueva C, Ruggiero C, Maggio M, et al. Plasma polyunsaturated fatty acids and age-related physical performance decline. Rejuvenation Res. 2009; 12 (1):25–32. Epub 2009/02/07. PubMed Central PMCID: PMC2674224. https://doi.org/10.1089/rej.2008.0799 PMID: 19196012

61. Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. Australas Med J. 2014; 7 (1):45–8. Epub 2014/02/26. PubMed Central PMCID: PMC3920109. https://doi.org/10.4066/AMJ.2013.1979 PMID: 24567766

62. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian scenario. Indian J Med Res. 2007; 125(3):217–30. Epub 2007/05/15. PMID: 17496352

63. Raheja BS, Sadikot SM, Phatak RB, Rao MB. Significance of the N-6/N-3 ratio for insulin action in diabetes. Ann N Y Acad Sci. 1993; 683:258–71. Epub 1993/06/14. PMID: 8352448

64. Simopoulos AP. Essential fatty acids in health and chronic disease. Am J Clin Nutr. 1999; 70(3 Suppl):560S–9S. Epub 1999/09/09.

65. Narasimhan S, Nagarajan L, Vaidya R, Gunasekaran G, Rajagopal G, Parthasarathy V, et al. Dietary fat intake and its association with risk of selected components of the metabolic syndrome among rural South Indians. Indian Journal of Endocrinology and Metabolism. 2016; 20(1):47–54. https://doi.org/10.4103/2230-8210.172248 PMID: 26904468