

# Dietary intakes of total polyphenol and its subclasses in relation to incidence of chronic kidney disease: a prospective population-based cohort study

**Parvin Mirmiran**

Nutrition and Endocrine Research Center, Research Institute for Endocrine Science, Shahid Beheshti University of Medical Science

**Emad Yuzbashian**

Nutrition and Endocrine Research Center, Research Institute for Endocrine Science, Shahid Beheshti University of Medical Science

**Pegah Rahbarinejad**

Nutrition and Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences

**Golaleh Asghari** (✉ [g\\_asghari@hotmail.com](mailto:g_asghari@hotmail.com))

Research Institute for Endocrine Science, Shahid Beheshti University of Medical Science

**Fereidoun Azizi**

Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences

---

## Research article

**Keywords:** Polyphenols, Glomerular Filtration Rate (GFR), Chronic Kidney Disease (CKD), Tehran Lipid and Glucose Study (TLGS)

**Posted Date:** August 31st, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-54796/v1>

**License:**   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

**Version of Record:** A version of this preprint was published on March 10th, 2021. See the published version at <https://doi.org/10.1186/s12882-021-02286-1>.

# Abstract

## Objective

Chronic Kidney Disease (CKD) is nowadays a public health challenge worldwide. Accordingly, this study is aiming to evaluate the association between long-term intake of total polyphenol and its subclasses, and the incidence of CKD.

## Methods

A sample of 3021 Iranian Adults (47% men) were selected from the the Tehran Lipid and Glucose Study population. The participants aged 20–79 years and had no diagnosis of CKD at baseline. Total polyphenol intake and its major subclasses including flavonoids, phenolic acids, stilbenes, and lignans, was assessed by a validated and reliable Food Frequency Questionnaire (FFQ). The of the were broadly categorized as flavonoids, phenolic acids, stilbenes, and lignans. The Modification of Diet in Renal Disease Study equation was used to calculate the Estimated Glomerular Filtration Rate (eGFR), and, CKD was defined as  $eGFR < 60 \text{ mL/min/1.73 m}^2$ . Hazard ratio and 95% confidence intervals of CKD by total polyphenols quartiles were assessed by Cox-regression analysis.

## Results

In this study, we documented 355 cases of diagnosed CKD over 11,058.464 person-years. The mean  $\pm$  SD age of participants was  $37.3 \pm 12.6$  years at baseline. After adjustment of the potential confounders, it was revealed that a moderate intake of lignans ( $\leq 6.8 \text{ mg}$ ) was negatively associated with the incidence of CKD, whereas there was no significant association between the higher amounts of lignan intake and CKD. No significant associations were observed between the consumption of total polyphenols and the incidence of CKD (HR: 0.97, 95% CI 0.67–1.40).

## Conclusions

Data of the current study suggest that in the case of lignan with protective properties, a moderate amount of lignan favorably reduced the incidence of CKD by approximately 32%, whereas higher amounts possessed a null effect.

## Background

Chronic kidney disease (CKD), as a global public health challenge, manifests by loss of kidney function or structural kidney damage (1, 2). Obesity, diabetes, hypertension and increased levels of inflammation and oxidative stress, as the underlying risk factors for cardiovascular disease (CVD), are also known as the most common chronic conditions associated with CKD (1, 3). In this regard, habitual dietary intake is

considered as an effective modifiable factor in the etiology of CKD. Therefore, adopting a healthy and feasible lifestyle appears to be a powerful strategy in the prevention of CKD (4).

It is believed that adherence to specific dietary patterns including the Mediterranean diet (5) and the Dietary Approaches to Stop Hypertension (DASH) (6, 7) has a favorable contribution in the renal function. An increasing body of evidence has consensus that plant-based diets characterized by higher intake of fruits, vegetables, nuts, spices, herbs, cereals, legume, seeds, chocolate, and tea better prevent the occurrence of chronic conditions (8). These plant-based food items are well-known for their diverse content of phytochemicals (9). Thus far, polyphenols are referred to as the major constituent of human consumed micronutrients; with considerable antioxidant and biological activities, they are believed to beneficially affect various chronic disorders (10, 11). Flavonoids, phenolic acids, stilbenes, and lignans are the four major subclasses of polyphenols (8). While several studies have investigated the effect of polyphenol-rich red grape juice (12), green tea, cocoa (13) and white wine (14) among patients with renal failure, there is an ongoing discussion about the CKD- preventive property of polyphenols in a regular diet. With regards to the lack of data on the relationship between long-term intake and polyphenols with kidney function among adults, this study aimed to investigate the association of long-term consumption of total polyphenol and its subclasses, including flavonoids, phenolic acids, stilbenes, and lignans with the incidence of CKD

## Methods

### Study population

This longitudinal study was performed within the framework of the ongoing community-based Tehran Lipid and Glucose Study (TLGS). The prospective TLGS was originally conducted to determine and prevent the risk factors for non-communicable diseases (NCDs) (15). In this respect, TLGS consists of 5 phases, the first of which was a cross-sectional study and began in 1999. Four other subsequent phases (phases II (2002–2005), III (2006–2008), IV (2009–2011), and V (2012–2015)) were performed as prospective follow-up surveys. The current study is based on the data of the third phase. Briefly, using multistage cluster random sampling methods, 15005 people  $\geq 3$  years of age were selected from three medical health centers in district 13 of Tehran.

Ultimately, a representative sample of 3021 individuals with 20- 79 years of age and complete data, were recruited and followed to the fifth phase. Based on the exclusion criteria, participants on pregnancy or lactating states, on energy consumption out of the predefined limits ( $800 < x < 4200$  kcal/d) or specific diets or with any history of myocardial infarction, cerebral vascular accident, cancers and CKD at baseline were excluded. Hence, a total of 2054 individuals were enrolled for the final follow-up analysis of 11058.464 person-years.

All participants were initially asked to provide written informed consent. The study protocol was also approved by the ethics committee research council of the Research Institute for Endocrine Science (RIES), Shahid Beheshti University of Medical Science, Tehran, Iran.

## Dietary assessment

The habitual food intake was evaluated by a validated and reliable semi-quantitative food-frequency questionnaire (FFQ) at baseline (16, 17). The individual consumption frequency of each food item was designated by trained and experienced dietitians on daily, weekly or monthly basis. The portion sizes were collected in household measures and converted to grams. The USDA Food Composition Table (FCT) was used to calculate and interpret the energy and nutrient content of each food item. The estimation of total polyphenol and subclasses' intake was based on the Phenol-Explorer database ([www.phenol-explorer.eu/contents](http://www.phenol-explorer.eu/contents)) (18).

## Measurement of covariates

The physical activity level of each participant was assessed by the Modifiable Activity Questionnaire which has previously been validated for the Iranian population (19). A metabolic equivalent (MET-h per week) was calculated according to a list of most common and daily routine activities.

Anthropometric measurements including weight and height were collected to the nearest 0.1 kg and 0.1 cm, respectively. The weight was recorded in light clothing via a SECA digital weighing scale (Seca 707; Seca Corporation; range 0.1–150 kg), and height was taken without shoes on. BMI was calculated as weight (kg) divided by square of height (m<sup>2</sup>). Arterial blood pressure was measured manually, using a mercury sphygmomanometer with a suitable cuff size for each participant after a 15-min rest in the supine position.

Systolic (SBP) and Diastolic blood pressures were determined by the initial tapping and disappearance of Korotkoff sound, respectively. Blood pressure was measured twice and the average was considered as participant's final blood pressure. Blood samples were taken from all participants at the TLGS research laboratory after 12 to 14 hours of overnight fasting.

Fasting plasma glucose (FPG) and 2-h plasma glucose (equivalent to 75 g anhydrous glucose; Cerestar EP) were measured by enzymatic colorimetric method using glucose oxidase, with both inter- and intra-assay CV being < 2%. Serum creatinine was measured under the standard colorimetric Jaffe\_Kinetic reaction method at baseline (2006–2008) and after 6 years of follow-up (2012–2015). Both Intra- and inter-assay CVs were below 3.1%; all analyses were performed using commercial kits (Pars Azmoon Inc.).

## Definition

In this study, the estimated GFR (eGFR) was expressed as ml/min/1.73m<sup>2</sup> of body surface area, using the Modification of Diet in Renal Disease (MDRD) equation (20). The MDRD equation is as follows:

$$eGFR = 186 \times (\text{Serum creatinine})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American})$$

Patients were classified based on individual eGFR levels pertain to the national kidney foundation guidelines (21); given this, eGFR  $\geq$  60 ml/min/1.73m<sup>2</sup> are considered as non-CKD patients and eGFR <

60 ml/min/1.73m<sup>2</sup> are those diagnosed with CKD. Hypertension was primarily defined as SBP/DBP  $\geq$  140/90 mm-Hg or current therapy for a definite diagnosis of hypertension (22). Furthermore, diabetes was defined in accordance with the criteria of the American Diabetes Association (ADA) as fasting plasma glucose  $\geq$  126 mg/dl, 2-h post 75-g glucose load  $\geq$  200 mg/dl or current therapy for a definite diagnosis of diabetes (23).

## Statistical analysis

In this study, the normality distribution of variables was assessed by the Kolmogorov–Smirnov test and Histogram chart. The participants' characteristics and nutritional states across quartiles of total polyphenols were reported as mean  $\pm$  SD for quantitative variables and percentage for categorical variables. Linear regression and Chi-square tests were used to investigate the trend of continuous and categorical variables in proportion to total polyphenols quartiles, respectively. Hazard ratio (HR) and 95% confidence intervals (CI) of incident CKD were assessed by quartiles of total polyphenols by Cox regression analysis; the lowest quartile of dietary exposures considered as a reference group. Moreover, three models were specified for the first being the crude, the second with adjustments for sex, age, physical activity and total calorie intake, and third additionally adjusted for BMI, diabetes and hypertension. The proportionality assumption underlying the Cox model was examined, and no evidence of violation was observed. All analyses were done using IBM SPSS version 16 (SPSS, Chicago, IL, USA) with the significance level set as  $P < 0.05$  (two-tailed).

## Results

In this study, the mean  $\pm$  SD age of participants was  $37.3 \pm 12.6$  years, with 47% being men. Within 11058.464 person-years of follow-up, 355 new cases of CKD were reported. Baseline characteristics and nutritional status of participants across quartiles of total polyphenols are stated in Table 1. The data had highlighted that across quartiles of total polyphenols, trends of age ( $P$  for trend = 0.015), BMI ( $P$  for trend = 0.001), energy ( $P$  for trend  $<$  0.001), and fat ( $P$  for trend = 0.003) had increased, whereas, the trend of carbohydrates was mitigated ( $P$  for trend  $<$  0.001) .

Table 1

Baseline characteristics and nutritional status of participants across quartiles of total polyphenols

	quartiles of total polyphenol				
	Q1	Q2	Q3	Q4	<i>P</i> for trend
Median (mg/d)	737	1201	1717	2682	
Age (year)	36.2 ± 12.4	37.4 ± 12.7	37.3 ± 12.5	38.3 ± 12.8	0.015
Male (%)	24	26	25	25	0.693
Body mass index (kg/m <sup>2</sup> )	26.3 ± 4.6	26.3 ± 4.7	26.9 ± 4.8	27.2 ± 4.8	0.001
Current smoking (%)	24	29	24	23	0.236
Physical activity (MET/hours per week)	27.7 ± 46.5	29.9 ± 46.6	29.4 ± 51.3	31.7 ± 49.5	0.261
Diabetes (%)	27	31	13	29	0.789
Hypertension (%)	21	22	28	28	0.117
eGFR (ml/min/1.73 m <sup>2</sup> )	76.2 ± 9.5	75.8 ± 10.1	76.1 ± 1.0	75.5 ± 9.5	0.266
Total energy intake (Kcal)	1756 ± 553	2176 ± 601	2417 ± 631	2769 ± 673	< 0.001
Protein (% of energy)	13.5 ± 2.6	13.7 ± 2.3	13.8 ± 2.3	13.7 ± 2.3	0.371
Carbohydrate (% of energy)	56.7 ± 7.5	56.3 ± 6.9	57.1 ± 7.2	59.4 ± 6.9	< 0.001
Fat (% of energy)	31.3 ± 7.6	32.3 ± 6.8	31.7 ± 7.1	30.4 ± 6.3	0.003
Whole grains (g/1000 kcal)	21.6 ± 25.0	26.8 ± 30.1	27.0 ± 33.3	27.7 ± 31.0	0.005
Vegetables (g/1000 kcal)	91.1 ± 56.1	115.9 ± 59.8	134.8 ± 75.5	149.7 ± 100.2	< 0.001
Fruits (g/1000 kcal)	94.0 ± 66.6	132.0 ± 74.1	174.7 ± 94.4	263.3 ± 130.4	< 0.001
Nuts (g/1000 kcal)	2.6 ± 3.6	2.8 ± 3.9	3.2 ± 3.8	4.0 ± 5.4	< 0.001
Abbreviations: eGFR, estimated glomerular filtration rate; MET, metabolic equivalent.					
Data are presented as mean ± s.d for continuous variables and percent for categorical variables.					

The HR for total polyphenol and its subclasses are described in Table 2. There were no significant associations between the consumption of total polyphenols and the incidence of CKD (HR: 0.97, 95% CI 0.67–1.40). Furthermore, the incidence of CKD was less significant among participants in the fourth quartile of flavonoids and phenolic acids as compared to those in the first quartile (HR: 1.07, 95% CI 0.74–1.55 and HR: 1.14, 95% CI 0.79–1.64, respectively). Across subclasses of polyphenols, lignans had a significant association with CKD in the multivariable-adjusted model. With that said, participants in the second and third quartile of lignans had a significantly reduced incident rate of CKD by 34% and 31%, respectively, comparing to those in the first quartile. Also, participants in the first and fourth quartiles of total dietary polyphenols were shown to be non-significantly associated with the incidence of CKD. Compared to participants in the first quartile of stilbenes, the HR was 0.64 (95% CI 0.48–0.87) for those in the last quartile of the unadjusted model and with a significant inverse but unstable trend that disappeared after adjusting for potential confounders.

Table 2

Multivariable-adjusted COX regression (95% CIs) for incidence of chronic kidney disease according to quartiles of the total polyphenols and its subgroups

	Total polyphenols Quartiles				P for trend
	Q1	Q2	Q3	Q4	
<i>Total Polyphenols</i>					
Median (mg/d)	737	1201	1717	2682	
Cases/ total	84/514	95/513	83/514	93/513	
Model 1	1	1.20 (0.90–1.62)	1.00 (0.73–1.35)	1.15 (0.85–1.54)	0.615
Model 2	1	1.20 (0.87–1.66)	0.92 (0.65–1.31)	0.99 (0.69–1.43)	0.598
Model 3	1	1.12 (0.81–1.55)	0.90 (0.63–1.28)	0.97 (0.67–1.40)	0.624
<i>Flavonoids</i>					
Median (mg/d)	33.11	55.85	82.65	125.47	
Cases/ total	83/514	86/513	93/514	93/513	
Model 1	1	1.08 (0.80–1.47)	1.13 (0.84–1.53)	1.14 (0.85–1.53)	0.401
Model 2	1	1.13 (0.81–1.57)	1.03 (0.74–1.44)	1.05 (0.73–1.52)	0.957
Model 3	1	1.12 (0.80–1.57)	1.09 (0.78–1.52)	1.07 (0.74–1.55)	0.852
<i>Phenolic acids</i>					
Median (mg/d)	37.21	61.71	92.21	163.62	
Cases/ total	85/514	91/513	86/514	93/513	
Model 1	1	1.09 (0.81–1.47)	1.03 (0.76–1.39)	1.11 (0.83–1.49)	0.587
Model 2	1	1.15 (0.83–1.58)	1.14 (0.82–1.60)	1.15 (0.80–1.64)	0.583

Model 1: Crude.

Model 2: Adjusted for sex, age, physical activity, and total calorie intake.

Model 3: Additionally adjusted for body mass index, diabetes, and hypertension.

	Total polyphenols Quartiles				P for trend
	Q1	Q2	Q3	Q4	
Model 3	1	1.14 (0.82–1.58)	1.13 (0.81–1.59)	1.14 (0.79–1.64)	0.600
<i>Lignans</i>					
Median (mg/d)	1.14	2.65	4.98	11.13	
Cases/ total	102/514	70/513	80/514	103/513	
Model 1	1	0.63 (0.47–0.86)	0.75 (0.56–1.00)	0.98 (0.74–1.28)	0.268
Model 2	1	0.66 (0.47–0.92)	0.70 (0.50–0.97)	1.06 (0.77–1.45)	0.089
Model 3	1	0.66 (0.47–0.94)	0.69 (0.49–0.97)	1.10 (0.80–1.52)	0.049
<i>Stilbens</i>					
Median (mg/d)	0.05	0.16	0.28	0.70	
Cases/ total	110/514	95/514	77/513	73/513	
Model 1	1	0.85 (0.65–1.12)	0.66 (0.49–0.88)	0.64 (0.48–0.87)	0.005
Model 2	1	1.16 (0.86–1.56)	0.99 (0.71–1.37)	1.10 (0.78–1.55)	0.779
Model 3	1	1.19 (0.87–1.62)	1.02 (0.73–1.42)	1.13 (0.80–1.61)	0.672
Model 1: Crude.					
Model 2: Adjusted for sex, age, physical activity, and total calorie intake.					
Model 3: Additionally adjusted for body mass index, diabetes, and hypertension.					

## Discussion

This study investigated the association of total dietary polyphenol and its major subclasses with the incidence of CKD among adults in Tehran, Iran. While high intake of lignans up to 6.8 mg is negatively associated with the incidence of CKD independent of the potential cofounders, no similar associations were depicted with higher values (> 6.8 mg). Also, it was observed that the incidence of CKD in the highest quartile of stilbenes was 36% lower comparing to the lowest quartile in the unadjusted model. There were no significant findings after controlling the confounding factors, which was specifically dependent on the effect of potential cofounders. Besides, no significant associations were detected between the consumption of total polyphenols and the incidence of CKD.

To the best of our knowledge, this is the first study that evaluated the association of long-term consumption of total polyphenol and its major subclasses with the incidence of CKD. This study has implied that a moderate amount of lignan ( $\leq 6.8$  mg) is CKD-protective, which can be attributed to the high content of antioxidants. Motivated by a piece of emerging evidence, reduced levels of oxidative stress, as a consequence of increased antioxidant defenses, correspondingly decreases the CVD risk factors (24). In this context, some epidemiological studies have emphasized that CVD and CKD share some common risk factors including low serum HDL cholesterol, hypertension, hypertriglyceridemia, and hyperglycemia (22, 25). The cardiovascular risk factors tend to progressively increase as a result of renal function reduction, however, the proper management of the cardiovascular system, could decrease the risk of CVD and CKD manifestations (22, 25). Therewith, data on the consumption of lignan remains inconsistent (26, 27); it is believed that a moderate intake promotes beneficial health effects. However, high amounts of lignan could act as estrogen antagonists (28) or inhibit enzymes involved in the metabolism of sex hormones such as 5 $\alpha$ -reductase and 17 $\beta$ -hydroxysteroid dehydrogenase (23). In other words, a higher intake of lignan is believed to have null effects on CVD risk factors, for which as few as two mechanisms have been proposed for (23). In fact, with higher intake of lignan and the mechanisms mentioned earlier, the increased CVD risk factors can decrease the level of free estradiol and testosterone in women and men, respectively (23). Therefore, it seems as only a moderate amount of lignan ( $\leq 6.8$  mg) may appear effective with an approximate 32% decrease of the CVD risk factors, and subsequently the risk of CKD.

Borges et al. performed a study to propose the CKD-reducing properties of green tea polyphenols by decreasing albuminuria among patients with diabetic nephropathy (4). The inhibition of inflammatory mediators (such as TNF- $\alpha$ ) is the possible mechanism behind this investigation. Within this context, it was also indicated that total polyphenol intake had no association with a lower risk of CKD (4). The results of another study by Cynthia et al. contradicted the previous evidence, mostly attributed to the intervention of multifactorial treatments received by the diabetic participants along with the green tea polyphenols. In this sense, a meta-analysis endorsed the preliminary support of polyphenol-rich interventions in the improvement of cardiovascular risk factors among hemodialysis patients (29). Despite individual studies indicating significant improvements, pooled results depicted no effect for most outcomes excepting myeloperoxidase, diastolic blood pressure, and triglycerides (29). Only myeloperoxidase, a measure of oxidative stress, had a large pooled effect size (29). Also, the individualized polyphenol metabolism as a result of inter-individual gastrointestinal microbiota differences, brought diversity to the range of responses among the population (29). In this respect, no specific associations were observed in the mentioned study, which could conceal the beneficial effect of total polyphenol consumption.

Concerning the current study, the potential limitations must be considered, as well. First, the consumption of total polyphenols and its subclasses were estimated by the Phenol-Explorer database ([www.phenol-explorer.eu/contents](http://www.phenol-explorer.eu/contents)) for the Iranian version not being available. Second, the albumin-to-creatinine ratio (ACR) was not assessed; the ACR could have helped us interpret the results more accurately. Third, this study did not take into account a creatinine double-checking procedure, which could have possibly

affected the findings. Finally, although the effect of potential confounders were adjusted, the impact of residual confounders could not be ruled out.

## Conclusions

In conclusion, the result of this prospective study did not confirm any associations between total polyphenols and the incidence of CKD. However, it was finalized that despite the CKD- protective effect of moderate lignan intake ( $\leq 6.8$  mg) by approximately 32% among adults of Tehran, higher amounts of lignan possess no significant effects. Therefore, there is no doubt that further research is required to differentiate the impact of low, moderate and high amounts of lignan intake on CKD incidence.

## Abbreviations

CKD

Chronic Kidney Disease

GFR

Glomerular Filtration Rate

TLGS

Tehran Lipid and Glucose Study

DASH

Dietary Approaches to Stop Hypertension

FFQ

Food-Frequency Questionnaire

FCT

Food Composition Table

MDRD

Modification of Diet in Renal Disease

RIES

Research Institute for Endocrine Sciences

TNF-a

Tumor necrosis factor-alpha

## Declarations

## Ethics approval and consent to participate

All participants were initially asked to provide written informed consent. The study protocol was also approved by the ethics committee research council of the Research Institute for Endocrine Science (RIES), Shahid Beheshti University of Medical Science, Tehran, Iran.

## Consent for publication

Not applicable' for that section.

## Availability of data and materials

Not applicable' for that section.

## Competing interests

The authors declare that they have no competing interests.

# Funding

This work was funded by a grant from the RIES, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

# Authors' contributions

The authors hereby appreciate the great contributions of the study participants. Overall, P.M. supervised the project and approved the final version of the manuscript to be submitted; G.A. and P.R. designed the research; E.Y. and P.R. analyzed and interpreted the data; F.A. and G.A. critically reviewed the manuscript; G.A., E.Y., and P.R. drafted the initial manuscript.

# Acknowledgements

We express our appreciation to TLGS participants and the research team members for their contribution to the study.

# References

1. Levey AS, Coresh J. Chronic kidney disease. *Lancet*. 2012;379(9811):165–80.
2. Foundation NK. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *American journal of kidney diseases: the official journal of the National Kidney Foundation*. 2002;39(2 Suppl 1):1–266.
3. Santoro A, Mancini E. Cardiac effects of chronic inflammation in dialysis patients. *Nephrol Dial Transplant*. 2002;17 Suppl 8:10 – 5.
4. Borges CM, Papadimitriou A, Duarte DA, Lopes de Faria JM, Lopes de Faria JB. The use of green tea polyphenols for treating residual albuminuria in diabetic nephropathy: A double-blind randomised clinical trial. *Scientific reports*. 2016;6:28282.

5. Asghari G, Farhadnejad H, Mirmiran P, Dizavi A, Yuzbashian E, Azizi F. Adherence to the Mediterranean diet is associated with reduced risk of incident chronic kidney diseases among Tehranian adults. *Hypertension research: official journal of the Japanese Society of Hypertension*. 2017;40(1):96–102.
6. Asghari G, Yuzbashian E, Mirmiran P, Azizi F. The association between Dietary Approaches to Stop Hypertension and incidence of chronic kidney disease in adults: the Tehran Lipid and Glucose Study. *Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association*. 2017;32(suppl\_2):ii224–30.
7. Yuzbashian E, Asghari G, Mirmiran P, Amouzegar-Bahambari P, Azizi F. Adherence to low-sodium Dietary Approaches to Stop Hypertension-style diet may decrease the risk of incident chronic kidney disease among high-risk patients: a secondary prevention in prospective cohort study. *Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association*. 2018;33(7):1159–68.
8. Scalbert A, Morand C, Manach C, Remesy C. Absorption and metabolism of polyphenols in the gut and impact on health. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*. 2002;56(6):276 – 82.
9. Amiot MJ, Riva C, Vinet A. Effects of dietary polyphenols on metabolic syndrome features in humans: a systematic review. *Obesity reviews: an official journal of the International Association for the Study of Obesity*. 2016;17(7):573–86.
10. Kuhnau J. The flavonoids. A class of semi-essential food components: their role in human nutrition. *World Rev Nutr Diet*. 1976;24:117–91.
11. Scalbert A, Williamson G. Dietary intake and bioavailability of polyphenols. *J Nutr*. 2000;130(8S Suppl):2073S-85S.
12. Castilla P, Echarri R, Davalos A, Cerrato F, Ortega H, Teruel JL, et al. Concentrated red grape juice exerts antioxidant, hypolipidemic, and antiinflammatory effects in both hemodialysis patients and healthy subjects. *Am J Clin Nutr*. 2006;84(1):252–62.
13. Rassaf T, Rammos C, Hendgen-Cotta UB, Heiss C, Kleophas W, Dellanna F, et al. Vasculoprotective Effects of Dietary Cocoa Flavanols in Patients on Hemodialysis: A Double-Blind, Randomized, Placebo-Controlled Trial. *Clinical journal of the American Society of Nephrology: CJASN*. 2016;11(1):108–18.
14. Migliori M, Panichi V, de la Torre R, Fito M, Covas M, Bertelli A, et al. Anti-inflammatory effect of white wine in CKD patients and healthy volunteers. *Blood purification*. 2015;39(1–3):218–23.
15. Azizi F, Ghanbarian A, Momenan AA, Hadaegh F, Mirmiran P, Hedayati M, et al. Prevention of non-communicable disease in a population in nutrition transition: Tehran Lipid and Glucose Study phase II. *Trials*. 2009;10(1):5.
16. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. *Public Health Nutr*. 2010;13(5):654–62.

17. Esfahani FH, Asghari G, Mirmiran P, Azizi F. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran Lipid and Glucose Study. *Journal of epidemiology*. 2010;20(2):150–8.
18. Perez-Jimenez J, Neveu V, Vos F, Scalbert A. Systematic analysis of the content of 502 polyphenols in 452 foods and beverages: an application of the phenol-explorer database. *J Agric Food Chem*. 2010;58(8):4959–69.
19. Momenan AA, Delshad M, Sarbazi N, Rezaei Ghaleh N, Ghanbarian A, Azizi F. Reliability and validity of the Modifiable Activity Questionnaire (MAQ) in an Iranian urban adult population. *Arch Iran Med*. 2012;15(5):279–82.
20. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999;130(6):461–70.
21. K/DOQI clinical. practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002;39(2 Suppl 1):1–266.
22. Eckardt KU, Coresh J, Devuyst O, Johnson RJ, Kottgen A, Levey AS, et al. Evolving importance of kidney disease: from subspecialty to global health burden. *Lancet*. 2013;382(9887):158–69.
23. Raffaelli B, Hoikkala A, Leppala E, Wahala K. Enterolignans. *Journal of chromatography B Analytical technologies in the biomedical life sciences*. 2002;777(1–2):29–43.
24. L.Gupta K, Sahni N. Dietary antioxidants and oxidative stress in predialysis chronic kidney disease patients. *J Nephropathol*. 2012;1(3):134–42.
25. Gansevoort RT, Correa-Rotter R, Hemmelgarn BR, Jafar TH, Heerspink HJ, Mann JF, et al. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet*. 2013;382(9889):339–52.
26. Nurmi T, Mursu J, Penalvo JL, Poulsen HE, Voutilainen S. Dietary intake and urinary excretion of lignans in Finnish men. *Br J Nutr*. 2010;103(5):677–85.
27. Morisset AS, Lemieux S, Veilleux A, Bergeron J, John Weisnagel S, Tchernof A. Impact of a lignan-rich diet on adiposity and insulin sensitivity in post-menopausal women. *Br J Nutr*. 2009;102(2):195–200.
28. Landete J. Plant and mammalian lignans: a review of source, intake, metabolism, intestinal bacteria and health. *Food Res Int*. 2012;46(1):410–24.
29. Marx W, Kelly J, Marshall S, Nakos S, Campbell K, Itsiopoulos C. The effect of polyphenol-rich interventions on cardiovascular risk factors in haemodialysis: A systematic review and meta-analysis. *Nutrients*. 2017;9(12):1345.