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Association between dietary phytochemical index, cardiometabolic risk factors and metabolic syndrome in Switzerland. The CoLaus study

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Abstract *Background and aims:* Plant-based diets are associated with reduced cardiometabolic risk factors (CRFs) and lower risk of metabolic syndrome (MetS), probably via phytochemicals acting synergistically. However, dietary phytochemical content estimation is challenging; therefore, the dietary phytochemical index (DPI) was proposed as a practical way to assess total dietary phytochemical content from phytochemical-rich foods (PRFs). We evaluated the association between DPI with CRFs and MetS and its components.

Methods and results: Cross-sectional analysis of 2009–2012 data of Colaus cohort study (Lausanne, Switzerland), including 3879 participants (mean age 57.6 ± 10.4 years, 53.5% women). Dietary intake was assessed via a validated food frequency questionnaire. DPI was calculated as the total energy intake percentage obtained from PRFs consumption and assessed as quartiles. Associations were determined using multivariable linear and logistic regression for CRFs and MetS, respectively. Median DPI value was 25.5 (interquartile range: 17.7–34.6). After multivariable-adjusted analyses, significant inverse associations were observed between the last two highest DPI quartiles and waist circumference (WC), body mass index (BMI), insulin, leptin, and hs-CRP. No significant associations were observed for MetS or its components except for central obesity, as subjects in the highest DPI quartile had lower odds (OR: 0.78; 95% CI: 0.62, 0.97) than those in lowest quartile.

Conclusion: A diet high in PRFs assessed via DPI is associated with lower WC, BMI, insulin, leptin, hs-CRP values, and lower odds of central obesity, indicating a potential protective effect of phytochemical intake on these CRFs and highlighting the importance of high PRFs intake in promoting cardiometabolic health.

Acronyms: CHUV, Lausanne University Hospital; CRFs, cardiometabolic risk factors; BP, blood pressure; MetS, metabolic syndrome; DPI, dietary phytochemical index; PRF, phytochemical-rich foods; CVD, cardiovascular disease; PBD, Plant-based diets; FFQ, food frequency questionnaires; hs-CRP, high-sensitive C-reactive protein; BMI, Body mass index; TNF-α, tumor necrosis factor-alpha; IL-6, interleukin-6; IL-1β, interleukin-1β; IDF, International Diabetes Federation; T2D, type 2 diabetes; WC, waist circumference; TC, total cholesterol.

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1. Introduction

Cardiometabolic risk factors (CRFs) include altered body weight, high blood pressure (BP), and metabolic disturbances related to glycemia, insulin, and lipids homeostasis. Clustering these conditions is known as metabolic syndrome (MetS), which increases cardiovascular disease (CVD) and type 2 diabetes (T2D) risk [1]. Plant-based diets (PBD), in which plant foods (mainly fruits, vegetables, nuts, and whole grains) provide most of the caloric intake, have been associated with reduced CRFs and MetS incidence [2,3]. This effect is partly mediated by the high amount of phytochemicals in PBD, including polyphenols and other bioactive compounds like carotenoids, glucosinolates, alkaloids, phytosterols, and fibers, among others [4–6]. There are approximately 27 000 reported phytochemicals in human foods; however, studies on the cardioprotective effects of phytochemicals focus on specific individual bioactive compounds or groups of phytochemicals and their action mechanisms; this approach does not reflect the complexity of dietary patterns in which the vast array of phytochemicals and their interactions need to be considered [7–9]. Furthermore, dietary phytochemical intake estimation is challenging; it relies mainly on linking food frequency questionnaires (FFQ) to food composition databases including phytochemicals, which is not always feasible due to high costs or accuracy as many databases are outdated or incomplete [10,11].

Therefore, to facilitate assessing the impact of diets high in phytochemical-rich foods (PRFs) and to better understand the effects of phytochemicals mixtures found in the human diet on health outcomes, a “Dietary phytochemical index” (DPI) was developed as a rough index of total dietary phytochemical content [12]. The DPI estimates the percentage of daily dietary calories supplied by PRFs, including fruits, vegetables, legumes, nuts, seeds, extra-virgin olive oil, whole grains, and alcoholic beverages such as wine, beer, and cider. Hence, a dietary pattern based mainly on healthy plant-based food could have a DPI value close to 100% and be associated with better health outcomes.

Evidence from cross-sectional studies conducted in Iran and South Korea has linked DPI with CRFs [13–17] and MetS [18–20], with inconsistent findings. Moreover, those associations are yet unexplored in European populations having different dietary patterns that could affect phytochemical intake. Therefore, we aimed to explore the association between DPI and CRFs and MetS in a population-based study of middle age participants living in Switzerland. We hypothesized that a higher DPI is inversely associated with CRFs and MetS.

2. Methods

2.1. Study population

Cross-sectional analysis of the CoLaus cohort, a population-based study on the epidemiology and genetic determinants of CRFs in Lausanne, Switzerland [21]. A representative sample was collected through simple, non-stratified random sampling of 19 830 individuals (35% of source population) aged between 35 and 75. Between June 2003 and May 2006, 6733 participants were enrolled. The first follow-up, conducted between April 2009 and September 2012, included 5064 of the initial participants and collected information on dietary intake for the first time; therefore, only data from this follow-up was used for the present study.

2.2. Dietary assessment and DPI calculation

Dietary intake for the previous four weeks was assessed using a validated, self-administered, semi-quantitative FFQ, including portion size [22]. The FFQ includes 97 food items accounting for more than 90% intake of calories, proteins, fat, carbohydrates, alcohol, vitamin D, retinol, and 85% of fiber, carotene, and iron. Seven consumption frequencies were provided for each item, and participants indicated the average serving size (smaller, equal, or bigger) compared with a reference size. Intake frequency was multiplied by the nutrient composition of the specified portion size expressed in milliliters (for drinks) and grams (for other food items) to determine caloric intake, which was based on the French CIQUAL food composition table [23].

DPI was operationalized as the percentage of dietary calories derived from foods rich in phytochemicals following McCarthy’s proposal [12]:

$$DPI = \frac{daily\ energy\ intake\ derivated\ from\ phytochemical\ rich\ foods\ (kcal)}{total\ daily\ energy\ intake\ (kcal)} \text{ x } 100$$

PRFs items available from FFQ included in the calculation as part of the numerator were whole grains (whole wheat bread, rye bread, and muesli), vegetables (green beans,

spinach, cauliflower, broccoli, tomatoes, carrots, green salad, green peas, corn, maize, avocado, natural vegetable soups, tomato sauce, and tofu), fruits (banana, apple, pear, plum, grapes, orange, mandarine, peach, apricot, melon, berries, kiwi, preserved fruit and fresh fruit juice), olive oil (for cooking), and alcohol (beer, wine, and champagne).

2.3. Outcomes measurement

CRFs included waist circumference (WC), body mass index (BMI), systolic and diastolic BP, fasting glucose, insulin, leptin, adiponectin, total, HDL and LDL-cholesterol, triglycerides, high-sensibility C reactive protein (hs-CRP), tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β). MetS and its components were defined according to the International Diabetes Federation (IDF) criteria [24] as follows: central obesity (waist circumference >94 cm in males, >80 cm in females), hypertension (systolic: $\geq$130 mm Hg or Diastolic: $\geq$85 mm Hg), hyperglycemia (fasting plasma glucose $\geq$5.6 mmol/l or previously diagnosed T2D), low HDL-cholesterol (<1.03 mmol/l in males & <1.29 mmol/l in females), hypertriglyceridemia ($\geq$1.7 mmol/l or specific treatment for this abnormality) and MetS (central obesity plus any other two additional components).

Body weight and height were measured with participants standing and wearing light indoor clothes without shoes. Body weight was measured in kilograms to the nearest 0.1 kg using a Seca® scale (Hamburg, Germany). Height was measured to the nearest 5 mm using a Seca® height gauge (Hamburg, Germany) [21]. BMI was computed and categorized according to World Health Organization guidelines, namely [25] undernourished (<18.5), normal (18.5 to <25), overweight (25 to <30), and obesity ($\geq$30). Waist and hip circumferences were measured as recommended [26]. BP was measured thrice on the left arm, with an appropriately sized cuff, after at least 10-min rest in seated position using an Omron® HEM-907 automated oscillometric sphygmomanometer (Matsusaka, Japan), and the last two measurements average was used for analyses [21].

Venous blood samples (50 ml) were drawn after overnight fasting. Chemistry assays, including glucose, insulin and serum lipids, were performed by Lausanne University Hospital (CHUV) Clinical Laboratory on fresh blood samples, whereas Pathway Diagnostics (Los Angeles, CA) measured adiponectin and leptin using enzyme-linked immunoassay (ELISA) (R&D Systems Inc.). CHUV Clinical Laboratory also measured TNF-α, IL-6, and IL-1β using multiplex particle-based flow cytometric cytokine assay (Luminex®) with the lowest detection limit of 0.2 pg/ml hs-CRP was assessed by immunoassay and latex HS (IMMULITE 1000—High; Diagnostic Products Corporation, Los Angeles, CA, USA) [21].

2.4. Covariates

Data on demographic characteristics and lifestyle information were collected using self-administered questionnaires. Confounding factors considered in adjustment were age (continuous), sex, educational level (university, high school, apprenticeship, and primary), physical activity (assessed by questionnaire [27] and expressed as total minutes/day), smoking status (never, former, and current), alcohol intake (abstainers, low, moderate and high intake), antihypertensive, hypolipidemic, antidiabetic or cardiovascular treatment, family history of CVD (presence of myocardial infarction or stroke in any of both parents), T2D and CVD presence (defined if participants reported it or if use of antidiabetes or cardiovascular treatment was indicated) and BMI (except for BMI as outcome and WC).

2.5. Inclusion and exclusion criteria

Inclusion criteria were written informed consent and willingness to participate in an interview, physical examination, and providing blood samples. Exclusion criteria were i) missing data on anthropometric measures, BP, dyslipidemia, insulin resistance, inflammation markers, and dietary caloric intake, ii) ongoing inflammation/infectious disorders (hs-CRP >20 mg/l) and iii) abnormal total energy intake (<850 kcal/day and >4500 kcal/day).

2.6. Statistical analysis

Statistical analyses were performed using Stata version 17.0 for Windows (Stata Corp, College Station, Texas, USA). Participants were categorized in DPI quartiles, and characteristics were assessed across groups and expressed as mean (standard deviation) or median (range or interquartile range) for continuous variables and as absolute numbers of participants (percentage) for categorical variables. Between-categories comparisons were made using ANOVA or Kruskal-Wallis's test for continuous variables and chi-square for categorical variables. Normal distribution of continuous variables was checked using histograms and the Shapiro-Francia test. Outcomes with a non-normal distribution (glucose, insulin, leptin, adiponectin, triglycerides, and inflammatory markers) were log-transformed. Multivariable analyses were performed using i) linear regression models for associations with CRFs and ii) logistic regression for associations with MetS and its components. In both cases, DPI was analyzed as continuous and categorical variable with the estimation of p-values for linear trend. Statistical significance was established for a two-sided test with $p < 0.05$.

2.7. Sensitivity analysis

Characteristics between included and excluded participants were compared to assess selection bias using chi-square or Student t-test. To assess the robustness of findings, interaction and subgroup analyses were applied for age (40—60 years and >60 years), sex, educational attainment (university, High school, Apprenticeship and Primary), alcohol intake (non-drinker, low intake, moderate intake, high intake) and BMI (undernourished, normal weight, overweight and obesity); these variables were selected based on

their known influence on cardiometabolic risk factors and their potential influence on the association with DPI. As alcohol has health-related harms and is a controversial DPI component, analyses with an index excluding alcohol items were performed. Lastly, non-linear DPI associations with MetS and its components were explored using cubic spline analysis with the multivariable models and four randomly assigned and connected knots.

3. Results

3.1. Participants characteristics

Of the 5064 participants in the first follow-up, 3879 (53% women, mean age 57.6 ± 10.4 years, MetS prevalence 36.8%) were included (Fig. 1). Their general characteristics across DPI quartiles are presented in Table 1. The higher the DPI quartile, the higher the participants' age, the woman's prevalence, the educational level, the percentage of non-smokers, alcohol consumers, familiar CVD antecedents, and the hypolipidemic drugs and dietary supplements used. Regarding CRFs distribution, participants in higher DPI quartiles had lower BMI, WC, insulin, adiponectin, triglycerides, and hs-CRP values and higher HDL-cholesterol. For the distribution of MetS and its components, the higher the DPI quartile, the lower the percentage of participants with hypertriglyceridemia and low HDL-cholesterol.

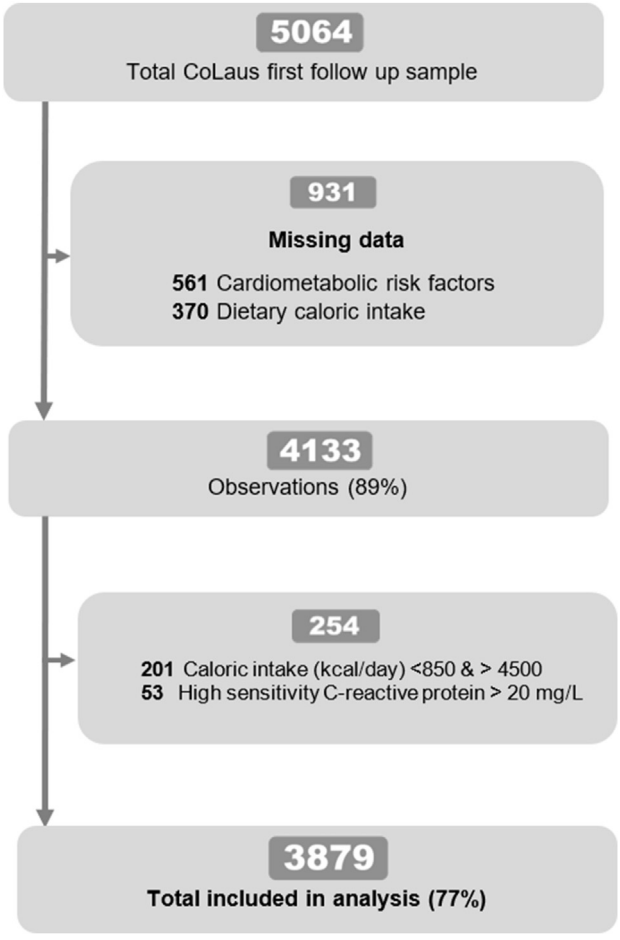

Fig. 1 Flowchart of participant selection.

3.2. Dietary intake across DPI quartiles

The median (IQR) DPI value for the included population was 25.5 (17.7–34.6). Table 1 shows a decrease in total daily energy intake and an increase in the daily energy intake from PRFs from the first to the last quartile. Distribution of PRFs intake across DPI quartiles is provided in Fig. 2. Compared with reference quartile (Q1), participants in fourth quartile (Q4) had a higher intake of vegetables, olive oil, whole grains and fruits. Alcohol consumption was higher in the third quartile (Q3). Fig. 3 displays the percentual PRFs caloric contribution to each DPI quartile. Fruits had the higher caloric contribution in all quartiles, followed by whole grains in Q4 and Q3 and vegetables in Q1.

3.3. Association of DPI with cardiometabolic risk factors

Table 2 reports associations of DPI quartiles with CRFs. In unadjusted analyses, inverse associations with WC, BMI, insulin, triglycerides, hs-CRP, TNF-α, and IL-1β and direct associations with adiponectin and HDL-cholesterol were observed. After multivariable-adjusted analyses, only inverse associations for WC, BMI, insulin, and hs-CRP remained significant. An inverse association emerged for leptin. No other associations were found for CRFs.

3.4. Association of DPI with metabolic syndrome and its components

Table 3 reports associations of DPI quartiles with MetS and its components. No associations for MetS were observed. Regarding MetS components, in unadjusted analyses, 35% and 36% lower odds of low HDL-cholesterol (OR: 0.65; 95% CI: 0.49, 0.87) and hypertriglyceridemia (OR: 0.64; 95% CI: 0.52, 0.79) were found in participants in Q4 compared to Q1. In multivariable-adjusted analyses, the above associations disappeared, but a 22% lower odds of central obesity (OR: 0.78; 95% CI: 0.62, 0.97) was revealed for individuals in Q4 compared to Q1.

3.5. Sensitivity analyses

Differences in characteristics between included and excluded participants are provided in Supplementary Table 1. Excluded participants had lower DPI values, lower educational levels, and a lower percentage of alcohol and dietary supplements intake; they had a higher percentage of smokers, T2D, family history of CVD, and antihypertensive and anti-diabetes medication use. Excluded participants also had higher values of BMI, WC, insulin resistance and T2D markers, triglycerides, hs-CRP, and IL-6 while presenting lower HDL- and LDL-cholesterol values. Prevalence of MetS and its components (except for hypertension) was also higher among excluded individuals.

Table 1 Characteristics of participants across DPI quartiles; CoLaus study, Lausanne, Switzerland, 2009–2012.

	DPI				
	Q1 (n = 972)	Q2 (n = 981)	Q3 (n = 960)	Q4 (n = 966)	p Value
DPI %, mean (SD)	12.5 (3.7)	21.6 (2.2)	29.8 (2.6)	43.4 (7.3)	
Daily total energy intake (Kcal/day), median (IQR)	1743 (1403–2211)	1730 (1384–2179)	1685 (1342–2087)	1681 (1330–2092)	**0.004**
Daily total energy intake (KJoules/day), median (IQR)	7293 (5870–9251)	7238 (5791–9117)	7050 (5615–8732)	7033 (5565–8753)	
Daily energy intake from PRFs (Kcal/day), median (IQR)	217 (155–297)	372 (295–468)	493 (393–623)	721 (569–914)	**< 0.001**
Daily energy intake from PRFs (KJoules/day), median (IQR)	908 (649–1243)	1556 (1234–1958)	2063 (1644–2607)	3017 (2381–3824)	
Demographic and lifestyle factors					
Age, mean (SD)	55.6 (10.5)	56.5 (10.1)	58.3 (10.4)	60.0 (10.0)	**< 0.001**
Sex, n (% women)	96 (40.7)	481 (49.0)	555 (57.8)	642 (66.4)	**< 0.001**
Ethnicity, n (% Caucasian)	896 (92.1)	919 (93.6)	906 (94.3)	904 (93.5)	0.26
Education attainment, n (%)					**0.007**
University	193 (19.8)	210 (21.4)	202 (21.0)	264 (27.3)	
High school	257 (26.4)	268 (27.3)	255 (26.5)	254 (26.2)	
Apprenticeship	367 (37.8)	348 (35.4)	360 (37.5)	301 (31.1)	
Primary	154 (15.8)	155 (15.8)	142 (14.8)	147 (15.2)	
Physical activity (total minutes/day), mean (SD)	440 (183)	436 (174)	443 (162)	447 (161)	0.57
Smoking status, n (%)					**< 0.001**
Current	242 (24.9)	199 (20.3)	184 (19.2)	161 (16.6)	
Former	325 (33.4)	392 (40.0)	371 (38.7)	399 (41.3)	
Never	404 (41.6)	388 (39.3)	402 (42.0)	406 (42.0)	
Alcohol intake (units/week), median (IQR)	3 (0–7)	4 (1–10)	4 (1–10)	4 (1–8)	**< 0.001**
Alcohol abstainers, n (%)	272 (28.0)	219 (22.0)	179 (19.0)	238 (25.0)	**< 0.001**
History of Hypertension, n (% yes)	389 (40.0)	399 (41.0)	394 (41.0)	398 (41.0)	0.95
History of CVD, n (% yes)	64 (6.6)	66 (6.7)	68 (7.1)	70 (7.2)	0.93
History of T2D, n (% yes)	83 (8.5)	96 (9.7)	96 (10.0)	89 (9.2)	0.69
Family history of CVD, n (% yes)	290 (35)	298 (35.7)	342 (41.2)	347 (41.8)	**0.004**
Treatments, n (% yes)					
Antihypertensive	252 (25.9)	247 (25.1)	251 (26.1)	262 (27.1)	0.80
Hypolipidemic	172 (17.7)	180 (18.3)	210 (21.8)	233 (24.1)	**0.001**
Antidiabetic	34 (3.5)	48 (4.8)	44 (4.5)	53 (5.4)	0.20
Dietary supplements consumption, n (% yes)	23 (2.3)	57 (5.8)	52 (5.4)	64 (6.6)	**< 0.001**
Cardiovascular risk factors distribution					
BMI, kg/m^2, mean (SD)	26.5 (4.7)	26.1 (4.5)	25.9 (4.1)	25.3 (4.3)	**< 0.001**
BMI categories n (%)					**< 0.001**
Normal	373 (38.3)	403 (41.1)	404 (42.1)	485 (50.2)	
Overweight	395 (40.6)	394 (40.1)	406 (42.2)	343 (35.5)	
Obesity	190 (19.5)	171 (17.4)	137 (14.2)	124 (12.8)	
Waist circumference, cm, mean (SD)	93.6 (13.5)	92.2 (12.6)	91.2 (12.3)	89 (12.3)	**< 0.001**
Systolic blood pressure (mm Hg), mean (SD)	125.8 (18.3)	125.7 (17.5)	126.3 (17.3)	126.2 (18.7)	0.88
Diastolic blood pressure (mm Hg), mean (SD)	78.4 (11.3)	78.2 (11.0)	78.3 (10.3)	77.5 (10.8)	0.27
Fasting glucose (mmol/L), median (IQR)[a]	5.7 (5.3–6.1)	5.7 (5.3–6.1)	5.7 (5.3–6.1)	5.6 (5.3–6.0)	0.10
Insulin (microIU/mL), median (IQR)[a]	6.9 (4.7–10.5)	6.8 (4.4. – 10.6)	6.3 (4.4–9.2)	6.0 (4.0–8.9)	**< 0.001**
Leptin (ng/mL), median (IQR)[a]	2.48 (0.91–6.52)	2.69 (0.93–6.40)	2.83 (1.07–6.44)	2.76 (1.04–6.32)	0.80
Adiponectin (μg/mL), median (IQR)[a]	3.39 (2.13–5.27)	3.58 (2.33–5.65)	3.94 (2.55–6.33)	4.38 (2.66–6.94)	**< 0.001**
Total cholesterol (mmol/L), mean (SD)	5,69 (1.00)	5.70 (1.02)	5.69 (1.05)	5.74 (1.03)	0.63
HDL-cholesterol (mmol/L), mean (SD)	1,56 (0.44)	1.62 (0.43)	1.67 (0.45)	1.73 (0.46)	**< 0.001**
LDL-cholesterol (mmol/L), mean (SD)	3,50 (0.92)	3.49 (0.91)	3.41 (0.93)	3.44 (0.92)	0.12

Triglycerides (mmol/L), median (IQR)[a]	1.2 (0.8−1.7)	1.1 (0.8−1.6)	1.1 (0.8−1.6)	1.1 (0.8−1.5)	**<0.001**
hs-CRP (mg/L), median (IQR)[a]	1.4 (0.7−2.8)	1.3 (0.7−2.8)	1.3 (0.7−2.4)	1.1 (0.6−2.3)	**<0.001**
TNFa (pg/mL), median (IQR)[a]	4.91 (2.81−8.68)	4.72 (2.45−8.19)	4.56 (2.58−7.98)	4.62 (2.42−7.92)	0.11
IL-6 (pg/mL), median (IQR)[a]	2.62 (0.98−7.87)	2.30 (0.89−7.60)	2.67 (1.01−8.14)	2.41 (0.92−7.79)	0.25
Il-1b (pg/mL), median (IQR)[a]	0.68 (0−2.41)	0.50 (0−2.48)	0.64 (0−2.60)	0.62 (0−2.13)	0.28
Distribution by metabolic syndrome and its components, n (%)					
Metabolic Syndrome (according to IDF criteria)[b]	374 (38.4)	349 (35.5)	361 (37.6)	347 (35.9)	0.49
Central obesity	611 (62.8)	637 (64.9)	636 (66.2)	608 (62.9)	0.33
Hypertension	505 (51.9)	500 (50.9)	522 (54.3)	522 (54.0)	0.36
Hyperglycemia	562 (57.8)	577 (58.8)	572 (59.5)	532 (55.0)	0.20
Low HDL-cholesterol	129 (13.2)	88 (8.9)	81 (8.4)	88 (9.1)	**0.001**
Hypertriglyceridemia	267 (27.4)	220 (22.4)	221 (23.0)	188 (19.4)	**<0.001**

Q, quartile. IQR, Interquartile range. SD, standard deviation. Kcal, kilocalorie. CVD, Cardiovascular disease. T2D, Type 2 diabetes. BMI, Body mass index. Kg, kilogram. m2, square meter. cm, centimeter. mm Hg, millimeter of mercury. mmol, millimole. L, Litter. microIU, micro-international unit. mL, milliliter. ng, nanogram. μg, micrograms. HDL, high-density lipoprotein. LDL, low-density lipoprotein. hs-CRP, high sensitivity C-reactive protein. TNFa, Tumor necrosis factor. Pg, picogram. IL-6, interleukin 6. IL-1b, Interleukin 1b.

Values expressed as mean ± standard deviation, median (interquartile range), or number of participants (percentage). Between-group comparisons made using chi-square for categorical variables and ANOVA or Kruskal-Wallis's test for continuous variables.

[a] Crude values. Transformation of values done in logarithmic scale before testing for statistical significance.

[b] Metabolic Syndrome components definition (according to IDF criteria): central obesity (waist circumference >94 cm in males, >80 cm in females), hypertension (Systolic: ≥130 mm Hg or Diastolic: ≥85 mm Hg), hyperglycemia (Fasting plasma glucose ≥5.6 mmol/l or previously diagnosed T2D), low HDL-cholesterol (<1.03 mmol/l in males & <1.29 mmol/l in females), hypertriglyceridemia (≥1.7 mmol/l or specific treatment for this abnormality). Metabolic Syndrome definition (according to IDF criteria): central obesity plus any other two additional components.

	Quartile 1 n = 972	Quartile 2 n = 981	Quartile 3 n = 960	Quartile 4 n = 960
Dietary phytochemical index %	13 (10, 16)	22 (20, 24)	30 (27, 32)	42 (40, 47)
Whole grains (grams/day)	4 (0, 16)	17 (2, 45)	48 (16, 75)	75 (37, 150)
Vegetables (grams/day)	134 (88, 193)	155 (111, 219)	174 (120, 249)	183 (123, 281)
Fruits (grams/day)	110 (54, 181)	194 (109, 324)	262 (143, 412)	428 (222, 635)
Olive oil (milliliters/day)	3 (1, 7)	5 (2, 10)	5 (4, 10)	7 (4, 10)
Alcoholic beverages (milliliters/day)	38 (5, 108)	59 (13, 161)	75 (13, 177)	59 (13, 155)

Fig. 2 Phytochemical-rich food groups' daily intake across DPI quartiles.
Results are expressed as median (range).

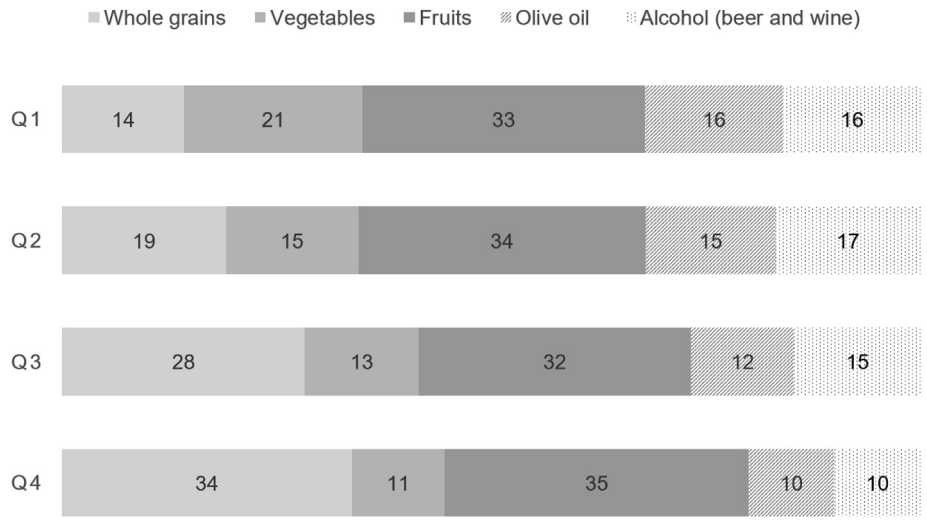

Fig. 3 Contribution of food groups' caloric intake across DPI quartiles.
Q, quartile.
Results are expressed as a percentage.

When considering potential effect modifications by several key variables, we found significant main effects of age on insulin ($p = 0.004$) and central obesity ($p = 0.02$), of sex on adiponectin ($p = 0.001$), and of alcohol intake on hypertension ($p = 0.03$). Upon further investigation in subgroup analyses (Supplementary Tables 1–6a), the significant association between DPI and WC persisted across age categories, women, those with high school and apprenticeship, and participants with low alcohol intake and abstainers. The association between DPI and BMI remained significant for age stratification, women, those with high school and apprenticeship, and those with low alcohol intake. The significant association observed for insulin remained only for individuals younger than 60 (confirming the interaction test results), both sexes, all educational levels except primary, those with adequate weight and overweight, and participants with low and high alcohol consumption. Regarding leptin associations, results after stratification remained significant for most subgroups, except for participants with primary education, those undernourished and with obesity, and those with low and high alcohol intake. The association between DPI and hs-CRP levels was significant only in participants younger than 60, both sexes, all educational levels except

Table 2 Associations of DPI across quartiles with cardiometabolic risk factors; CoLaus study, Lausanne, Switzerland, 2009–2012.

	DPI				
	Q1 (n = 972)	Q2 (n = 981)	Q3 (n = 960)	Q4 (n = 966)	p Trend[a]
Anthropometric measurements					
Waist circumference (cm)					**< 0.001**
Model 1		−1.40* (−2.53,-0.27)	−2.40** (−3.54,-1.26)	−4.56** (−5.69,-3.42)	
Model 2	Reference	−0.87 (−1.89, 0.15)	−1.55* (−2.59,-0.52)	−3.42** (−4.47,-2.37)	
Model 3		−0.85 (−1.97, 0.26)	−0.80 (−1.94, 0.34)	−2.79** (−3.94,-1.64)	
Body mass index (kg/m^2)					**< 0.001**
Model 1		−0.37 (−0.76, 0.03)	−0.65* (−1.05,-0.26)	−1.21** (−1.60,-0.81)	
Model 2	Reference	−0.31 (−0.69, 0.08)	−0.58* (−0.97,-0.19)	−1.12** (−1.52,-0.72)	
Model 3		−0.34 (−0.75, 0.07)	−0.34 (−0.77, 0.08)	−0.91** (−1.33,-0.48)	
Blood pressure					
Systolic blood pressure (mm Hg)					0.512
Model 1		−0.13 (−1.73, 1.47)	0.46 (−1.15, 2.07)	0.32 (−1.29, 1.92)	
Model 2	Reference	−0.03 (−1.42, 1.36)	0.07 (−1.35, 1.48)	−0.60 (−2.04, 0.83)	
Model 3		0.38 (−1.19, 1.95)	−0.19 (−1.79, 1.42)	−0.38 (−2.00, 1.25)	
Diastolic blood pressure (mm Hg)					0.572
Model 1		−0.24 (−1.21, 0.72)	−0.16 (−1.13, 0.81)	−0.91 (−1.88, 0.06)	
Model 2	Reference	0.01 (−0.94, 0.96)	0.28 (−0.68, 1.25)	−0.27 (−1.25, 0.70)	
Model 3		0.07 (−0.99, 1.13)	−0.04 (−1.12, 1.04)	−0.29 (−1.39, 0.80)	
Markers of insulin resistance and diabetes					
Log Fasting glucose (mmol/L)					0.676
Model 1		−0.001 (−0.02, 0.01)	−0.001 (−0.01, 0.01)	−0.01 (−0.02, 0.001)	
Model 2	Reference	0.001 (−0.01, 0.01)	0.001 (−0.01, 0.01)	−0.001 (−0.02, 0.01)	
Model 3		−0.001 (−0.01, 0.01)	0.001 (−0.01, 0.01)	0.001 (−0.01, 0.01)	
Log Insulin (microIU/mL)					**< 0.001**
Model 1		−0.01 (−0.07, 0.04)	−0.09* (−0.15,-0.03)	−0.14** (−0.20,-0.08)	
Model 2	Reference	−0.01 (−0.07, 0.04)	−0.10** (−0.15,-0.04)	−0.16** (−0.22,-0.10)	
Model 3		−0.02 (−0.07, 0.04)	−0.08* (−0.13,-0.02)	−0.10** (−0.16,-0.05)	
Log Leptin (ng/mL)					**< 0.001**
Model 1		0.04 (−0.08, 0.16)	0.06 (−0.06, 0.18)	0.05 (−0.07, 0.17)	
Model 2	Reference	−0.08 (−0.18, 0.03)	−0.20** (−0.31,-0.09)	−0.35** (−0.46,-0.24)	
Model 3		−0.07 (−0.17, 0.03)	−0.14* (−0.24,-0.04)	−0.22** (−0.32,-0.11)	
Log Adiponectin (ng/mL)					0.126
Model 1		0.07* (0.01, 0.14)	0.18** (0.11, 0.24)	0.25** (0.18, 0.31)	
Model 2	Reference	0.02 (−0.04, 0.08)	0.06* (0.001, 0.12)	0.06* (0.001, 0.12)	
Model 3		−0.001 (−0.07, 0.07)	0.03 (−0.04, 0.10)	0.05 (−0.02, 0.11)	
Dyslipidemia markers					
Total cholesterol (mmol/L)					0.259
Model 1		0.02 (−0.07, 0.11)	0.001 (−0.09, 0.09)	0.05 (−0.04, 0.15)	
Model 2	Reference	−0.01 (−0.10, 0.08)	−0.06 (−0.15, 0.04)	−0.03 (−0.13, 0.06)	
Model 3		−0.06 (−0.16, 0.04)	−0.10 (−0.20, 0.001)	−0.05 (−0.15, 0.05)	
HDL-cholesterol (mmol/L)					0.158
Model 1		0.06* (0.02, 0.10)	0.12** (0.08, 0.16)	0.18** (0.14, 0.22)	
Model 2	Reference	0.03 (−0.01, 0.07)	0.05* (0.01, 0.08)	0.07** (0.03, 0.10)	
Model 3		0.001 (−0.04, 0.04)	0.02 (−0.02, 0.05)	0.03 (−0.01, 0.06)	
LDL-cholesterol (mmol/L)					0.097
Model 1		−0.01 (−0.10, 0.07)	−0.09* (−0.17,-0.01)	−0.06 (−0.14, 0.02)	
Model 2	Reference	−0.02 (−0.10, 0.07)	−0.09* (−0.18,-0.01)	−0.07 (−0.15, 0.02)	
Model 3		−0.04 (−0.13, 0.05)	−0.11* (−0.21,-0.02)	−0.06 (−0.15, 0.03)	
Log Triglycerides (mmol/L)					0.408
Model 1		−0.05* (−0.10,-0.01)	−0.05* (−0.10,-0.01)	−0.10** (−0.14,-0.06)	
Model 2	Reference	−0.04 (−0.08, 0.001)	−0.03 (−0.07, 0.01)	−0.06* (−0.10,-0.02)	
Model 3		−0.03 (−0.07, 0.02)	−0.01 (−0.06, 0.04)	−0.03 (−0.07, 0.02)	
Cardiovascular/Inflammatory markers					
Log hs-CRP (mg/L)					**< 0.001**
Model 1		−0.04 (−0.13, 0.05)	−0.10* (−0.19,-0.01)	−0.19** (−0.28,-0.11)	
Model 2	Reference	−0.06 (−0.15, 0.03)	−0.16** (−0.25,-0.07)	−0.29** (−0.38,-0.20)	
Model 3		−0.03 (−0.12, 0.06)	−0.12* (−0.21,-0.02)	−0.18** (−0.28,-0.09)	
Log TNF-alpha (pg/mL)					0.097
Model 1		−0.08 (−0.17, 0.01)	−0.08 (−0.18, 0.01)	−0.11* (−0.20,-0.01)	
Model 2	Reference	−0.08 (−0.18, 0.01)	−0.09 (−0.18, 0.001)	−0.12* (−0.21,-0.02)	
Model 3		−0.07 (−0.17, 0.04)	−0.07 (−0.18, 0.04)	−0.10 (−0.21, 0.01)	
Log Interleukin 6 (pg/mL)					0.781
Model 1		−0.05 (−0.19, 0.10)	0.08 (−0.07, 0.22)	−0.06 (−0.21, 0.08)	
Model 2	Reference	−0.04 (−0.18, 0.11)	0.10 (−0.05, 0.25)	−0.03 (−0.18, 0.12)	
Model 3		−0.09 (−0.27, 0.08)	0.08 (−0.10, 0.25)	−0.03 (−0.21, 0.15)	

(*continued on next page*)

Table 2 (*continued*)

	DPI				
	Q1 (n = 972)	Q2 (n = 981)	Q3 (n = 960)	Q4 (n = 966)	p Trend[a]
Log Interleukin 1b (pg/mL)					0.249
Model 1		−0.01 (−0.16, 0.15)	−0.01 (−0.16, 0.15)	−0.16* (−0.32,-0.01)	
Model 2	Reference	0.01 (−0.15, 0.16)	0.03 (−0.12, 0.19)	−0.10 (−0.26, 0.06)	
Model 3		−0.001 (−0.18, 0.18)	0.03 (−0.16, 0.21)	−0.12 (−0.30, 0.06)	

Q, quartile. cm, centimeter. Kg, kilogram. m2, square meter. mm Hg, millimeters of mercury. mmol, millimole. L, liter. microIU, microInternational units. mL, mililiter. ng, nanogram. mg, milligram. pg, picogram. Log, Log-transformed variable. HDL, high-density lipoprotein. LDL, low-density lipoprotein. hs-CRP, High sensitivity C-reactive protein. TNF-alpha, tumor necrosis factor-alpha.
Values expressed as standardized regression coefficients β and (95% confidence interval).
Q1: reference group.
P-value: *= <0.05 **= <0.001.
Model 1: crude model. Model 2: adjusted by age and sex. Model 3: additionally adjusted by educational level, smoking status, alcohol consumption, physical activity, lipid-lowering medication use (statins, only for serum lipids), antihypertensive medication use (only for blood pressure), antidiabetic drug treatment use (only for markers of insulin resistance and diabetes), cardiovascular medication use (only for blood pressure and serum lipids), family history of CVD, presence of T2D, presence of CVD and BMI (except for waist circumference and body mass index as outcomes).
[a] P-trend estimated for Model 3.

primary, individuals with normal weight, and those with low alcohol intake. For central obesity, results were significant only for women (as indicated by interaction analyses), participants older than 60 or with low alcohol intake. When excluding alcoholic sources of phytochemicals from the DPI, all significant results were maintained, and J-shaped significant associations were observed for total cholesterol (TC) and LDL-cholesterol (Supplementary Table 6b). Finally, there was no evidence of non-linear associations between DPI and MetS and its components after cubic spline analyses (Supplementary Fig. 1).

4. Discussion

To our knowledge, this is the first study in a European country associating total dietary phytochemical intake using DPI with CRFs, MetS, and its components. Our results indicate an inverse association between DPI and WC, BMI, insulin, leptin, hs-CRP, and lower odds of central obesity for participants in the highest DPI quartile. No other significant associations were observed in the primary analyses.

4.1. Dietary intake across DPI quartiles

The observed distribution of total and PRF-derived daily energy intake across quartiles suggests that, when applying DPI, emphasis should not only be on the quantity but also the sources of calories consumed, particularly PRFs. By prioritizing the consumption of PRFs, individuals in the higher quartiles increase their phytochemical intake without merely relying on higher caloric intake. This highlights the importance of considering the quality and composition of the diet when evaluating the association between dietary phytochemical intake and CRFs. When food groups were assessed as DPI caloric contributors, fruits were the principal contributor in each quartile, followed by whole grains, highlighting the importance of these food groups as DPI contributors. Furthermore, the relative contribution of alcoholic beverages decreased as quartiles increased. This decrease can be attributed to the higher caloric intake from other PRFs, such as whole grains and fruits, as mentioned above. The findings suggest that participants in higher DPI quartiles prioritize healthier PRFs, leading to a more balanced dietary pattern.

4.2. Association of DPI with cardiometabolic risk factors

After multivariable-adjusted analyses, DPI was inversely associated with WC, BMI, insulin, leptin, and hs-CRP. Associations for anthropometric measures remained in most stratified analyses and were in line with results reported in a systematic review assessing the results of two cross-sectional and one longitudinal studies [28], but contrary to two Iranian cross-sectional studies [15,16]. In our Q4 participants, the high intake of fruits and whole grains rich in phytochemicals and with a low glycemic index could support our results as these food groups have been inversely related to weight gain and WC [29] owing to mechanisms like fatty acid β-oxidation stimulation, increased thermogenesis, appetite suppression and anti-adipogenic effects of phytochemicals [16,30,31]. It should be noted that attributing these results to either a lower caloric intake, the phytochemicals' effects, or a combination of both, remains challenging. For insulin, the inverse association varied according to subgroup analyses but is consistent with those reported in an Iranian longitudinal study [32]; certain phytochemicals, particularly polyphenols, have been shown to regulate insulin production and secretion, protect pancreatic β-cells and enhance the uptake of insulin-dependent glucose transporter 4 (GLUT4) [33]. The inverse association for leptin persisted robustly, being this the first time associations between DPI, leptin and adiponectin are described. Phytochemical supplementation in animal and human studies seemed to decrease leptin secretion and serum levels and increase its hypothalamic signaling [31,34]. Finally, hs-CRP inverse association remained only when stratified by sex and for

Table 3 Associations of DPI across quartiles with metabolic syndrome and its components; CoLaus study, Lausanne, Switzerland, 2009–2012.

	DPI				
	Q1 (n = 972)	Q2 (n = 981)	Q3 (n = 960)	Q4 (n = 966)	p Trend[a]
Metabolic syndrome (N cases)	374	349	361	347	0.176
Model 1		1.04 (0.87, 1.25)	1.08 (0.90, 1.29)	0.89 (0.75, 1.07)	
Model 2	1.0 (Reference)	1.11 (0.92, 1.35)	1.18 (0.97, 1.43)	0.97 (0.79, 1.18)	
Model 3		0.96 (0.76, 1.20)	1.00 (0.79, 1.26)	0.84 (0.66, 1.06)	
Central obesity (N cases)	611	637	636	608	**0.046**
Model 1		1.09 (0.91, 1.32)	1.16 (0.96, 1.40)	1.00 (0.83, 1.21)	
Model 2	1.0 (Reference)	1.01 (0.83, 1.22)	0.95 (0.78, 1.16)	0.72** (0.59, 0.87)	
Model 3		1.03 (0.82, 1.28)	1.05 (0.84, 1.32)	0.78* (0.62, 0.97)	
Hypertension (N cases)	505	500	522	522	0.407
Model 1		0.96 (0.80, 1.15)	1.10 (0.92, 1.32)	1.09 (0.91, 1.30)	
Model 2	1.0 (Reference)	0.94 (0.77, 1.14)	1.02 (0.83, 1.24)	0.90 (0.74, 1.11)	
Model 3		0.97 (0.74, 1.28)	1.13 (0.86, 1.49)	1.04 (0.78, 1.38)	
Hyperglicemia (N cases)	562	577	572	532	0.554
Model 1		1.04 (0.87, 1.25)	1.08 (0.90, 1.29)	0.89 (0.75, 1.07)	
Model 2	1.0 (Reference)	1.11 (0.92, 1.35)	1.18 (0.97, 1.43)	0.97 (0.79, 1.18)	
Model 3		1.16 (0.92, 1.46)	1.17 (0.92, 1.48)	1.08 (0.85, 1.37)	
Low HDL-cholesterol (N cases)	129	88	81	88	0.891
Model 1		0.64* (0.48, 0.86)	0.60** (0.45, 0.81)	0.65* (0.49, 0.87)	
Model 2	1.0 (Reference)	0.67* (0.50, 0.90)	0.67* (0.49, 0.90)	0.77 (0.57, 1.03)	
Model 3		0.84 (0.59, 1.20)	0.82 (0.56, 1.18)	1.01 (0.70, 1.46)	
Hypertriglyceridemia (N cases)	267	220	221	188	0.365
Model 1		0.76* (0.62, 0.94)	0.79* (0.64, 0.97)	0.64** (0.52, 0.79)	
Model 2	1.0 (Reference)	0.80* (0.65, 0.99)	0.89 (0.72, 1.10)	0.76* (0.61, 0.95)	
Model 3		0.88 (0.69, 1.14)	0.92 (0.71, 1.19)	0.85 (0.65, 1.11)	

Q, quartile. Ref, reference.
Metabolic Syndrome components definition (according to IDF criteria): central obesity (waist circumference >94 cm in males, >80 cm in females), hypertension (Systolic: ≥130 mm Hg or Diastolic: ≥85 mm Hg), hyperglycemia (Fasting plasma glucose ≥5.6 mmol/l or previously diagnosed T2D), low HDL-cholesterol (<1.03 mmol/l in males & <1.29 mmol/l in females), hypertriglyceridemia (≥1.7 mmol/l or specific treatment for this abnormality). Metabolic Syndrome definition (according to IDF criteria): central obesity plus any other two additional components.
Values expressed as odds ratios and (95% confidence interval).
Q1: reference group.
P-value: *=<0.05 **=<0.001.
Model 1: crude model. Model 2: adjusted by age and sex. Model 3: additionally adjusted by educational level, smoking status, alcohol consumption, physical activity, lipid-lowering medication use (statins, only for serum lipids), antihypertensive medication use (only for blood pressure), antidiabetic drug treatment use (only for markers of insulin resistance and diabetes), cardiovascular medication use (only for blood pressure and serum lipids), family history of CVD, presence of T2D, presence of CVD and BMI (except for waist circumference and body mass index as outcomes).
[a] P-trend estimated for Model 3.

most educational levels; this finding differs from two Iranian cross-sectional studies [13,14] but coincides with a South Korean cross-sectional study [17] and a Swiss cross-sectional article [35] reporting inverse associations between a dietary pattern high in fruits and vegetables and inflammatory markers. Polyphenols, flavonoids, and carotenoids regulate hs-CRP serum levels by inhibiting pro-inflammatory enzymes, removing and diminishing reactive-oxygen species and free radicals production, protecting cells from oxidative stress and inflammation, and blocking neural signalization to lymphocytes B [17]. Overall, our results suggest that high PRFs intake is associated with lower WC, BMI, insulin, leptin, and hs-CRP levels.

4.3. Association of DPI with metabolic syndrome and its components

After confounders adjustment, no association was observed for MetS; as for its components, only 22% decreased odds for central obesity among participants in Q4 compared to Q1 was found. Two recently published meta-analyses [33,36] on DPI associations with MetS support our findings for central obesity. Possible explanations imply higher dietary fiber and protein intake and lower dietary fat and reduced caloric intake from PRFs [33], which have also been shown to reduce oxidative stress, promote thermogenesis, inhibit adipocyte differentiation, and reduce adipogenesis [36]. Still, after sex subgroup analyses, results remained significant only for women, suggesting other mechanisms are implied. Phytochemicals like resveratrol, carotenoids, and phytosterols could improve hormone levels and emulate the estrogen role in regulating female body weight [33,36]. Overall, our results indicate that high PRFs intake decreases the odds of central obesity, particularly in those older than 60, women, and participants with low alcohol intake.

The analyses robustness with a DPI excluding alcoholic beverages and the observation of new associations for TC and LDL-cholesterol is a relevant finding. Given the health-

related consequences of alcohol consumption [37], we consider it possible to formulate a healthier DPI calculation without including alcoholic phytochemical sources. Lastly, the dose-response relation between DPI and MetS and its components showed a general protective trend for DPI at higher values (i.e., highest quartile) for all MetS components and without indications of non-linearity. Similar findings were reported in South Korean cross-sectional studies for central obesity [18] and hypertension [38].

4.4. Strengths and limitations

This is the first study conducted in a European population that assessed the associations between DPI and several CRFs, MetS, and its components, addressing an important research gap as previous studies have predominantly centered on populations in Iran and South Korea, regions characterized by different dietary patterns and phytochemical intake compared to European countries. Another novel contribution of our study is exploring the association between DPI and adipokines, namely leptin and adiponectin, shedding light on novel pathways through which a high dietary phytochemical intake may influence cardiometabolic health. We have also incorporated several interactions and subgroup analyses (age, educational attainment, BMI, and alcohol intake) not previously explored in studies investigating DPI and CRFs, and MetS. Lastly, we introduced a modified version of the DPI, excluding alcoholic beverage items. Comparing the results between the original DPI and our modified version represents a novel approach, as previous studies conducted in Iran and South Korea omitted alcoholic beverages from their main analysis due to cultural and religious aspects. Our findings with the modified DPI demonstrated robustness and unveiled additional inverse associations between the modified DPI and serum lipids, indicating that including alcoholic beverage items in DPI is unnecessary.

We also recognize limitations. First, cross-sectional designs cannot discard reverse causality directionality. To reduce its impact, individuals with characteristics possibly influencing diet were excluded, we controlled for several confounders, and additionally, some of our findings align with results on DPI associations from cohort studies [29,32,39]. Second, our sample size is smaller than studies reporting significant associations between DPI and MetS [19,38]; therefore, we might be unpowered to find other reported associations. Third, we cannot dismiss a selection bias toward healthier participants being included, as indicated by sensitivity analysis; this bias is common in observational studies, and its impact is hard to determine [40]. Fourth, the FFQ used in this study does not include PRFs groups like pulses, nuts, and seeds, which have been included in other studies with different findings than ours [13,15,19,20]; this might have led to lower DPI values and thus biased estimates. Fifth, the original DPI does not consider the correlations between energy and phytochemical content of the included foods, as it does not include phytochemical-rich non-caloric beverages like tea and coffee [12], which intake is common in the Swiss population. Future studies should develop a modified DPI version considering these issues. Finally, given the nature of our design, sources for residual confounding like inter-individual variability related to phytochemicals bioavailability and variability on PRFs phytochemical content (due to seasonality, cultivar, and preservation, among others) must be considered.

4.5. Public health/clinical implications and future outlook

Evidence to understand phytochemicals' interactions and their potential human health implications is becoming stronger than for individual compounds [8]. DPI, proposed as a simple and inexpensive method for total phytochemical intake assessment, can be considered a proxy for PBD, providing insights into diet quality and promoting healthy and sustainable dietary patterns that contribute to planetary health.

So far, no cut-off point for an ideal DPI value has been set; however, our results indicate dietary energy intake from PRFs close to 40% could benefit cardiometabolic health and agrees with results from a longitudinal study for weight control [29]. This threshold might be used as guideline in clinical settings when using DPI to evaluate a healthy diet. Nevertheless, any increase beyond 40% should be encouraged by promoting whole grains and fruit intake, which could lead to higher health benefits than those observed in this study; these PRFs consumption was low than the recommended amount for Swiss population [41], and their health benefits have been repeatedly shown. Pulses are sustainable and affordable PRFs; more European intake studies are required to validate their contribution to cardiometabolic health [42]. Further research on DPI associations with cardiometabolic health should consider a healthier reformulation of the original index by including phytochemical-rich beverages like green tea and coffee despite their null caloric contribution [43,44] and conversely, excluding alcoholic beverages items given the well-established hazardous effects of alcohol intake on overall health [37]. Additionally, as the energy content of PRFs may not necessarily correlate with their actual phytochemical intake, assigning weights to phytochemical-rich food groups based on their phytochemical content when calculating the index could potentially address this concern. These proposed adaptations would enhance the precision and utility of DPI, advancing our understanding of the complex interplay between overall dietary phytochemical intake and health outcomes. Lastly, it is crucial to advance research on total dietary phytochemical intake using DPI and cardiometabolic health by making prospective analyses and comparing DPI with other established dietary indices.

In conclusion, the primary contributors to DPI calculation were fruits and whole grains, particularly in the last two quartiles. A high DPI is associated with lower WC, BMI, insulin, leptin, and hs-CRP values indicating a potential protective effect of high dietary phytochemical intake on these factors. A high DPI is also associated with lower odds

of central obesity, particularly in people older than 60 and women. Notably, a DPI that excluded alcoholic beverages revealed robust results and uncovered additional associations with TC and LDL cholesterol when compared with original DPI formulation. Future research applying DPI should consider correlations between phytochemicals and energy contents of food and the incorporation of phytochemical-rich non-caloric beverages. Overall, our findings support the importance of considering the intake of PRFs to promote cardiometabolic health and sustainable dietary patterns that contribute to individual and planetary health.

Authors' contributions

MG, OHF, TM, and PMV: conceptualization and methodology. MG: investigation, data curation, formal analysis, writing - original draft. ZMRD, PFR, M-Gl, AB, TM, OHF, and PMV: writing – review, and editing. OHF and PMV: supervision. PMV: data manager. All authors read and approved final manuscript.

Ethical disclosure

The institutional Ethics Committee of the University of Lausanne, which afterward became the Ethics Commission of Canton Vaud (www.cer-vd.ch), approved the baseline CoLaus study (reference 16/03). The approval was renewed for the first follow-up (reference 33/09). The full decisions of the CER-VD can be obtained from the authors upon request. The study was performed in agreement with the Helsinki Declaration and its former amendments and in accordance with the applicable Swiss legislation. All participants gave their signed informed consent before entering the study.

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Data availability

Information on data availability can be found in the supplementary material.

Declaration of competing interest

The authors have nothing to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2023.07.018.

References

[1] Tune JD, Goodwill AG, Sassoon DJ, Mather KJ. Cardiovascular consequences of metabolic syndrome. Transl Res 2017;183:57–70. https://doi.org/10.1016/j.trsl.2017.01.001.
[2] Cicero AFG, Fogacci F, Colletti A. Food and plant bioactives for reducing cardiometabolic disease risk: an evidence based approach. Food Funct 2017;8:2076–88. https://doi.org/10.1039/C7FO00178A.
[3] Noce A, Di Lauro M, Di Daniele F, Pietroboni Zaitseva A, Marrone G, Borboni P, et al. Natural bioactive compounds useful in clinical management of metabolic syndrome. Nutrients 2021;13. https://doi.org/10.3390/nu13020630.
[4] Thakur M, Singh K, Khedkar R. 11 - phytochemicals: Extraction process, safety assessment, toxicological evaluations, and regulatory issues. In: Prakash B, editor. Functional and preservative properties of phytochemicals. Academic Press; 2020. p. 341–61.
[5] Sharifi-Rad J, Rodrigues CF, Sharopov F, Docea AO, Can Karaca A, Sharifi-Rad M, et al. Diet, lifestyle and cardiovascular diseases: linking pathophysiology to cardioprotective effects of natural bioactive compounds. Int J Environ Res Publ Health 2020;17. https://doi.org/10.3390/ijerph17072326.
[6] Parihar A, Parihar MS. Bioactive food components in the prevention of cardiovascular diseases. In: Mérillon J-M, Ramawat KG, editors. Bioactive molecules in food. Cham: Springer International Publishing; 2017. p. 1–21.
[7] Jacobs DR, Tapsell LC. Food synergy: the key to a healthy diet. Proc Nutr Soc 2013;72:200–6. https://doi.org/10.1017/S0029665112003011.
[8] Natarajan TD, Ramasamy JR, Palanisamy K. Nutraceutical potentials of synergic foods: a systematic review. J Ethnic Foods 2019;6:27. https://doi.org/10.1186/s42779-019-0033-3.
[9] Barabási A-L, Menichetti G, Loscalzo J. The unmapped chemical complexity of our diet. Nature Food 2020;1:33–7. https://doi.org/10.1038/s43016-019-0005-1.
[10] Rothwell JA, Knaze V, Zamora-Ros R. Polyphenols: dietary assessment and role in the prevention of cancers. Curr Opin Clin Nutr Metab Care 2017;20. https://doi.org/10.1097/mco.0000000000000424.
[11] Gamba M, Asllanaj E, Raguindin PF, Glisic M, Franco OH, Minder B, et al. Nutritional and phytochemical characterization of radish (Raphanus sativus): a systematic review. Trends Food Sci Technol 2021;113:205–18. https://doi.org/10.1016/j.tifs.2021.04.045.
[12] McCarty MF. Proposal for a dietary "phytochemical index". Med Hypotheses 2004;63:813–7. https://doi.org/10.1016/j.mehy.2002.11.004.
[13] Bahadoran Z, Golzarand M, Mirmiran P, Saadati N, Azizi F. The association of dietary phytochemical index and cardiometabolic risk factors in adults: tehran Lipid and Glucose Study. J Hum Nutr Diet 2013;26:145–53. https://doi.org/10.1111/jhn.12048.
[14] Edalati S, Alipour B, Rashidkhani B. Association between dietary intake of phytochemicals and hs-CRP in healthy women from tehran: a holistic approach using dietary phytochemical index. Nutr Food Sci Res 2018;5:11–6. https://doi.org/10.29252/nfsr.5.3.11.
[15] Dehghani Firouzabadi F, Jayedi A, Asgari E, Farazi M, Noruzi Z, Djafarian K, et al. The association of dietary phytochemical index with metabolic syndrome in adults. Clin Nutr Res 2021;10:161–71. https://doi.org/10.7762/cnr.2021.10.2.161.
[16] Asgari E, Jayedi A, Dehghani Firouzabadi F, Noruzi Z, Farazi M, Djafarian K, et al. Association of the dietary phytochemical index with general and central obesity in a sample of Iranian adults. J Funct Foods 2021;83:104546. https://doi.org/10.1016/j.jff.2021.104546.
[17] Kim C, Park K. Association between phytochemical index and inflammation in Korean adults. Antioxidants 2022;11. https://doi.org/10.3390/antiox11020348.

[18] Im J, Kim M, Park K. Association between the phytochemical index and lower prevalence of obesity/abdominal obesity in Korean adults. Nutrients 2020;12. https://doi.org/10.3390/nu12082312.
[19] Kim M, Park K. Association between phytochemical index and metabolic syndrome. Nutr Res Prac 2020;14:252–61. https://doi.org/10.4162/nrp.2020.14.3.252.
[20] Vasmehjani AA, Darabi Z, Nadjarzadeh A, Mirzaei M, Hosseinzadeh M. The relation between dietary phytochemical index and metabolic syndrome and its components in a large sample of Iranian adults: a population-based study. BMC Publ Health 2021;21:1587. https://doi.org/10.1186/s12889-021-11590-2.
[21] Firmann M, Mayor V, Vidal PM, Bochud M, Pécoud A, Hayoz D, et al. The CoLaus study: a population-based study to investigate the epidemiology and genetic determinants of cardiovascular risk factors and metabolic syndrome. BMC Cardiovasc Disord 2008;8:6. https://doi.org/10.1186/1471-2261-8-6.
[22] Bernstein L, Huot I, Morabia A. Amélioration des performances d'un questionnaire alimentaire semi-quantitatif comparé à un rappel des 24 heures. Sante Publique 1995;7:403–13.
[23] ANSES-CIQUAL French food composition table. French agency for food environmental and occupational health and safety. 2016.
[24] Alberti KGMM, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the international diabetes federation. Diabet Med 2006;23:469–80. https://doi.org/10.1111/j.1464-5491.2006.01858.x.
[25] A healthy lifestyle - WHO recommendations. Fact sheets: World health organization. 2010.
[26] Lean MEJ, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. Br Med J 1995;311:158. https://doi.org/10.1136/bmj.311.6998.158.
[27] Bernstein M, Sloutskis D, Kumanyika S, Sparti A, Schutz Y, Morabia A. Data-based approach for developing a physical activity frequency questionnaire. Am J Epidemiol 1998;147:147–54.
[28] Carnauba RA, Chaves DFS, Baptistella AB, Paschoal V, Naves A, Buehler AM. Association between high consumption of phytochemical-rich foods and anthropometric measures: a systematic review. Int J Food Sci Nutr 2017;68:158–66. https://doi.org/10.1080/09637486.2016.1229761.
[29] Mirmiran P, Bahadoran Z, Golzarand M, Shiva N, Azizi F. Association between dietary phytochemical index and 3-year changes in weight, waist circumference and body adiposity index in adults: tehran Lipid and Glucose study. Nutr Metab 2012;9:108. https://doi.org/10.1186/1743-7075-9-108.
[30] Rupasinghe HPV, Sekhon-Loodu S, Mantso T, Panayiotidis MI. Phytochemicals in regulating fatty acid β-oxidation: potential underlying mechanisms and their involvement in obesity and weight loss. Pharmacol Therapeut 2016;165:153–63. https://doi.org/10.1016/j.pharmthera.2016.06.005.
[31] Ahmad B, Friar EP, Vohra MS, Garrett MD, Serpell CJ, Fong IL, et al. Mechanisms of action for the anti-obesogenic activities of phytochemicals. Phytochemistry 2020;180:112513. https://doi.org/10.1016/j.phytochem.2020.112513.
[32] Bahadoran Z, Mirmiran P, Tohidi M, Azizi F. Dietary phytochemical index and the risk of insulin resistance and β-cell dysfunction: a prospective approach in Tehran lipid and glucose study. Int J Food Sci Nutr 2015;66:950–5. https://doi.org/10.3109/09637486.2015.1111867.
[33] Mehranfar S, Jalilpiran Y, Ejtahed H-S, Seif E, Shahrestanaki E, Mahdavi-Gorabi A, et al. Association of dietary phytochemical index with cardiometabolic risk factors. A systematic review and meta-analysis on observational studies. Int J Vitam Nutr Res 2022:1–18. https://doi.org/10.1024/0300-9831/a000763.
[34] Murugan DD, Balan D, Wong P-F. Adipogenesis and therapeutic potentials of antiobesogenic phytochemicals: insights from preclinical studies. Phytother Res 2021;35:5936–60. https://doi.org/10.1002/ptr.7205.
[35] Piccand E, Vollenweider P, Guessous I, Marques-Vidal P. Association between dietary intake and inflammatory markers: results from the CoLaus study. Publ Health Nutr 2019;22:498–505. https://doi.org/10.1017/s1368980018002355.
[36] Wei C, Liu L, Liu R, Dai W, Cui W, Li D. Association between the phytochemical index and overweight/obesity: a meta-analysis. Nutrients 2022;14:1429.
[37] World Health Organization. Global status report on alcohol and health 2018. World Health Organization; 2019.
[38] Jo U, Park K. Phytochemical index and hypertension in Korean adults using data from the Korea national health and nutrition examination survey in 2008–2019. Eur J Clin Nutr 2022. https://doi.org/10.1038/s41430-022-01155-w.
[39] Golzarand M, Bahadoran Z, Mirmiran P, Sadeghian-Sharif S, Azizi F. Dietary phytochemical index is inversely associated with the occurrence of hypertension in adults: a 3-year follow-up (the Tehran Lipid and Glucose Study). Eur J Clin Nutr 2015;69:392–8. https://doi.org/10.1038/ejcn.2014.233.
[40] Odgaard-Jensen J, Vist GE, Timmer A, Kunz R, Akl EA, Schünemann H, et al. Randomisation to protect against selection bias in healthcare trials. Cochrane Database Syst Rev 2011;2011:Mr000012. https://doi.org/10.1002/14651858.MR000012.pub3.
[41] Schneid Schuh D, Campos Pellanda L, Guessous I, Marques-Vidal P. Trends and determinants of change in compliance to dietary guidelines in a Swiss community-dwelling sample. Prev Med 2018;111:198–203. https://doi.org/10.1016/j.ypmed.2018.03.008.
[42] Viguiliouk E, Blanco Mejia S, Kendall CWC, Sievenpiper JL. Can pulses play a role in improving cardiometabolic health? Evidence from systematic reviews and meta-analyses. Ann N Y Acad Sci 2017;1392:43–57. https://doi.org/10.1111/nyas.13312.
[43] Aghababayan S, Sheikhi Mobarakeh Z, Qorbani M, Abbasvandi F, Tiznobeyk Z, Aminianfar A, et al. Dietary phytochemical index and benign breast diseases: a case-control study. Nutr Cancer 2020;72:1067–73. https://doi.org/10.1080/01635581.2019.1658795.
[44] Bahadoran Z, Karimi Z, Houshiar-rad A, Mirzayi HR, Rashidkhani B. Dietary phytochemical index and the risk of breast cancer: a case control study in a population of Iranian women. Asian Pac J Cancer Prev APJCP 2013;14:2747–51. https://doi.org/10.7314/apjcp.2013.14.5.2747.