Moslehi *et al. Nutrition & Metabolism* (2024) 21:79
https://doi.org/10.1186/s12986-024-00854-4

Nutrition & Metabolism

RESEARCH Open Access

Ultra-processed foods and the incidence of pre-diabetes and type 2 diabetes among Iranian adults: the Tehran lipid and glucose study

Nazanin Moslehi[1*], Maryam Mahdavi[2], Parvin Mirmiran[3*] and Fereidoun Azizi[4]

Abstract

Background No study has investigated the association between ultra-processed food (UPF) and pre-diabetes development. Furthermore, prior investigations on the association between UPF and the risk of type 2 diabetes (T2D) were primarily conducted in Europe and America, and studies in other regions are lacking. We investigated the association between ultra-processed foods and the risk of pre-diabetes and T2D in a cohort of Iranians.

Methods This prospective study, with a sample size of 1954 for pre-diabetes and 2457 for T2D, was conducted among adults' participants (aged ≥ 18 years) from the Tehran Lipid and Glucose Study (TLGS). We defined UPF intake using NOVA calcification as a proportion of total energy, and calculated its average intake during the follow-ups. The hazard ratios (HR) and 95% confidence intervals (95% CI) for pre-diabetes/T2D across tertiles of total UPF and per 10% of its increment were examined using Cox proportional hazards models. We also investigated the possibility of non-linear association using a restricted cubic spline regression.

Results We identified 766 and 256 cases of pre-diabetes and T2D, respectively, during a median follow-up of 7 years for pre-diabetes and 8.6 years for T2D. In the multivariable adjusted model, a 10% increase in total UPF intake was associated with a 12% higher risk of pre-diabetes (HR = 1.12; 95% 1.02, 1.23). The incidence of pre-diabetes was also higher in those in tertile 3 than those in tertile 1 (HR = 1.28; 95% CI = 1.07, 1.52). Following additional adjustment for diet quality, the results remained unchanged. Spline regression demonstrated a J-shaped association between UPF and the risk of pre-diabetes; the risk of pre-diabetes did not increase until UPF consumption exceeded about 24% of total energy intake. Of the individual UPF, hydrogenated fat/mayonnaise/ margarine group was related to an increased risk of pre-diabetes. The total UPF and its individual items were not associated with T2D.

Conclusions This study found a positive, non-linear relationship between total UPF and the risk of pre-diabetes in Iranian adults. Our data could not show any significant association between UPF and T2D risk.

*Correspondence:
Nazanin Moslehi
moslehinazanin@yahoo.com; moslehinazanin@sbmu.ac.ir
Parvin Mirmiran
mirmiran@endocrine.ac.ir; parvin.mirmiran@gmail.com

Full list of author information is available at the end of the article

© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Keywords Impaired fasting glucose, Impaired glucose tolerance, NOVA classification, Industrial foods, Dysglycemia, The middle east region, Iran

Introduction

Worldwide food consumption habits have altered dramatically, with fresh and minimally processed food being steadily replaced by ultra-processed food (UPF). This transition, which originated in high-income nations, is presently taking place in low- and middle-income countries as well [1]. Worldwide estimates range from 10% to more than 50% of daily energy intake from UPF, with the United States and the United Kingdom reporting the highest contribution [2, 3]. The increased availability of highly processed food products is causing an increase in the consumption of UPFs in Iran. In a cohort of Iranian adults, the median proportion of UPF consumption was 12.7% of total energy intake for overweight or obese individuals and 14.1% for normal-weight individuals [4]. UPFs undergo different industrial processing, which can alter the characteristics of the foods and potentially produce contamination. Moreover, substances added to foods as flavor enhancers, preservatives, colorings, or emulsifiers, as well as materials used for packaging, may have adverse effects on health [5]. The nutritional composition of UPFs is generally poor, and therefore, their high consumption may lower the quality of the diet [6]. The health consequences of UPF consumption are currently of interest and have been investigated in numerous studies.

High UPF consumption adversely related to cardiometabolic health variables [7, 8] and increased cardiovascular and all-cause mortality [9, 10], according to prospective cohort studies. In terms of type 2 diabetes (T2D) risk, prospective studies from western countries consistently demonstrated a positive association between UPF and T2D occurrence [11–15]. However, in some studies, the increased risk of T2D was significant between the extreme groups of total UPF consumption, and results for moderate UPF intakes were null [12–14]. With regards to specific subgroups of UPF, research on the populations of the Netherlands and the United States revealed contradictory associations between types of UPF and T2D [14, 15]. On the other hand, the British and French cohorts demonstrated a potential link between all types of UPF products and the increase in T2D incidence [11, 12]. We could find only one prospective study that examined the UPF-diabetes association in a non-western population [16]. The study's findings showed 18–32% higher risk of T2D from quartiles 2–4 UPF consumption in middle-aged Korean adults. Furthermore, the study demonstrated the presence of variability in results according to UPF subgroups [16].

In addition to the limited number of studies investigating the association between UPF and T2D in other regions, such as the Middle East, no study has investigated the association between UPF and pre-diabetes incidence. Therefore, the current prospective study aimed to examine the association between UPF consumption and the risk of pre-diabetes and T2D in Iranian adults using the data from the Tehran Lipid and Glucose Study (TLGS).

Methods

Study population

We conducted the present prospective investigation using data from the TLGS. In 1999, the TLGS began as a population-based prospective cohort study, sampling individuals aged 3 to 69 who resided in district 13 of Tehran [17]. The objective of the TLGS was to ascertain the risk factors and associated outcomes of non-communicable diseases. At 3-year intervals, follow-up examinations were conducted to ensure that the information of the participants remained updated. The present study defined the third examination cycle (2005–2008) as the baseline because the Food Frequency Questionnaire (FFQ) was first administered at this time. Participants were followed to the sixth examination (2016–2018). Figure 1 illustrates the process of participants' selection for the current study. Out of the 3687 participants who provided dietary data during the third examination cycle, 2644 were chosen as follows: they were all at least 18 years old, did not have T2D, were not pregnant, and had follow-up information.

We excluded those with pre-diabetes at baseline (n=310), missing information to define pre-diabetes at baseline (n=154) or follow-up (n=57), incident diabetes during follow-up (n=71), missing covariates (n=60), and energy intake outside of sex-specific percentiles 1 and 99 (n=38) from the 2644 participants, leaving 1954 participants to be analyzed for the pre-diabetes outcome.

We also investigated the outcome of T2D in 2457 individuals who remained after excluding those who lacked sufficient information to establish their diabetes status at follow-up (n=33), had missing covariates (n=106), or reported energy consumption outside of sex-specific percentiles 1 and 99 (n=48).

The TLGS received approval from the Human Research Review Committee of the Endocrine Research Center at Shahid Beheshti University. All participants were given written, informed consent prior to recruitment. The research ethics committees of the Research Institute for Endocrine Sciences at Shahid Beheshti University of

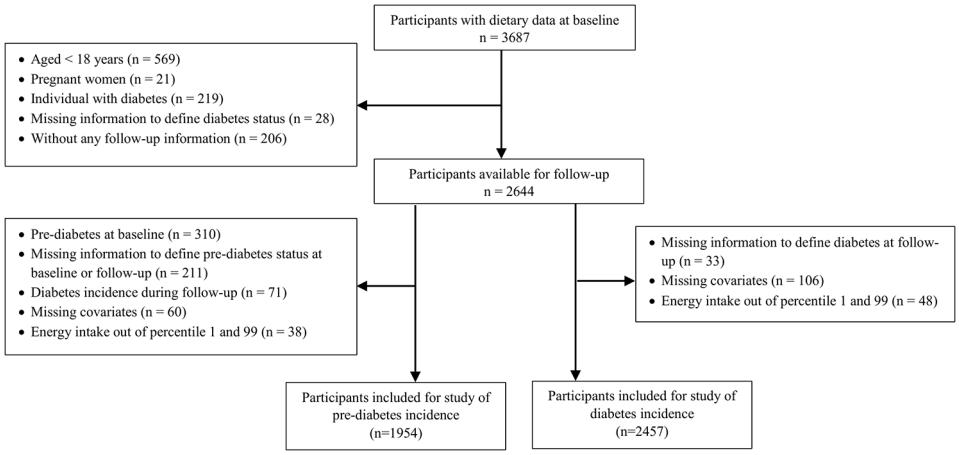

Fig. 1 Selection of the participants

Medical Sciences also granted approval for the current study (IR.SBMU.ENDOCRINE.REC.1403.023).

Dietary assessment

We determined the participants' regular dietary consumption through FFQ and an in-person interview. The participants were asked regarding the frequency and amount of consumption of 168 prevalent food and beverage items that were ingested within the previous year. Based on the daily intake of each item and the food composition tables, energy and nutrient intake were estimated. The nutrient composition of food products not included in the Iranian food composition table, such as cooked legumes or white or red meat, was determined using the United States Department of Agriculture's (USDA) food composition table. The validity and reliability of the questionnaire for assessing food consumption have been confirmed [18, 19].

We determined the UPF consumption by taking into account the following food items classified by NOVA: cakes, biscuits, crackers, ham/sausage, burgers, creamy cheese, ice creams, chocolate milk, pizza, candies, chocolates, mayonnaise, margarine, hydrogenated fats, carbonated soft drinks, potato chips, and pufak [20, 21]. We determined the total intake of UPF as a proportion of the total daily energy intake (% of energy). Moreover, to investigate the individual categories of UPF, the abovementioned food items were grouped into five categories: 1- hydrogenated fat/ mayonnaise/ margarine; 2- packaged snacks and confectioneries (including cakes, biscuits, crackers, candies, chocolates, potato chips, and pufak); 3- ready-to-eat/heat dishes (including ham/sausage, burgers, and pizza); 4- dairy products (including ice cream, creamy cheese, and chocolate milk); and 5- soft drinks. We preferred the energy ratio to the weight ratio because all UPF items had energy content.

We calculated the average intake of energy, UPF, and other dietary variables using the dietary data from the third examination up to the last FFQ completed before the onset of pre-diabetes/T2D or the last follow-up for those without the outcomes to quantify long-term intake and reduce inter-individual variation.

Non-dietary assessment

Socio-demographic and medical information of the participants, including birth date, smoking, education, occupation, marital status, family history of diabetes, and medications, was recorded using a questionnaire. Participants were categorized into current smokers, ex-smokers, and non-smokers based on smoking status; low (<6 years), middle (6–12 years), and high (>12 years) based on educational level; having a full-time job (yes or no) based on occupation; married and living alone (never married, widowed, or divorced) based on marital status. Physical activity during leisure, job, and household activities was assessed using a Persian translation of the Modifiable Activity Questionnaire (MAQ) and determined as the metabolic equivalent of task (MET) minutes per week [22]. For statistical analysis, we classified participants into two groups: less than 600 and equal to or more than 600 Met-min/week.

Anthropometric variables, including weight, height, and waist circumference, were measured using a standard protocol. The body mass index (BMI) was computed by dividing the weight (in kilograms) by the square of the height (in square meters).Waist circumference adjusted for BMI was determined using the residual method [23].

After 15 min of rest, a standardized mercury sphygmomanometer (Riester, Jungingen, Germany) was employed to measure systolic and diastolic blood pressure in the right arm in a seated position. A 30-second interval was used to measure blood pressure twice, and the participant's blood pressure was determined as the average of

the two measurements. Hypertension was defined as systolic blood pressure≥140 mmHg, diastolic blood pressure≥90 mmHg, and/or taking anti-hypertensive medications based on the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [24].

Participants' biochemical characteristics, such as fasting serum glucose, triglycerides, and high-density lipoprotein cholesterol (HDL-C), were assessed from a serum sample taken following a 12- to 14-hour overnight fast. 2-hour serum glucose levels were also tested 2 h after consuming 75 g of oral glucose. The biochemical measurements have been done on the day of blood collection with the enzymatic colorimetric method using commercial kits (Pars Azmun commercial kits, Tehran, Iran). Intra- and inter-coefficients of variation were 2.2% for fasting glucose, 0.6 and 1.6% for triglycerides, and 0.5 and 2% for HDL-C.

Outcome definition

Pre-diabetes and T2D diagnoses were performed based on the criteria of the American Diabetes Association [25]. Pre-diabetes was defined as impaired fasting glucose (fasting serum glucose 100–125 mg/dl) or /and impaired glucose tolerance (2-hour serum glucose 140–199 mg/dL). T2D was diagnosed as fasting serum glucose being ≥126 mg/dL, 2-h serum glucose being ≥200 mg/dL, or glucose-lowering medication.

Statistical analysis

Participants' characteristics across tertile categories of UPF were determined and compared using the analysis of variance (ANOVA) for normal-distributed continuous variables, the Kruskal-Wallis test for non-normal-distributed continuous variables, and the chi-squared test for categorical variables. Results were reported as mean±standard deviation for normally distributed continuous variables, median (percentiles 25, 75) for skewed variables, and number (percentage) for categorical variables. Hazard ratios (HR) and 95% confidence intervals (CI) for pre-diabetes and T2D were estimated using Cox proportional hazards regression across tertiles of UPF. The person-years for each participant were estimated from the baseline to the date of the pre-diabetes/T2D incidence, the date of the last follow-up, or the end date of the study. The event date of the occurrence of pre-diabetes/ T2D was defined as the midpoint between the data of the follow-up examination during which the events were found for the first time and the most recent follow-up examination prior to diagnosis. The test for trends through tertiles of UPF was determined with the median for each tertile category assigned to each participant in that category and then treating the variable as continuous. Considering UPF as a continuous variable, HR (95% CI) was also estimated per 10% increment in the proportion of energy intake from UPF consumption. We reported the results in unadjusted, sex- and BMI-adjusted, and multivariable adjusted models. We also created an additional model by including the Healthy Eating Index (HEI)-2015 [26] (continuous score) in the multivariable adjusted model to control the confounding potential of overall diet quality. We derived the HEI-2015 score, which ranges from 0 to 100 (higher values indicating better food quality), by combining the 13 dietary component scores [26, 27]. The variables included in the multivariable adjusted model were: sex (female/male), BMI (continuous), waist circumference adjusted for BMI (continuous), family history of diabetes (yes/no), education (low, middle, and high), energy intake (continuous), fasting glucose (continuous), triglycerides-to-HDL-C ratio (continuous), and hypertension (yes/no). We initially selected the covariates based on prior studies [16, 28, 29]. Variables that showed a univariate association with outcomes at a p-value less than 0.2 were then included in the statistical models. Age was defined as the time scale. We tested the proportional-hazard assumption using the Schoenfeld residual test, which confirmed the assumption's validity.

In the multivariable-adjusted model, we also examined the risk of pre-diabetes/T2D per 10% increment in UPF consumption in subgroups of sex, smoking (smokers and non-smokers (never-smoker and ex-smoker)), BMI status (<25 and ≥25 kg/m^2), abdominal obesity (yes/no), family history of diabetes (yes/no), and fiber intakes (≤9.1 and >9.1 g/1000 kcal). Abdominal obesity was defined as waist circumference≥89 cm in males and ≥91 cm in females [30]. Fiber intake was categorized based on the median intake of the study population. The P-value for the implicative interaction between each subgroup and UPF consumption on pre-diabetes/T2D was obtained with the inclusion of the interaction term in the unadjusted model.

The potential of non-linear associations between UPF and pre-diabetes/T2D was examined using restricted cubic spline regression in the multivariable adjusted model. We defined three knots at the 5th, 50th, and 90th percentiles of UPF, and we set the median of the lowest tertile of UPF as a reference.

Finally, the HR (95% CI) for pre-diabetes/T2D were separately estimated per one standard deviation increase in energy percentage from UPF components (the five categories) in the multivariable-adjusted model. Statistical analyses were performed using STATA 14 (StataCorp, College Station, Texas, USA).

Results

Ultra-processed food and pre-diabetes incidence

The mean baseline age of participants included in the pre-diabetes investigation was 37.9 years, and 53.7% were female. The median (25th, 75th percentiles) for UPF consumption was 91.2 g/day (54, 150) and 13.4% of energy (8.78, 19.0). The relative contributions of each component to total energy intake from UPF were as follows: hydrogenated fat, mayonnaise, and margarine (38.2%), packaged snacks and confectioneries (32.1%), dairy products (13.9%), ready-to-eat/heat dishes (12.4%), and soft drinks (3.3%).

Table 1 displays the demographic and clinical characteristics of participants at baseline, as well as their dietary intakes in the total population and across tertiles of UPF. Participants in the highest tertile of proportion UPF were younger, more likely to be female and living alone, and had lower BMI, waist circumference, fasting serum glucose, triglycerides-to-HDL-C ratio, and systolic and diastolic blood pressure compared to those in the lowest tertile. Energy and the proportion of dietary fat increased, while the proportion of dietary carbohydrates, protein, and HEI decreased from tertile 1 into tertile 3.

During a median (25th, 75th percentile) follow-up of 7 years (3.8, 8.9), pre-diabetes developed in 766 individuals. Table 2 shows the association between UPF consumption and the risk of pre-diabetes. In the unadjusted model, those within tertile 3 showed a 24% higher risk of pre-diabetes compared to those within tertile 1 (HR = 1.24; 95% CI = 1.04, 1.49). The increased risk remained significant

Table 1 Characteristics of participants for the pre-diabetes database in total and according to tertile categories of ultra-processed food consumption (% of daily energy intake) *

Characteristics	Total population	Tertile 1	Tertile 2	Tertile 3	*P*-value †
Number	1954	651	652	651	-
Median intakes, % kcal	13.4	6.83	13.4	21.4	-
Baseline characteristics					
Age, year	37.9 ± 12.7	42.6 ± 13.2	36.7 ± 12.0	34.3 ± 11.4	< 0.001
Female, n (%)	1049 (53.7)	343 (52.7)	332 (50.9)	374 (57.5)	0.050
Smoking status, n (%)					0.208
Never	1537 (78.7)	512 (79.2)	511 (78.5)	514 (78.6)	
Current	167 (8.5)	67 (10.3)	50 (7.7)	50 (7.7)	
Former	250 (12.8)	72 (11.1)	91 (14.0)	87 (13.4)	
Education, n (%)					0.001
Low	235 (12.0)	103 (15.8)	66 (10.1)	66 (10.1)	
Middle	1181 (60.4)	358 (55.0)	406 (62.3)	417 (64.1)	
High	538 (27.5)	190 (29.2)	180 (27.6)	168 (25.8)	
Full time job, n (%)	962 (49.2)	306 (47.0)	352 (54.0)	304 (46.7)	0.012
Marital status					< 0.001
Married	1446 (74.0)	514 (79.0)	488 (74.8)	444 (68.2)	
Living alone	508 (26.0)	137 (21.0)	164 (25.2)	207 (31.8)	
Low Physical activity level ‡, n (%)	740 (37.9)	242 (37.2)	246 (37.7)	252 (38.7)	0.846
Family history type 2 diabetes, %	618 (31.6)	228 (35.0)	183 (28.1)	207 (31.8)	0.026
Body mass index, kg/m^2	26.5 ± 4.58	27.1 ± 4.40	26.2 ± 4.53	26.3 ± 4.74	0.001
Waist circumference, Cm	88.1 ± 12.7	89.9 ± 11.6	87.4 ± 12.9	87.1 ± 13.4	< 0.001
Fasting blood glucose, mg/dL	85.1 ± 6.26	85.8 ± 6.06	84.8 ± 6.35	84.8 ± 6.32	0.004
Triglycerides-to-HDL-C ratio	1.16 (0.76, 1.86)	1.26 (0.81, 1.91)	1.09 (0.76, 1.82)	1.13 (0.70, 1.83)	< 0.001
Systolic blood pressure, mmHg	110 ± 15.2	112 ± 16.60	109 ± 14.87	108 ± 13.7	< 0.001
Diastolic blood pressure, mmHg	72.6 ± 10.3	74.2 ± 10.2	72.1 ± 10.4	71.6 ± 10.2	< 0.001
Anti-hypertensive mediation, n (%)	39 (2.0)	19 (2.9)	12 (1.8)	8 (1.2)	0.088
Dietary characteristics§					
Total energy intake, Kcal	2421 ± 786	2325 ± 750	2415 ± 748	2524 ± 845	< 0.001
Carbohydrate intake, % of energy	58.0 ± 6.31	61.2 ± 6.12	58.3 ± 5.29	54.7 ± 5.72	< 0.001
Fat intake, % of energy	30.8 ± 6.05	27.2 ± 5.13	30.4 ± 4.74	34.8 ± 5.65	< 0.001
Protein intake, % of energy	14.0 ± 2.25	14.9 ± 2.26	14.1 ± 2.00	13.2 ± 2.17	< 0.001
Ultra-processed food intake, % of energy	13.4 (8.78, 19.1)	6.83 (4.69, 8.78)	13.4 (11.9, 15.0)	21.4 (19.0, 25.4)	< 0.001
Healthy Eating Index-2015 score	63.8 ± 7.88	64.7 ± 8.70	63.7 ± 7.52	63.1 ± 7.27	< 0.001

* Results are reported as mean ± standard deviation, median (percentiles 25, 75), and number (percentage). † P-values show differences across tertiles based on ANOVA (normally distributed variables), the Kruskal-Wallis test (non-normally distributed variables), and the Chi-squared test (categorical variables). ‡ Less than 600 Met-min/week. § Cumulative average intake

Table 2 Hazard ratios (95% confidence intervals) for pre-diabetes incidence according to proportion of ultra-process food consumption

	Tertile 1	Tertile 2	Tertile 3	*p*-trend	Continuous (per 10% increment)	*p*-value
Ultra-processed food, % of energy						
Cases/populations	286/651	231/652	249/651	-	766/1954	-
Median intakes, % kcal	6.83	13.4	21.4	-	13.4	-
Unadjusted	1	0.95 (0.80,1.14)	1.24 (1.04,1.49)	0.014	1.11 (1.01,1.22)	0.028
Sex and BMI-adjusted	1	0.95 (0.79,1.13)	1.25 (1.05,1.49)	0.013	1.11 (1.01,1.21)	0.031
Multivariable adjusted *	1	0.99 (0.83,1.19)	1.28 (1.07,1.52)	0.007	1.12 (1.02,1.23)	0.014
Multivariable adjusted + diet quality †	1	0.99 (0.83, 1.18)	1.27 (1.06, 1.52)	0.009	1.12 (1.02, 1.23)	0.018

* Adjusted for sex, BMI (continuous), waist circumference adjusted for BMI (continuous), family history diabetes (yes/no), education (<6, 6–12, and ≥12 years of education), physical activity (<600 and ≥600 metabolic equivalent task minutes/week), energy intake (continuous), fasting serum glucose (continuous), triglycerides to HDL-C ratio, and hypertension (yes/no). Age is considered as the time scale. † Adjusted for all variables included in multivariable adjusted model plus Healthy Eating Index (HEI)-2015 (continuous)

in the sex- and BMI-adjusted model, as well as the multivariable-adjusted model. The HR for pre-diabetes was 1.28 (95% CI=1.07, 1.52) in tertile 3 compared to tertile 1 in the multivariable-adjusted model. When UPF was treated as a continuous variable, each 10% increase in UPF consumption was related to a 12% higher risk of pre-diabetes in the multivariable-adjusted model (HR=1.12; 95% CI=1.02, 1.23). Results did not change after the inclusion of HEI-2015 in the model.

Figure 2A demonstrates results for associations between UPF and pre-diabetes in different subgroups of participants. The HRs for pre-diabetes were more than 1 per 10% increase in UPF consumption in all subgroups, but the positive associations became significant in females (HR=1.14; 95% CI=1.00, 1.30), non-smokers (HR=1.14; 95% CI=1.03, 1.26), individuals with a BMI≥25 kg/m2 (HR=1.13; 95 CI=1.01, 1.25), and those without a family history of diabetes (HR=1.16; 95% CI=1.03, 1.30). However, no significant interaction was observed between each subgroup and UPF consumption on the risk of pre-diabetes.

Figure 3A demonstrates the spline curve for the association between UPF and pre-diabetes. This curve indicates a non-linear relationship between UPF and pre-diabetes, exhibiting a J-shaped pattern. Compared to the reference group for UPF consumption, the HR for pre-diabetes did not increase until consumption of UPF constituted about 24% of total energy intake.

Looking at individual UPF components (Supplementary Table), we found a 13% higher risk of pre-diabetes associated with one standard deviation increase in the proportion of energy intake from hydrogenated fat, mayonnaise, and margarine subgroups (HR=1.13; 95% CI=1.05, 1.22).

Ultra-processed food and type 2 diabetes incidence

The mean baseline age of 2457 individuals included in the diabetes investigation was 38.5 years, and 54.1% were female. The median (25th, 75th percentiles) for UPF consumption was 91.3 g/day (54.7, 151) and 13.1% of energy (8.7, 18.5). UPF components made comparable contributions to those in the pre-diabetes database.

Compared to the lowest tertile of UPF, participants in the highest tertile were younger, more likely to be female, less likely to be current smokers, and had a lower BMI, waist circumference, fasting serum glucose and triglycerides-to-HDL-C ratio, and systolic and diastolic blood pressure. From tertile 1 to 3, there was a significant increase in energy intake and the proportion of fat to total energy, while the proportion of carbohydrates and protein decreased. The overall quality of diet assessed as HEI was also decreased from tertile 1 to 3 of UPF consumption (Table 3).

We identified 258 new cases of T2D during a median (25th, 75th percentiles) follow-up of 8.6 years (6.5, 9.5). No significant association between UPF consumption and the risk of diabetes across the tertile categories of UPF and UPF as a continuous variable was observed (Table 4). Furthermore, the associations between UPF and T2D were not significant in any subgroups (Fig. 2B).

The spline curve suggested a non-linear risk pattern for T2D with UPF (J-shaped), but the T2D risk was not significantly higher compared to reference groups at any levels of UPF consumption (Fig. 3B).

None of the individual categories of UPF showed a significant association with the risk of T2D (Supplementary Table).

Discussion

In this prospective investigation, a higher intake of UPF significantly increased the risk of pre-diabetes. However, dose-response analysis revealed a J-shaped association between UPF and the risk of pre-diabetes, where the risk of pre-diabetes did not increase until UPF consumption exceeded about 24% of total energy intake. Of the individual UPF, hydrogenated fat/mayonnaise/ margarine showed a significant positive association with the risk of

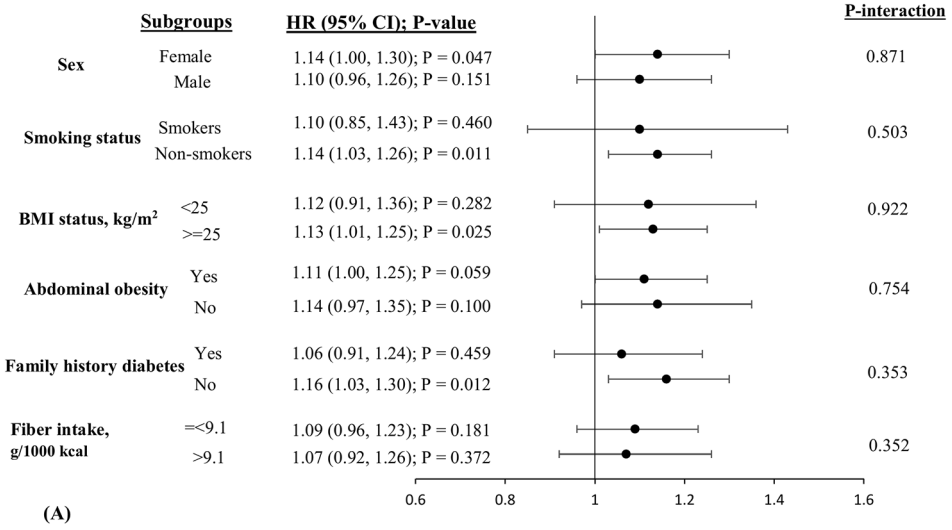

Fig. 2 Subgroup analysis of the association between ultra-processed food (per 10% increase as a percentage of daily energy intake) and risk of pre-diabetes (**A**) and type 2 diabetes (**B**). Adjusted for sex, BMI (continuous), waist circumference adjusted for BMI (continuous), family history diabetes (yes/no), education (< 6, 6–12, and ≥ 12 years of education), physical activity (< 600 and ≥ 600 metabolic equivalent task minutes/week), energy intake (continuous), fasting serum glucose (continuous), triglycerides to HDL-C ratio, and hypertension (yes/no). Age is considered as the time scale

pre-diabetes. This study found no significant association between UPF consumption and T2D risk.

Pre-diabetes is a highly prevalent condition with a substantial burden on human health [31]. Pre-diabetes can develop in one out of two individuals with normoglycemia. During their lifetime, 70–75% of individuals with pre-diabetes will develop T2D [32, 33]. In addition to T2D, the risk of diabetes-related complications, cardiovascular disease, cancer, and mortality increases in individuals with pre-diabetes [34–37]. The current study's findings, which show that UPF consumption increases the risk of pre-diabetes, are clinically significant, given the global increase in both UPF consumption and pre-diabetes prevalence. Although we could not find a significant association between UPF and T2D, the increased risk of pre-diabetes attributed to UPF may increase the risk of T2D in the future. The positive association was observed independent of energy and the overall quality of the diet, suggesting other characteristics of UPF may be involved in the association. Non-nutritive substances produced during industrial processing, such as advanced glycation end products and acrylamide, may increase insulin resistance. The endocrine-disrupting effects of substances added as emulsifiers, preservatives, flavoring, and coloring, as well as food-packaged substances such as bisphenols and phthalates, may also lead

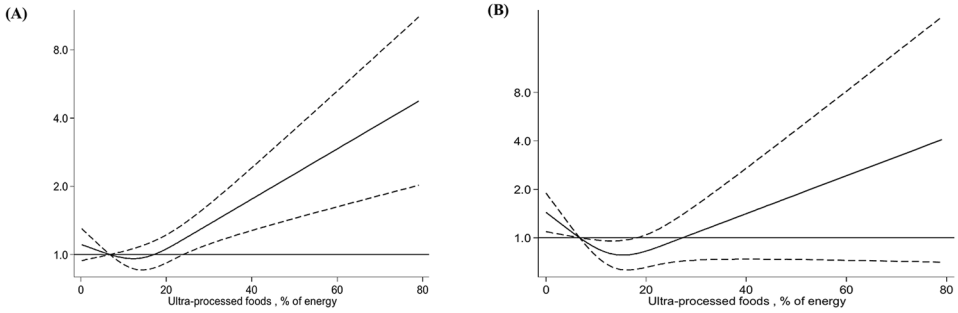

Fig. 3 Multivariable adjusted spline curve for association between ultra-processed foods and risk of pre-diabetes (**A**) and type 2 diabetes (**B**). Hazard ratio showed by solid line and 95% confidence interval by dash lines. Adjusted for sex, BMI (continuous), waist circumference adjusted for BMI (continuous), family history diabetes (yes/no), education (< 6, 6–12, and ≥ 12 years of education), physical activity (< 600 and ≥ 600 metabolic equivalent task minutes/week), energy intake (continuous), fasting serum glucose (continuous), triglycerides to HDL-C ratio, and hypertension (yes/no). Age is considered as the time scale. The median of ultra-processed food in the first tertile was used as the reference value

Table 3 Characteristics of participants for the type 2 diabetes database in total and according to tertile categories of ultra-processed food consumption (% of daily energy intake) *

Characteristics	Total population	Tertile 1	Tertile 2	Tertile 3	*P*-value †
Number	2457	818	820	819	-
Median intakes, % kcal	13.1	6.69	13.1	21.1	-
Baseline characteristics					
Age, year	38.5 ± 13.6	43.6 ± 13.8	37.4 ± 12.7	34.5 ± 12.6	< 0.001
Female, n (%)	1329 (54.1)	429 (52.4)	422 (51.5)	478 (58.4)	0.010
Smoking status, n (%)					0.045
Never	1936 (78.8)	648 (79.2)	644 (78.5)	644 (78.6)	
Current	208 (8.5)	83 (10.1)	68 (8.3)	57 (7.0)	
Former	313 (12.7)	87 (10.6)	108 (13.2)	118 (14.4)	
Education, n (%)					< 0.001
Low	633 (25.8)	155 (18.9)	100 (12.2)	78 (9.5)	
Middle	1491 (60.7)	431 (52.7)	521 (63.5)	539 (65.8)	
High	333 (13.6)	232 (28.4)	199 (24.3)	202 (24.7)	
Full time job, n (%)	1161 (47.3)	376 (46.0)	421 (51.3)	364 (44.4)	0.013
Marital status					< 0.001
Married	1792 (72.9)	653 (79.8)	607 (74.0)	532 (65.0)	
Living alone	665 (27.1)	165 (20.2)	213 (26.0)	287 (35.0)	
Low Physical activity level ‡, n (%)	957 (38.9)	316 (38.6)	313 (38.2)	328 (40.0)	0.719
Family history type 2 diabetes, n (%)	819 (33.3)	296 (36.2)	252 (30.7)	271 (33.1)	0.063
Body mass index, kg/m^2	26.8 ± 4.82	27.4 ± 4.52	26.7 ± 4.86	26.4 ± 5.03	< 0.001
Waist circumference, Cm	89.0 ± 13.3	90.9 ± 11.8	88.7 ± 13.5	87.3 ± 14.1	< 0.001
Fasting blood glucose, mg/dL	87.0 ± 8.62	88.2 ± 8.99	86.5 ± 8.29	86.2 ± 8.46	< 0.001
Triglycerides-to-HDL-C ratio	1.21 (0.77, 1.94)	1.34 (0.86, 2.07)	1.14 (0.77, 1.86)	1.14 (0.71, 1.88)	0.004
Systolic blood pressure, mmHg	111 ± 15.8	114 ± 16.8	110 ± 15.1	109 ± 15.1	< 0.001
Diastolic blood pressure, mmHg	73.2 ± 10.5	74.8 ± 10.1	72.7 ± 10.5	72.0 ± 10.7	< 0.001
Anti-hypertensive mediation, n (%)	61 (2.5)	29 (3.5)	17 (2.1)	15 (1.8)	0.055
Dietary characteristics§					
Total energy intake, Kcal	2424 ± 777	2322 ± 735	2449 ± 768	2502 ± 816	< 0.001
Carbohydrate intake, % of energy	58.1 ± 6.20	61.3 ± 6.16	58.3 ± 5.25	54.9 ± 5.47	< 0.001
Fat intake, % of energy	30.6 ± 5.86	26.9 ± 4.98	30.3 ± 4.61	34.5 ± 5.33	< 0.001
Protein intake, % of energy	14.1 ± 2.36	15.0 ± 2.47	14.3 ± 2.20	13.2 ± 2.06	< 0.001
Ultra-processed food intake, % of energy	13.1 (8.67, 18.5)	6.69 (4.73, 8.67)	13.1 (11.7, 14.7)	21.1 (18.5, 24.6)	< 0.001
Healthy Eating Index-2015 score	63.6 ± 7.97	64.4 ± 8.73	63.3 ± 7.78	63.1 ± 7.29	0.004

* Results are reported as mean ± standard deviation, median (percentiles 25, 75), and number (percentage). † P-values show differences across tertiles based on ANOVA (normally distributed variables), the Kruskal-Wallis test (non-normally distributed variables), and the Chi-squared test (categorical variables). ‡ Less than 600 Met-min/week. § Cumulative average intake

Table 4 Hazard ratio (95% confidence interval) for type 2 diabetes incidence according to ultra-process food consumption

	Tertile 1	Tertile 2	Tertile 3	*p*-trend	Continuous (per 10% increment)	*p*-value
Ultra-processed food, % of energy						
Cases/populations	111/818	73/820	74/819	-	258/2457	-
Median intakes, % kcal	6.69	13.1	21.1	-	13.1	-
Unadjusted	1	0.82 (0.60,1.10)	1.01 (0.75,1.37)	0.984	0.97 (0.81,1.16)	0.728
Sex and BMI-adjusted	1	0.77 (0.57,1.04)	0.94 (0.70,1.27)	0.661	0.93 (0.79,1.11)	0.448
Multivariable adjusted *	1	0.81 (0.60,1.10)	0.93 (0.68,1.26)	0.601	0.94 (0.79,1.12)	0.507
Multivariable adjusted + diet quality †	1	0.81 (0.60, 1.10)	0.94 (0.69, 1.28)	0.657	0.95 (0.79, 1.13)	0.556

* Adjusted for sex, BMI (continuous), waist circumference adjusted for BMI (continuous), family history diabetes (yes/no), education (<6, 6–12, and ≥12 years of education), physical activity (<600 and ≥600 metabolic equivalent task minutes/week), energy intake (continuous), fasting serum glucose (continuous), triglycerides to HDL-C ratio, and hypertension (yes/no). Age is considered as the time scale

† Adjusted for all variables included in multivariable adjusted model plus Healthy Eating Index (HEI)-2015 (continuous)

to glucose hemostasis impairment [5, 16]. Moreover, of the individual UPF items, hydrogenated fats/margarine/mayonnaise was related to an increased risk of pre-diabetes in our study, which partly may be due to their high content of saturated fatty acids and trans-fatty acids. Hydrogenated fats are the primary source of industrially produced trans fats [38, 39]. They are commonly utilized to produce other foods such as margarine, shortening, and bakery products. Industrial trans fatty acids, by altering lipid profiles and causing inflammation, may promote insulin resistance and reduce glucose tolerance [38].

Different subgroups had similar risk estimates for pre-diabetes for every 10% increase in UPF in the present study. However, the positive association was statistically significant in females, nonsmokers, individuals with a BMI of 25 kg/m2 or more, and people who did not have a family history of diabetes. Subgroup analyses revealed no significant interaction, suggesting the association between UPF and pre-diabetes may not vary based on sex, smoking status, BMI status, abdominal obesity, family history of diabetes, and dietary fiber intake.

Multiple studies, predominantly conducted among western populations, have reported the association between UPF and the risk of T2D. Prospective studies from the United Kingdom, Spain, the Netherlands, and the United States reported, respectively, a 44%, 53%, 56%, and 46% increased risk of T2D in the highest vs. lowest categories of UPF consumption [12–15]. A recent meta-analysis of 7 observational studies from western populations suggested a 37% higher risk of T2D in the highest vs. lowest categories of UPF intake (HR=1.37, 95% CI=1.20 to 1.56). However, there was moderate heterogeneity across the studies (I^2=52%) [8]. A Korean study indicates a lower magnitude of association between UPF and T2D, with a risk 32% higher in quartile 4 vs. 1 (HR=1.32; 95% CI=1.11, 1.56) [16]. Despite the overall positive association between extreme UPF consumption and the risk of T2D, some studies demonstrated no significant association in the middle UPF categories compared to the lowest category. For instance, the UK Biobank study found no association between the risk of T2D in the second and third quartiles of UPF, with respective mean contributions of 15.4% and 23.6%, and the increased risk of T2D compared to the first quartile [12]. In terms of weight ratio, the mean UPF consumption in our study was 5.4%, which was lower than France (17.3%), the United Kingdom (22.1%), Spain (9.5%), the Netherlands (35.9%), and the United States (36.1%). Therefore, the lower contribution of UPF in our study may lead to null findings for T2D. On the other hand, the Korean study, with a similar contribution to ours (4.9%), also reported an increased risk of T2D [16]. The Korean study's mean follow-up time was 12.9 years, which was higher than ours (mean: 7.8 years). This may indicate that our study's follow-up period may not be sufficient to observe the increased risk of T2D attributed to UPF consumption. Consistent with this hypothesis, a meta-analysis found that the risk of T2D for both moderate and high consumption of UPF was higher in studies lasting more than 10 years [40]. Differences in the contributions of food items to the total intake of UPF in our investigation compared to the other studies may also result in different findings. In the western population, sugary beverages, breads, and cereals have contributed most to the overall intake of UPF [12, 14, 15]. Moreover, sugary beverages in the western population include artificially sweetened beverages, but we have no data on artificially sweetened beverages. In the Korean study, sugar-sweetened beverages were the most commonly consumed UPF items, followed by ready-to-eat or heat-mixed dishes, including instant noodles and pizza/hamburgers [16]. Furthermore, despite using the NOVA definition to classify the foods as UPF in these studies, the definition of UPF is not uniform across the studies because the evaluation of some country-specific industrial products needs researchers' interpretation. Therefore, inconsistent findings may result from differences in the definition of overall UPF consumption among the studies [41].

The results of the current study provide some perspective about the association between UPF and T2D

in the Middle East region, with benefits from a population-based study of the TLGS. The association between UPF and T2D may vary in different regions because of differences in the amount of UPF, the contribution of their components, the degree of processing, and the composition of UPF across countries [5]. Therefore, this study offers a more comprehensive understanding of the associations between UPF and T2D compared to previous studies, most of which focused on western populations. Repeated assessments of dietary intakes during the follow-up and using the average intake are among the strengths of this study, which can reduce within-person variability and better capture the long-term dietary intake. Furthermore, we conducted various subgroup analyses to explore the potential influence of these variables on the relationship between UPF and pre-diabetes/T2D. Investigating the possibility of non-linear associations, which is a complement of the more general statistical methods of categorization and linearization, is another strength of the study. This study also provides evidence on the association between UPF and pre-diabetes that has not been previously examined.

The investigation is, however, subject to certain limitations. First, the FFQ did not include all varieties of UPF items due to its lack of a specific design to evaluate UPF intake. Additionally, the FFQ lacked detailed information about the distinction between industrial and non-industrial types of certain food items. Therefore, there is a likelihood of underestimating UPF consumption and misclassifying food items. Nevertheless, the absence of dietary assessment methods that are specifically designed to assess food processing is a common limitation of the existing studies on the association between UPF and diabetes. Indeed, only a few questionnaires exist at present that specifically designed to evaluate food processing using NOVA classification. However, the generalizability of these questionnaires to other populations is restricted [41]. Second, despite the FFQ's demonstrated reliability and validity for measuring food intakes [18], the data collected by this questionnaire are susceptible to self-reporting bias [42]. Third, the study's participants were adults living in a district of Tehran, which is not a nationally representative sample. Therefore, the findings of the study have limited generalizability. Finally, despite controlling for most potential covariates, residual or unmeasured (i.e., alcoholic drinks) confounders may still exist.

Conclusion

In conclusion, we observed a positive, non-linear association between total UPF consumption and the risk of pre-diabetes. Total UPF was not significantly related to the risk of T2D. More research is required in the Middle East regions to determine whether the UPFs should be regarded as a potential dietary risk factor for pre-diabetes/T2D.

Abbreviations

ANOVA	Analysis of Variance
BMI	Body Mass Index
CI	Confidence Interval
FFQ	Food Frequency Questionnaire
T2D	Type 2 Diabetes
HDL-C	High Density Lipoprotein Cholesterol
HR	Hazard Ratio
TLGS	Tehran Lipid and Glucose Study
UPF	ultra-processed food

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12986-024-00854-4.

Supplementary Material 1

Acknowledgements

We thank the participants in the Tehran Lipid and Glucose Study for their enthusiastic participation and the personnel of the Research Institute for Endocrine Sciences, Tehran Lipid and Glucose Study Unit, for their invaluable assistance.

Author contributions

NM: The conception and design of the study, conducted statistical analyses, and drafted the manuscript. MM : conducted statistical analyses and helped in interpretation and preparation of the manuscript. PM and FA: Conceptual design of the study and contributed to the critical revision of the manuscript. All authors read and approved the final manuscript.

Funding

This work was supported by Shahid Beheshti University Medical Sciences, Tehran, Iran. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The research ethics committees of the Research Institute for Endocrine Sciences at Shahid Beheshti University of Medical Sciences granted approval for the current study (IR.SBMU.ENDOCRINE.REC.1403.023). Everyone who participated in the Tehran Lipid and Glucose Study provided informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Nutrition and Endocrine Research Center, Research Institute for Endreocrine Sciences, Shahid Beheshti University of Medical Sciences, No. 24, Shahid Arabi St., Yemen Blvd., Chamran Exp., Tehran 1985717413, Iran
[2]Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Department of Clinical Nutrition and Dietetics, Faculty of Nutrition and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, No. 7, Shahid Hafezi St., Farahzadi Blvd., Shahrak-e-qods, Tehran 1985717413, Iran

[4]Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: 13 June 2024 / Accepted: 17 September 2024
Published online: 09 October 2024

References

1. Monteiro CA, Moubarac JC, Cannon G, et al. Ultra-processed products are becoming dominant in the global food system. Obes Rev. 2013;14:21–8.
2. Marino M, Puppo F, Del Bo' C, et al. A systematic review of worldwide consumption of ultra-processed foods: findings and criticisms. Nutrients. 2021;13:2778.
3. Ruggiero E, Esposito S, Costanzo S, et al. Ultra-processed food consumption and its correlates among Italian children, adolescents and adults from the Italian Nutrition & Health Survey (INHES) cohort study. Public Health Nutr. 2021;24:6258–71.
4. Mirmiran P, Moslehi N, Golzarand M, et al. Ultra-processed foods consumption and the risk of metabolically unhealthy phenotype in normal-weight and overweight/obese adults: a prospective investigation. Int J Food Sci Nutr. 2023;74:522–31.
5. Almarshad MI, Algonaiman R, Alharbi HF, et al. Relationship between ultra-processed food consumption and risk of diabetes mellitus: a mini-review. Nutrients. 2022;14:2366.
6. Martini D, Godos J, Bonaccio M, et al. Ultra-processed foods and nutritional dietary profile: a meta-analysis of nationally representative samples. Nutrients. 2021;13:3390.
7. Pagliai G, Dinu M, Madarena M, et al. Consumption of ultra-processed foods and health status: a systematic review and meta-analysis. Br J Nutr. 2021;125:308–18.
8. Vitale M, Costabile G, Testa R, et al. Ultra-processed foods and human health: a systematic review and meta-analysis of prospective cohort studies. Adv Nutr. 2024;15:100121.
9. Bonaccio M, Di Castelnuovo A, Costanzo S, et al. Ultra-processed food consumption is associated with increased risk of all-cause and cardiovascular mortality in the Moli-Sani Study. Am J Clin Nutr. 2021;113:446–55.
10. Yuan L, Hu H, Li T, et al. Dose-response meta-analysis of ultra-processed food with the risk of cardiovascular events and all-cause mortality: evidence from prospective cohort studies. Food Funct. 2023;14:2586–96.
11. Srour B, Fezeu LK, Kesse-Guyot E, et al. Ultraprocessed food consumption and risk of type 2 diabetes among participants of the NutriNet-Santé prospective cohort. JAMA Intern Med. 2020;180:283–91.
12. Levy RB, Rauber F, Chang K, et al. Ultra-processed food consumption and type 2 diabetes incidence: a prospective cohort study. Clin Nutr. 2021;40:3608–14.
13. Llavero-Valero M, Escalada-San Martín J, Martínez-González MA, et al. Ultra-processed foods and type-2 diabetes risk in the SUN project: a prospective cohort study. Clin Nutr. 2021;40:2817–24.
14. Duan M-J, Vinke PC, Navis G, et al. Ultra-processed food and incident type 2 diabetes: studying the underlying consumption patterns to unravel the health effects of this heterogeneous food category in the prospective Lifelines cohort. BMC Med. 2022;20:7.
15. Chen Z, Khandpur N, Desjardins C, et al. Ultra-processed food consumption and risk of type 2 diabetes: three large prospective US cohort studies. Diabetes Care. 2023;46:1335–44.
16. Cho Y, Ryu S, Kim R, et al. Ultra-processed food intake and risk of type 2 diabetes in Korean adults. J Nutr. 2024;154:243–51.
17. Azizi F, Zadeh-Vakili A, Takyar M. Review of rationale, design, and initial findings: Tehran lipid and glucose study. Int J Endocrinol Metab. 2018;16(4 Suppl):e84777.
18. Mirmiran P, Esfahani FH, Mehrabi Y, et al. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. Public Health Nutr. 2010;13:654–62.
19. Esfahani FH, Asghari G, Mirmiran P, et al. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran lipid and glucose study. J Epidemiol. 2010;20:150–8.
20. Moubarac J-C, Parra DC, Cannon G, et al. Food classification systems based on food processing: significance and implications for policies and actions: a systematic literature review and assessment. Curr Obes Rep. 2014;3:256–72.
21. Monteiro CA, Cannon G, Levy RB, et al. Ultra-processed foods: what they are and how to identify them. Public Health Nutr. 2019;22:936–41.
22. Momenan AA, Delshad M, Sarbazi N et al. Reliability and validity of the Modifiable Activity Questionnaire (MAQ) in an Iranian urban adult population. 2012.
23. Romaguera D, Ängquist L, Du H, et al. Dietary determinants of changes in waist circumference adjusted for body mass index–a proxy measure of visceral adiposity. PLoS ONE. 2010;5:e11588.
24. Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. JAMA. 2003;289:2560–71.
25. ElSayed NA, Aleppo G, Aroda VR, et al. 2. Classification and diagnosis of diabetes: standards of care in diabetes—2023. Diabetes Care. 2023;46:S19–40.
26. Reedy J, Lerman JL, Krebs-Smith SM, et al. Evaluation of the healthy eating Index-2015. J Acad Nutr Diet. 2018;118:1622–33.
27. National Cancer Institute. HEI-2015 Dietary Components, constituents, and Scoring standards. https://epi.grants.cancer.gov/hei/hei-2020-table1.html. Updated Feb 22, 2022.
28. Bozorgmanesh M, Hadaegh F, Ghaffari S, et al. A simple risk score effectively predicted type 2 diabetes in Iranian adult population: population-based cohort study. Eur J Public Health. 2011;21:554–9.
29. Hu PL, Koh YLE, Tan NC. The utility of diabetes risk score items as predictors of incident type 2 diabetes in Asian populations: an evidence-based review. Diabetes Res Clin Pract. 2016;122:179–89.
30. Delavari A, Forouzanfar MH, Alikhani S, et al. First nationwide study of the prevalence of the metabolic syndrome and optimal cutoff points of waist circumference in the Middle East: the national survey of risk factors for noncommunicable diseases of Iran. Diabetes Care. 2009;32:1092–7.
31. Hostalek U. Global epidemiology of prediabetes-present and future perspectives. Clin Diabetes Endocrinol. 2019;5:5.
32. Tabák AG, Herder C, Rathmann W, et al. Prediabetes: a high-risk state for diabetes development. Lancet. 2012;379:2279–90.
33. Ligthart S, van Herpt TT, Leening MJ, et al. Lifetime risk of developing impaired glucose metabolism and eventual progression from prediabetes to type 2 diabetes: a prospective cohort study. Lancet Diabetes Endocrinol. 2016;4:44–51.
34. Huang Y, Cai X, Chen P, et al. Associations of prediabetes with all-cause and cardiovascular mortality: a meta-analysis. Ann Med. 2014;46:684–92.
35. Huang Y, Cai X, Mai W, et al. Association between prediabetes and risk of cardiovascular disease and all cause mortality: systematic review and meta-analysis. BMJ. 2016;355:i5953.
36. Keesari PR, Jain A, Ganampet NR, et al. Association between prediabetes and breast cancer: a comprehensive meta-analysis. Breast Cancer Res Treat. 2024;204:1–13.
37. Schlesinger S, Neuenschwander M, Barbaresko J, et al. Prediabetes and risk of mortality, diabetes-related complications and comorbidities: umbrella review of meta-analyses of prospective studies. Diabetologia. 2022;65:275–85.
38. Kummerow FA. The negative effects of hydrogenated trans fats and what to do about them. Atherosclerosis. 2009;205:458–65.
39. Bhandari SD, Delmonte P, Honigfort M, et al. Regulatory changes affecting the production and use of fats and oils: focus on partially hydrogenated oils. J Am Oil Chem Soc. 2020;97:797–815.
40. Delpino FM, Figueiredo LM, Bielemann RM, et al. Ultra-processed food and risk of type 2 diabetes: a systematic review and meta-analysis of longitudinal studies. Int J Epidemiol. 2022;51:1120–41.
41. Dinu M, Bonaccio M, Martini D, et al. Reproducibility and validity of a food-frequency questionnaire (NFFQ) to assess food consumption based on the NOVA classification in adults. I Int J Food Sci Nutr. 2021;72:861–9.
42. Althubaiti A. Information bias in health research: definition, pitfalls, and adjustment methods. J Multidiscip Healthc. 2016;9:211–7.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.