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The association of dietary phosphorus with blood pressure: Results from a secondary analysis of the PREMIER Trial

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Abstract

Inconsistent findings exist for the association between dietary phosphorus intake and blood pressure (BP). We examined the longitudinal association between urinary excretion and dietary intake of phosphorus (total, plant, animal, and added) with BP.

This is a secondary analysis of PREMIER, a randomized behavioral intervention study in adults (25–79y) with BP, measured at six months, as the primary outcome. We classified total phosphorus intake from dietary recalls into plant, animal, and added phosphorus. We modeled six month change of phosphorus intake (from 24h dietary recalls, N = 622) and excretion (from 24h urine collection, N = 564) on BP, using linear regression crude and adjusted for intervention, age, race, sex, income, education, study site, and change in energy intake (kcal/d), sodium intake (mg/d), fitness (heart rate, bpm), and DASH diet index.

Baseline phosphorus intake was 1154 mg/d (95%CI 1126, 1182) with 38%, 53%, and 10% from plant, animal, and added phosphorus, respectively. Total phosphorus intake was not associated with significant changes in BP. Increased urinary phosphorus excretion was associated with a significant increase in DBP [0.14 mmHg/100 mg (0.01, 0.28), adjusted]. In several analyses, phosphorus type (plant, animal, or added) significantly modified the association between phosphorus intake and BP. For example, added phosphorus (but not plant or animal) was

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associated with increases in SBP and DBP, 1.24 mmHg/100 mg (0.36, 2.12) and 0.83 mmHg/100 mg (0.22, 1.44), respectively, crude.

These findings suggest that the type of phosphorus may modify the association between phosphorus intake and BP. Trial registration (clinicaltrials.gov).

Keywords

phosphorus; blood pressure; randomized trial; diet; urinary excretion

Introduction

Dietary phosphorus intake and urinary phosphorus excretion may be associated with beneficial or adverse changes in blood pressure. Several studies have found reduced blood pressure or lower risk of hypertension among those consuming more total dietary phosphorus [1–3]. However, these studies have either been cross-sectional [2,3] or have depended on food frequency questionnaires [1]. A recent systematic review of randomized trials and prospective observational studies did not find a consistent association of total dietary phosphorus intake with blood pressure [4].

Greater urinary phosphorus excretion was associated with reduced risk of cardiovascular disease events in the Heart and Soul study, a prospective observational study in a population with normal to moderately impaired kidney function, mean estimated GFR 71 ml /min per 1.73 m^2 (SD 22) [5]. Conversely, dietary phosphorus intake has been associated with several adverse health outcomes including increased blood pressure [6], greater left ventricular mass [7], impaired endothelial function [8,9], greater carotid intima-media thickness [10], and higher risk of all-cause mortality [11].

Dietary phosphorus exists in a variety of forms, with some suggesting that specific types of phosphorus, such as dairy, may be associated with positive health outcomes [1], while others, such as added phosphorus, may be associated with negative health outcomes [10,12]. However, these studies have been limited in their ability to classify phosphorus within foods due to their use of food frequency questionnaires or inability to account for multiple types of phosphorus within specific foods. Phosphate is the most common form of phosphorus in animal products [13]. A combination of phytate and phosphate occur in plant foods [14–16]. Additionally, phosphorus is added commercially to foods in a variety of forms (e.g. sodium phosphates, calcium phosphates, and phosphoric acids) [17].

The objective of this study was to investigate the associations dietary phosphorus intake (total, plant, animal, and added phosphorus) and urinary phosphorus excretion with changes in blood pressure in participants of a completed randomized behavioral intervention trial, PREMIER.

Methods

Study design

This is a secondary analysis of PREMIER, a completed randomized behavioral intervention trial of adult men and women with non-optimal blood pressure assigned to one of three behavioral interventions. Change in blood pressure from baseline to six months was the primary outcome. A detailed description of the trial has been reported [18,19]. Briefly, PREMIER participants were adults 25 years old or older (range 25–79y) with a BMI of 18.5–45 kg/m^2, a systolic blood pressure of 120–159 mmHg, and a diastolic blood pressure of 80–95 mmHg. PREMIER participants were randomized to one of three behavioral interventions (Advice Only, Established, or Established + DASH). Participants were enrolled between September 1999 and June 2001 at four US centers (Baton Rouge, Louisiana; Baltimore, Maryland; Durham, North Carolina, and Portland, Oregon). All participants consumed self-selected diets throughout the study period. Study staff involved in data collection were unaware of participant treatment assignments and those involved in administering the intervention were unaware of outcome data.

Participants randomized to Advice Only received two 30 minute sessions in which they were provided with general advice to lose weight (if overweight), reduce sodium intake, increase physical activity, limit alcohol, and eat a healthy diet pattern. Those randomized to the Established and Established + DASH interventions participated in 14 group and four individual intervention sessions throughout the six month intervention. Those randomized to Established and Established + DASH were counseled to lose weight (by increasing physical activity and reducing calorie intake), reduce sodium intake, and increase physical activity. Those on the Established + DASH intervention were further instructed to follow a DASH-type diet (specifically increasing intake of fruits, vegetables, and low-fat dairy and reducing saturated and total fat intake), and to replace high fat, high calorie foods with fruits and vegetables.

We would expect the Advice Only and Established interventions to result in reduced total phosphorus intake, due to overall reduction in calorie intake, but not result in a systematic change in dietary sources of phosphorus. We would expect the Established + DASH intervention to result in increased plant (fruits and vegetables) and animal (dairy) phosphorus intake due to the higher phosphorus content of a DASH-type diet.

Urinary phosphorus excretion and dietary phosphorus intake

A single 24 hour urine collections and a two 24 hour dietary recall interviews were collected at baseline and again at six months (total of two 24 hour urine collections, four dietary recalls). Urine samples were analyzed for phosphorus content at the Core Laboratory for Clinical Studies at Washington University, St. Louis, Missouri.

Dietary recall interviews were performed by the Diet Assessment Center at The Pennsylvania State University. During these interviews, the name and amount of each food consumed during the past 24 hours was collected. Every effort was made to get specific detail about the foods (including brand names and other product details, preparation method and recipe ingredients if known). Dietary data were analyzed using the Nutrition Data

System (NDS-R, 2001, Nutrition Coordinating Center, University of Minnesota, Minnesota), a nutrient database with macro- and micro-nutrient content (including total phosphorus) of over 18,000 unique foods entries.

For the current analysis, we divided the total phosphorus content of each food item into three phosphorus types (plant, animal, or added) in units of mg phosphorus per 100 g food. For each food item, we identified a manufacturer supplied ingredient list from the USDA Branded Products Database [20] for the exact or similar food to determine the presence or absence of plant, animal, and/or added phosphorus. Plant phosphorus-containing ingredients included grains, nuts, seeds, fruits, and vegetables. Animal phosphorus-containing ingredients included meat, fish, dairy, and eggs. Added phosphorus-containing ingredients included phosphates and phosphoric acids. The total phosphorus content of each food (as reported in the nutrient database) was divided evenly into the phosphorus types present in a particular food.

Blood pressure

Paired blood pressure measurements were taken on four separate days at baseline and three to four separate days at six months using a random-zero sphygmomanometer. For a given visit, blood pressures were reported as the mean of all available measurements. Those without blood pressure measurements at six months, or those taking anti-hypertensive medication at six months, had their three month measurement carried forward. Those without a three month measurement had their blood pressure imputed using values from participants in the Advice Only group [21].

Statistical analysis

We estimated participants' phosphorus intake, phosphorus excretion, and blood pressure as the mean of all available measurements for each time point (Supplemental Figure 1).

We examined the association of change in urinary phosphorus excretion and dietary phosphorus intake (total, plant, animal, and added) with change in systolic and diastolic blood pressure from baseline to six months using Spearman's rank correlation coefficient and linear regression models. To account for the influence of intervention on the association between phosphorus and blood pressure, we (a) adjusted for intervention arm and (b) examined the association separately by intervention arm by including an interaction term with the phosphorus exposure. Difference in the association of phosphorus intake and excretion with blood pressure by intervention group were compared using analysis of covariance (ANCOVA) with a significance level of P-interaction < 0.05 followed by pairwise comparisons using Tukey's Honest Significant Difference (HSD) with a significance level of $P < 0.05$. Differences in the association between phosphorus intake and blood pressure by phosphorus type (plant, animal, or added) overall were compared using analysis of variance (ANOVA) with a significance level of P-interaction < 0.05, followed by three pairwise comparisons with a significance level of $P < 0.05$. Differences in the association between phosphorus intake and blood pressure by phosphorus type (plant, animal, or added) by intervention group were compared first using ANCOVA for the phosphorus type by intervention interaction with a significance level of P-interaction < 0.05, followed by an ANOVA comparing the three phosphorus types within each intervention group with a significance level of *P*-interaction < 0.05, followed by three pairwise comparisons with a significance level of $P < 0.05$. We further adjusted for age, race, sex, study center, income, education level, and change in total energy intake (kcal/d), sodium intake (mg/d), fitness level (heart rate, bpm), and DASH diet index. We performed a sensitivity analysis further adjusting for change in weight.

We adjusted phosphorus intake (total, plant, animal, and added) for energy intake using the residual method [22]. Income and education were modelled ordinally. Fitness level was estimated using heart rate at the end of the second stage of a 10-minute submaximal treadmill exercise test at baseline and six months (or the last available heart rate for participants unable to complete the test) [19]. DASH diet index was estimated using study-specific quintiles of intake of fruits, vegetables, nuts and legumes, whole grains, low-fat dairy, sodium, red and processed meats, and sweetened beverages (soda) [23]. Models examining plant, animal, or added phosphorus types included all three phosphorus types in the model.

Results

Baseline characteristics

At baseline, when all participants were consuming their usual diet, mean total phosphorus intake was 1154 mg/d (95%CI 1126, 1182) with 38%, 53%, and 10% coming from plant, animal, and added phosphorus, respectively (Table 1). Mean phosphorus intakes from plant, animal, and added phosphorus were 429 mg/d (95%CI 415, 443), 619 mg/d (95%CI 599, 639), and 106 mg/d (95%CI 101, 111), respectively (Supplemental Tables 1–3). Those with higher total phosphorus intake had higher urinary phosphorus excretion, higher potassium, sodium, calcium, and total energy intake, and consumed a lower percent of total phosphorus from plant and added phosphorus, a higher percent from animal phosphorus, had a higher overall DASH diet index, and a higher level of fitness (lower heart rate). Those with higher total phosphorus intake were also more likely to be white, male, and weighed more, had higher incomes, and had higher levels of education. Adjustment for total energy intake did not substantively change results. (Supplemental Table 4).

At baseline, mean urinary phosphorus excretion was 937 mg/d (95%CI 910, 963) (Table 2). There were significant differences in baseline urinary phosphorus excretion by intervention group (*P*-interaction = 0.025); those assigned to the Established intervention had significantly lower urinary phosphorus excretion than those assigned to Established + DASH ($P = 0.027$). Those with higher urinary phosphorus excretion were not significantly different with respect to age, diastolic blood pressure, or education level. Those with higher urinary phosphorus excretion had higher total phosphorus intake, as well as higher potassium, sodium, calcium, and total energy intake. Those with higher urinary phosphorus excretion did not consume a significantly different percent of total phosphorus from plant, animal, or added phosphorus compared to those with lower urinary phosphorus excretion. Trends were similar for energy-adjusted urinary phosphorus excretion (Supplemental Table 5).

Change from baseline to six months

From baseline to six months, both systolic and diastolic blood pressure decreased overall, and for all intervention groups ($P < 0.001$) (Table 3). Total phosphorus intake did not change overall ($P = 0.174$) or for Advice Only ($P = 0.078$) but decreased for Established ($P = 0.002$), and increased for Established + DASH ($P = 0.012$). Urinary phosphorus excretion decreased overall ($P < 0.002$), and for Advice Only ($P < 0.001$) and Established ($P = 0.007$), but did not significantly change for Established + DASH ($P = 0.928$). Overall, participants did not change intake of plant ($P = 0.967$) or animal ($P = 0.910$) phosphorus while they decreased intake of added phosphorus ($P < 0.001$). Those assigned to the Advice Only intervention did not change intake from plant, animal, or added phosphorus ($P = 0.097$, 0.191, and 0.499, respectively). Those assigned to the Established intervention significantly decreased intake from animal ($P = 0.011$) and added ($P < 0.001$) phosphorus, but not plant phosphorus ($P = 0.817$). Those assigned to the Established + DASH intervention did not significantly change intake from plant phosphorus ($P = 0.066$), increased intake from animal phosphorus ($P < 0.001$), and decreased intake from added phosphorus ($P < 0.001$).

Compared to Advice Only, Established had a greater decrease in systolic and diastolic blood pressure ($P < 0.001$ and $p = 0.008$, respectively) and a significantly different change in added phosphorus intake ($P = 0.001$). Compared to Advice Only, Established + DASH had a greater decrease in systolic and diastolic blood pressure ($P < 0.001$), a significantly different change in total phosphorus intake ($P = 0.007$), urinary phosphorus excretion ($P = 0.027$), plant phosphorus intake ($P = 0.036$), animal phosphorus intake ($P = 0.001$), and added phosphorus intake ($P < 0.001$). Compared to Established, Established + DASH had a significantly different change in total phosphorus intake ($P < 0.001$) and animal phosphorus intake ($P < 0.001$).

From baseline to six months, energy intake significantly decreased for all three interventions ($P < 0.001$). (Supplemental Table 6). Potassium intake significantly increased for Established + DASH interventions ($P < 0.001$), but not Advice Only or Established ($P = 0.91$ and 0.33, respectively). Sodium intake decreased significantly for all three interventions ($P = 0.002$ Advice only, $P < 0.001$ Established and Established + DASH).). Compared to Advice Only, sodium intake decreased significantly more for Established and Established + DASH ($P < 0.001$). Calcium intake increased significantly for Established + DASH ($P < 0.001$) but not Advice Only or Established ($P = 0.19$ and 0.074, respectively).

Association of phosphorus and blood pressure

Increased total phosphorus intake was non-significantly negatively correlated with changes in systolic and diastolic blood pressure ($P = 0.828$ and 0.893, respectively), while urinary phosphorus excretion was non-significantly positively correlated with changes in systolic blood pressure and significantly positively correlated with changes in diastolic blood pressure ($P = 0.198$ and 0.019, respectively) (Figure). Increased plant phosphorus intake was non-significantly negatively correlated with changes in systolic and diastolic blood pressure ($P = 0.144$ and 0.060, respectively), animal phosphorus intake had a weak and inconsistent correlation ($P = 0.736$ and 0.939, respectively), and added phosphorus had a significant positive correlation ($P < 0.001$, both) (Supplemental Figure 2).

Change in total phosphorus intake was not significantly associated with changes in systolic or diastolic blood pressure crude (*P* = 0.764 and 0.732, respectively) nor after adjustment for age, race, sex, income, education level, study site, and change in energy intake (kcal/d), sodium intake (mg/d), fitness (heart rate, bpm), and DASH diet index (*P* = 0.454 and 0.201, respectively) (Table 4). There were also no significant differences in the association of total phosphorus intake and systolic or diastolic blood pressure by intervention in either model.

In all participants, increased urinary phosphorus excretion was non-significantly associated with increased systolic and significantly associated with increased diastolic blood pressure both crude (*P* = 0.069 and 0.005, respectively) and adjusted (*P* = 0.267 and 0.035, respectively) and there was a significant interaction by intervention. The association of urinary phosphorus excretion with systolic and diastolic blood pressure was significantly different between the Advice Only and Established + DASH groups both crude (*P* = 0.015 and 0.005, respectively) and adjusted (*P* = 0.010 and 0.006, respectively). Among those on the Established + DASH intervention, increased urinary phosphorus excretion significantly associated with increased systolic and diastolic blood pressure both crude (*P* = 0.004 and $P <$ 0.001, respectively) and adjusted (*P* = 0.014 and 0.002, respectively).

The type of phosphorus (plant, animal, or added) significantly modified the association between phosphorus intake and blood pressure in the crude, but not in the adjusted model. Overall, added phosphorus intake had a significantly different association with systolic and diastolic blood pressure than plant (*P* = 0.004 and 0.003, respectively, crude) and animal (*P* = 0.009 and 0.014, respectively, crude) phosphorus. Increased added phosphorus intake was associated with significant increases in systolic and diastolic blood pressure (*P* = 0.006 and 0.008, respectively, crude). Among the Advice Only group (but not Established or Established + DASH), added phosphorus intake had a significantly different association with systolic and diastolic blood pressure than plant (*P* = 0.005 and 0.021, respectively, crude) or animal (*P* = 0.001 and 0.008, respectively, crude) phosphorus. Among the Advice Only group, increased added phosphorus intake was associated with significant increases in systolic and diastolic blood pressure (*P* = 0.003 and 0.022, respectively, crude).

Additional adjustment for change in weight attenuated the results overall (Supplemental Table 7). However, the association between urinary phosphorus excretion and both systolic and diastolic blood pressure was still significantly different between Advice Only and Established + DASH (*P* = 0.030 and 0.017, respectively). Increased urinary phosphorus excretion was associated with decreased systolic blood pressure among those on Advice Only (*P* = 0.035) and increased diastolic blood pressure among those on Established + DASH (*P* = 0.018).

Discussion:

In this secondary analysis of a randomized behavioral intervention trial, we found that increases in total dietary phosphorus intake were not associated with changes in blood pressure. However, the type of phosphorus (plant, animal, or added) significantly modified the association between phosphorus intake and blood pressure. Increased added phosphorus intake was significantly (in the crude model) associated with increases in systolic and diastolic blood pressure. Increases in urinary phosphorus excretion were also associated with increases in diastolic blood pressure overall and in those assigned to the Established and Established + DASH interventions.

These findings may help explain the inconsistent results found in previous studies of an association between dietary phosphorus intake and urinary phosphorus excretion with blood pressure. Several studies have found total dietary phosphorus intake is associated with beneficial [1–3], adverse [10,11,24], or no consistent [3,4] cardiovascular health-related outcomes. However we found added phosphorus (but not plant or animal phosphorus) may be associated with harmful changes in blood pressure. Failure to account for the type of phosphorus may have contributed to the inconsistent findings of prior studies.

Furthermore, while one prospective observational study found urinary phosphorus excretion associated with reduced incidence of cardiovascular disease [5], they were not able to account for lifestyle and dietary patterns. We found that the association between urinary phosphorus excretion and blood pressure varied by behavioral intervention group, a proxy for lifestyle and dietary patterns. This is in line with a secondary analysis of the Dietary Approaches to Stop Hypertension (DASH) trial, which found that the percentage of urinary phosphorus excreted in the urine varied significantly by dietary pattern [25].

The strengths of PREMIER include the large sample size, detailed and repeated dietary interviews conducted by trained researchers, careful and repeated blood pressure measurements, six month intervention, high follow up rate, large dietary contrast between individuals, and randomized design. Strengths of the current study include the detailed stratification of the total phosphorus content from the 3,755 unique foods consumed by PREMIER participants into plant, animal, and added phosphorus. One other study classified phosphorus from added phosphorus, but the assumed phosphorus-containing ingredients were used at the maximum allowed by European Union regulations [10]. This could significantly over-estimate intake from added phosphorus, and potentially bias associations.

The study has several limitations. PREMIER, like all studies using 24 hour dietary recalls, depends on self-reported dietary intake. The use of trained interviewers and repeated dietary recalls in PREMIER improves the accuracy. Second, estimates of dietary intake are only as accurate as the nutrition database underlying the estimates. We stratified total phosphorus into plant, animal, and added phosphorus using the USDA Branded Products Database but were unable to stratify plant phosphorus into phytate vs. non-phytate nor animal into dairy vs. non-dairy. If phytate but not non-phytate plant phosphorus is associated with beneficial changes in blood pressure, our results may have been attenuated. Furthermore, we were not able to precisely estimate the relative contribution of plant, animal, and added phosphorus within specific foods. This may have led to an under or over estimate of the intake of specific types of phosphorus. Finally, the added phosphorus only accounted for 10% of total phosphorus intake in PREMIER participants, limiting statistical power. However, this may reflect typical added phosphorus intakes in a general population. Randomized trials suggesting a harmful effect of added phosphorus to cardiovascular health have supplemented diets with much higher levels of added phosphorus [6,8,9].

The current study has implications for future research and policy. Several studies have proposed urinary phosphorus excretion as a proxy for dietary phosphorus intake [26–28]. However, a recent study found that the phosphorus excretion varies significantly by dietary pattern [25]. The current study further suggests that urinary phosphorus excretion may be an inappropriate proxy for dietary phosphorus intake based on the observation that urinary phosphorus excretion is associated with harmful changes in blood pressure, while total phosphorus intake was not associated with changes in blood pressure. However, increased urinary phosphorus excretion may be a risk factor of increased blood pressure. Studies using multiple 24h urine collections would be useful to better define key dietary and non-dietary factors that determine urinary phosphorus excretion.

Our results do not support recent calls for required labelling of total phosphorus on food packages. While in certain populations, such as those with chronic kidney disease, dietary phosphorus is a nutrient to limit, our findings suggest that the type of phosphorus may have an important effect on its association with health outcomes in a general population. Prior to advocating labeling, we need stronger and more consistent evidence for an association between specific types dietary phosphorus intake with health outcomes. Adding an additional nutrient without clear guidance to the public as to whether the nutrient is beneficial or harmful does not provide actionable information and could distract from an already crowded nutrition panel. In addition to the importance of other nutrients (such as potassium and sodium) and the ratio of phosphorus to other nutrients (such as the calcium to phosphorus ratio), our study suggests that additional studies are required to examine the association of specific types of phosphorus with health outcomes.

Conclusions

In this secondary analysis of a randomized behavioral intervention trial, we found that increases in total dietary phosphorus intake were not associated with changes in blood pressure. However, the type of phosphorus (plant, animal, or added) significantly modified the crude association between phosphorus intake and blood pressure. These findings may help explain the inconsistent associations found in previous studies, and suggests that additional studies are required to examine the association of specific types of phosphorus with blood pressure and other health outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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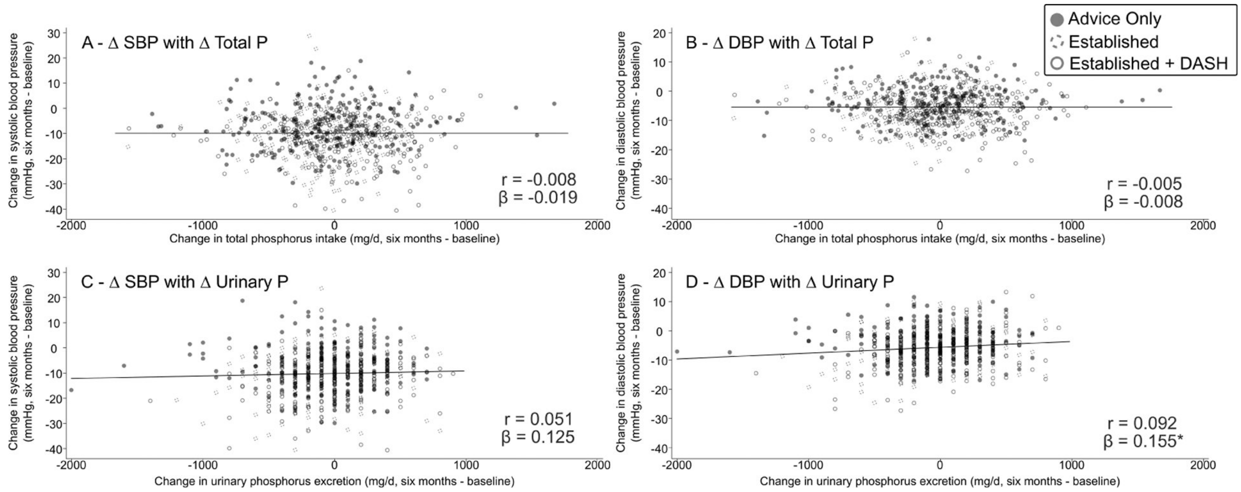

Figure.

24h dietary recall interviews, urinary phosphorus excretion from a single 24h urine collection, and blood pressure from three to four pairs of measurements at each time point.

r = Pearson correlation coefficient.

Trend line and β's from univariate linear regression. β's represent change in blood pressure (mmHg) per 100mg/d increase in phosphorus.

*significantly different than zero, $p < 0.05$.

wo data points from the Advice Only intervention were truncated from the top left panel at (−2500, −6.75) and (−2100, 11.25). Black line represents zero (no change in blood pressure)

Table 1.

Baseline characteristics of PREMIER participants by quartile of total phosphorus intake.

	Total	**Q1**	**Q2**	**Q3**	**Q4**	***P*-trend***
Total phosphorus intake (mg/d), median (range)	1110 (284, 3001)	715 (284, 857)	989 (859, 1110)	1236 (1110, 1405)	1624 (1405, 3001)	
n (%)	806 (100.0)	202 (25.1)	201 (24.9)	202 (25.1)	201 (24.9)	
Intervention						0.231
Advice Only	271 (33.6)	79 (39.1)	64 (31.8)	64 (31.7)	64 (31.8)	
Established	267 (33.1)	59 (29.2)	76 (37.8)	72 (35.6)	60 (29.9)	
Established + DASH	268 (33.3)	64 (31.7)	61 (30.3)	66 (32.7)	77 (38.3)	
Age	50.0 ± 8.9	50.5 ± 9.0	49.9 ± 8.6	49.7 ± 9.1	49.7 ± 8.9	0.35
Race (White)	519 (64.4)	86 (42.6)	128 (63.7)	140 (69.3)	165 (82.1)	**< 0.001**
Sex (Male)	308 (38.2)	35 (17.3)	65 (32.3)	85 (42.1)	123 (61.2)	**< 0.001**
Weight (kg)	95.3 ± 18.9	90.4 ± 17.0	93.3 ± 17.5	96.0 ± 17.8	101.5 ± 21.2	**< 0.001**
BMI at Run-in	33.0 ± 5.8	33.0 ± 5.7	32.6 ± 5.7	33.3 ± 5.5	33.3 ± 6.4	0.344
Systolic Blood Pressure (mmHg)	134.9 ± 9.6	135.0 ± 10.4	135.1 ± 9.4	135.1 ± 9.0	134.2 ± 9.5	0.422
Diastolic Blood Pressure (mmHg)	84.8 ± 4.2	84.5 ± 4.3	84.6 ± 4.1	85.1 ± 4.0	85.0 ± 4.2	0.171
Education Level						**< 0.001**
High School or less	74 (9.2)	27 (13.4)	15 (7.5)	21 (10.4)	11 (5.5)	
College or some college	472 (58.6)	136 (67.3)	122 (60.7)	107 (53.0)	107 (53.2)	
Postgraduate Work	260 (32.3)	39 (19.3)	64 (31.8)	74 (36.6)	83 (41.3)	
Income						**< 0.001**
< $30,000	84 (10.8)	35 (18.2)	19 (9.7)	20 (10.5)	10 (5.0)	
$30,000-$59,999	253 (32.6)	68 (35.4)	63 (32.1)	60 (31.6)	62 (31.2)	
$60,000+	440 (56.6)	89 (46.4)	114 (58.2)	110 (57.9)	127 (63.8)	
Study Site						**< 0.001**
A	208 (25.8)	78 (38.6)	45 (22.4)	48 (23.8)	37 (18.4)	
B	147 (18.2)	34 (16.8)	41 (20.4)	39 (19.3)	33 (16.4)	
C	223 (27.7)	54 (26.7)	64 (31.8)	52 (25.7)	53 (26.4)	
D	228 (28.3)	36 (17.8)	51 (25.4)	63 (31.2)	78 (38.8)	
Fitness (heart rate, bpm)	130 ± 14	132 ± 14	131 ± 14	131 ± 14	128 ± 15	**0.002**
DASH Diet Index	24 ± 5	22 ± 4	24 ± 5	23 ± 5	25 ± 5	**< 0.001**
Total Phosphorus Intake (mg/d), mean ± SD	1154 ± 408	683 ± 132	987 ± 72	1246 ± 84	1702 ± 278	**< 0.001**
Urinary Phosphorus Excretion (mg/d)	937 ± 384	752 ± 323	895 ± 316	956 ± 349	1149 ± 429	**< 0.001**
Percent Phosphorus Excretion	87 ± 39	113 ± 48	91 ± 32	77 ± 28	68 ± 27	**< 0.001**
Phosphorus intake from plant (mg/d)	429 ± 198	269 ± 95	382 ± 119	449 ± 147	616 ± 222	**< 0.001**

	Total	Q1	Q2	Q3	Q4	*P*-trend*
Phosphorus intake from animal (mg/d)	619 ± 293	336 ± 118	506 ± 124	684 ± 151	951 ± 293	**< 0.001**
Phosphorus intake from added phosphorus (mg/d)	106 ± 69	77 ± 52	99 ± 58	113 ± 67	135 ± 81	**< 0.001**
Percent of phosphorus intake from plant	38 ± 12	40 ± 13	39 ± 11	36 ± 12	36 ± 12	**0.001**
Percent of phosphorus intake from animal	53 ± 13	49 ± 14	51 ± 12	55 ± 11	55 ± 12	**< 0.001**
Percent of phosphorus intake from added phosphorus	10 ± 6	11 ± 7	10 ± 6	9 ± 5	8 ± 5	**< 0.001**
Energy (kcal/d)	1946 ± 633	1376 ± 354	1739 ± 365	2087 ± 415	2586 ± 614	**< 0.001**
Potassium (mg/d)	2523 ± 903	1660 ± 506	2278 ± 530	2619 ± 525	3540 ± 777	**< 0.001**
Sodium (mg/d)	3128 ± 1230	2240 ± 822	2766 ± 803	3360 ± 924	4148 ± 1371	**< 0.001**
Calcium (mg/d)	738 ± 354	412 ± 156	639 ± 189	796 ± 220	1107 ± 372	**< 0.001**

Values are means ± SDs or number (percentage), unless otherwise noted.

* p-trend from univariate linear regression using continuous total phosphorus intake for continuous variables and ANOVA for categorical variables.

Bold indicates statistically significant at the $p < 0.05$ level.

Table 2.

Baseline characteristics of PREMIER participants by quartile of urinary phosphorus excretion.

	Total	Q1	Q2	Q3	Q4	*P*-trend*
Urinary Phosphorus Excretion (mg/d), median (range)	900 (100, 3300)	600 (100, 700)	800 (800, 900)	1000 (1000, 1100)	1400 (1200, 3300)	
n (%)	801 (100.0)	262 (32.7)	206 (25.7)	133 (16.6)	200 (25.0)	
Intervention						**0.025**
Advice Only	271 (33.8)	96 (36.6)	75 (36.4)	38 (28.6)	62 (31.0)	
Established	267 (33.3)	93 (35.5)	69 (33.5)	43 (32.3)	62 (31.0)	
Established + DASH	263 (32.8)	73 (27.9)	62 (30.1)	52 (39.1)	76 (38.0)	
Age	50.0 ± 8.9	50.3 ± 9.5	50.9 ± 8.9	49.8 ± 8.8	48.9 ± 8.2	0.064
Race (White)	512 (64.2)	121 (46.4)	129 (63.2)	102 (76.7)	160 (80.4)	**< 0.001**
Sex (Male)	305 (38.3)	50 (19.2)	58 (28.4)	64 (48.1)	133 (66.8)	**< 0.001**
Weight (kg)	95.4 ± 18.8	88.3 ± 16.8	92.3 ± 15.9	98.8 ± 19.6	105.5 ± 18.7	**< 0.001**
BMI at Run-in	33.1 ± 5.8	31.9 ± 5.3	32.4 ± 5.7	33.6 ± 6.3	34.9 ± 5.6	**< 0.001**
Systolic Blood Pressure (mmHg)	134.8 ± 9.6	134.1 ± 9.7	136.1 ± 10.0	135.6 ± 9.5	134.0 ± 8.9	0.859
Diastolic Blood Pressure (mmHg)	84.8 ± 4.2	84.0 ± 4.0	84.8 ± 4.2	85.2 ± 4.1	85.4 ± 4.3	**< 0.001**
Education Level						0.09
High School or less	73 (9.2)	29 (11.1)	14 (6.9)	12 (9.0)	18 (9.0)	
College or some college	467 (58.6)	161 (61.7)	123 (60.3)	75 (56.4)	108 (54.3)	
Postgraduate Work	257 (32.2)	71 (27.2)	67 (32.8)	46 (34.6)	73 (36.7)	
Income						**< 0.001**
< $30,000	83 (10.8)	41 (16.6)	19 (9.7)	10 (7.7)	13 (6.6)	
$30,000-$59,999	251 (32.7)	91 (36.8)	59 (30.3)	44 (33.8)	57 (29.1)	
$60,000+	434 (56.5)	115 (46.6)	117 (60.0)	76 (58.5)	126 (64.3)	
Study Site						**< 0.001**
A	210 (26.2)	96 (36.6)	58 (28.2)	29 (21.8)	27 (13.5)	
B	143 (17.9)	37 (14.1)	35 (17.0)	26 (19.5)	45 (22.5)	
C	220 (27.5)	76 (29.0)	62 (30.1)	39 (29.3)	43 (21.5)	
D	228 (28.5)	53 (20.2)	51 (24.8)	39 (29.3)	85 (42.5)	
Fitness (heart rate, bpm)	130 ± 15	132 ± 13	130 ± 14	129 ± 17	129 ± 15	**0.036**
DASH Diet Index	24 ± 5	23 ± 5	24 ± 5	24 ± 5	24 ± 5	0.673
Total Phosphorus (mg/d)	1152 ± 409	965 ± 345	1124 ± 351	1234 ± 400	1372 ± 427	**< 0.001**
Urinary Phosphorus Excretion (mg/d), mean ± SD	937 ± 383	558 ± 125	847 ± 50	1043 ± 50	1455 ± 302	**< 0.001**
Percent Phosphorus Excretion	87 ± 39	65 ± 27	84 ± 32	94 ± 35	116 ± 41	**< 0.001**
Phosphorus intake from plant (mg/d)	428 ± 199	366 ± 173	415 ± 168	476 ± 238	490 ± 205	**< 0.001**

	Total	Q1	Q2	Q3	Q4	*P*-trend*
Phosphorus intake from animal (mg/d)	618 ± 295	506 ± 242	610 ± 264	652 ± 278	751 ± 338	**< 0.001**
Phosphorus intake from added phosphorus (mg/d)	106 ± 69	92 ± 62	99 ± 69	106 ± 64	131 ± 74	**< 0.001**
Percent of phosphorus intake from plant	38 ± 12	39 ± 13	37 ± 11	39 ± 13	36 ± 12	0.133
Percent of phosphorus intake from animal	53 ± 13	51 ± 13	54 ± 12	52 ± 13	54 ± 12	0.123
Percent of phosphorus intake from added phosphorus	10 ± 6	10 ± 7	9 ± 6	9 ± 6	10 ± 6	0.84
Energy (kcal/d)	1944 ± 634	1716 ± 538	1871 ± 540	2017 ± 589	2269 ± 724	**< 0.001**
Potassium (mg/d), mean (sd)	2519 ± 903	2180 ± 799	2485 ± 799	2652 ± 932	2911 ± 942	**< 0.001**
Sodium (mg/d), mean (sd)	3121 ± 1233	2685 ± 1079	2979 ± 979	3362 ± 1242	3676 ± 1397	**< 0.001**
Calcium (mg/d), mean (sd)	736 ± 353	623 ± 313	707 ± 333	770 ± 323	892 ± 383	**< 0.001**

Values are means ± SDs or number (percentage), unless otherwise noted.

*p-trend from univariate linear regression using continuous total phosphorus intake for continuous variables and ANOVA for categorical variables.

Bold indicates statistically significant at the p < 0.05 level.

Table 3.

Baseline values and crude change from baseline to six months for blood pressure, urinary phosphorus excretion, and dietary phosphorus intake by intervention arm for participants of PREMIER.

	Overall		Advice Only		Established		Established + DASH	
	Baseline	Change at 6 Months	Baseline	Change at 6 Months	Baseline	Change at 6 Months	Baseline	Change at 6 Months
Systolic blood pressure (mmHg)	134.9	**−9.4**	134.2	**−6.6[A]**	135.5	**−10.5[B]**	134.9	**−11.1[B]**
	(134.2, 135.6)	**(−10.1, −8.7)**	(133.1, 135.4)	**(−7.7, −5.4)**	(134.4, 136.7)	**(−11.7, −9.4)**	(133.8, 136.0)	**(−12.2, −9.9)**
Diastolic blood pressure (mmHg)	84.8	**−5.2**	84.8	**−3.8[A]**	85.0	**−5.5[B]**	84.6	**−6.4[B]**
	(84.5, 85.1)	**(−5.7, −4.8)**	(84.3, 85.3)	**(−4.6, −3.0)**	(84.5, 85.5)	**(−6.3, −4.7)**	(84.1, 85.1)	**(−7.2, −5.6)**
Total phosphorus intake (mg/d)	1154	−21	1129	−45[B]	1150	**−82[B]**	1184	**65[A]**
	(1126, 1182)	(−50, 9)	(1080, 1177)	(−96, 5)	(1101, 1199)	**(−133, −30)**	(1135, 1232)	**(14, 117)**
Urinary phosphorus excretion (mg/d)	937	**−53**	931	**−92[B]**	903	**−70[AB]**	977	2[A]
	(910, 963)	**(−83, −24)**	(885, 976)	**(−142, −41)**	(857, 949)	**(−121, −20)**	(931, 1023)	(−48, 53)
Plant phosphorus intake (mg/d)	429	0	426	−21[B]	424	−3[AB]	437	23[A]
	(415, 443)	(−15, 14)	(402, 449)	(−45, 4)	(400, 448)	(−28, 22)	(414, 461)	(−2, 48)
Animal Phosphorus intake (mg/d)	619	−1	605	−28[B]	620	**−56[B]**	631	**80[A]**
	(599, 639)	(−26, 24)	(570, 640)	(−70, 14)	(585, 656)	**(−99, −13)**	(596, 666)	**(37, 123)**
Added phosphorus intake (mg/d)	106	**−19**	97	3[A]	106	**−23[B]**	115	**−38[B]**
	(101, 111)	**(−25, −13)**	(89, 106)	(−6, 13)	(98, 114)	**(−33, −13)**	(107, 123)	**(−48, −28)**

Table 4.

Association of change in phosphorus intake and excretion from baseline to six months with change in systolic and diastolic blood pressure by intervention group in participants of PREMIER.

		Overall		Advice Only		Established		Established + DASH		*p*-INTERACTION[‡]	
		Crude[*]	Adjusted[†]	Crude	Adjusted[†]	Crude	Adjusted[†]	Crude	Adjusted[†]	Crude	Adjusted[†]
Change in systolic blood pressure (mmHg per 100mg/d increase in phosphorus)	Total Phosphorus	0.03	−0.10	0.11	−0.02	−0.13	−0.16	0.02	−0.15	0.575	0.881
		(−0.14, 0.20)	(−0.36, 0.16)	(−0.15, 0.38)	(−0.42, 0.38)	(−0.48, 0.23)	(−0.69, 0.37)	(−0.26, 0.31)	(−0.57, 0.27)		
	Urinary Excretion	0.17	0.11	−0.12	−0.23	0.32	0.32	**0.51**	**0.43**	**0.014**	**0.007**
		(−0.01, 0.36)	(−0.08, 0.30)	(−0.39, 0.15)[B]	(−0.51, 0.06)[B]	(−0.04, 0.69)[AB]	(−0.06, 0.70)[AB]	**(0.16, 0.85)**[A]	**(0.09, 0.78)[A]**		
	P-Interaction[§]	**0.015**	0.102	**0.006**	-	0.106	-	0.206	-	**0.047**[‖]	0.266[‖]
	Plant Phosphorus	−0.19	−0.30	0.20	0.00	−0.47	−0.34	−0.23	−0.51	0.344	-
		(−0.54, 0.16)	(−0.77, 0.16)	(−0.47, 0.87)	(−0.77, 0.76)	(−1.08, 0.14)	(−1.08, 0.39)	(−0.79, 0.34)	(−1.20, 0.18)		
	Animal Phosphorus	0.02	−0.10	0.01	−0.18	0.04	−0.09	0.02	−0.02	0.990	-
		(−0.18, 0.22)	(−0.37, 0.17)	(−0.30, 0.32)	(−0.58, 0.22)	(−0.36, 0.45)	(−0.58, 0.40)	(−0.34, 0.38)	(−0.45, 0.41)		
	Added Phosphorus	**1.24**	0.85	**2.36**	**2.05**	0.45	0.46	0.88	0.08	0.219	-
		(0.36, 2.12)	(−0.15, 1.85)	**(0.80, 3.93)**	**(0.39, 3.70)**	(−1.28, 2.19)	(−1.42, 2.33)	(−0.48, 2.24)	(−1.47, 1.63)		
Change in diastolic blood pressure (mmHg per 100mg/d increase in phosphorus)	Total Phosphorus	0.02	−0.12	0.05	−0.06	0.03	−0.07	−0.02	−0.22	0.889	0.705
		(−0.10, 0.14)	(−0.30, 0.06)	(−0.14, 0.23)	(−0.34, 0.22)	(−0.21, 0.28)	(−0.44, 0.31)	(−0.21, 0.18)	(−0.51, 0.08)		
	Urinary Excretion	**0.18**	**0.14**	−0.06	−0.10	**0.34**	**0.29**	**0.42**	**0.39**	**0.003**	**0.004**
		(0.05, 0.31)	**(0.01, 0.28)**	(−0.24, 0.13)	(−0.30, 0.10)[B]	**(0.09, 0.59)**	**(0.02, 0.55)[AB]**	**(0.19, 0.66)**	**(0.15, 0.63)[A]**		
	P-Interaction[§]	**0.008**	0.111	**0.031**	-	0.617	-	0.206	-	**0.033**[‖]	0.110[‖]
	Plant Phosphorus	−0.20	**−0.38**	0.04	−0.02	−0.21	−0.31	−0.35	**−0.74**	0.457	-
		(−0.44, 0.05)	**(−0.71, −0.06)**	(−0.43, 0.50)	(−0.55, 0.52)	(−0.63, 0.21)	(−0.83, 0.20)	(−0.74, 0.04)	**(−1.23, −0.26)**		

		Overall		Advice Only		Established		Established + DASH		*p*-INTERACTION‡	
	Animal Phosphorus	0.04	−0.09	0.00	−0.18	0.09	−0.10	0.05	0.00	0.87	-
		(−0.10, 0.18)	(−0.28, 0.09)	(−0.21, 0.21)	(−0.46, 0.11)	(−0.18, 0.37)	(−0.44, 0.25)	(−0.19, 0.30)	(−0.30, 0.30)		
	Added Phosphorus	**0.83**	0.21	**1.26**	0.76	0.98	0.41	0.40	−0.39	0.474	-
		(0.22, 1.44)	(−0.49, 0.91)	**(0.19, 2.34)**	(−0.40, 1.92)	(−0.22, 2.18)	(−0.91, 1.72)	(−0.53, 1.34)	(−1.48, 0.70)		

Values are means (95% CIs).

Bold indicates change is statistically different than zero at the $p < 0.05$ level.

Different superscript letters (A,B) indicate statistically significantly different six-month change in a given outcome between intervention groups at the $p < 0.05$ level.

Values are means (95% CIs).

[*] Adjusted for intervention group.

[†] Adjusted for age, white race, male sex, income, education level, study site, and change in energy intake (kcal/d) and sodium intake (mg/d), fitness (heart rate, bpm), and DASH diet index.

Bold indicates statistically different than zero at the $p < 0.05$ level.

Different superscript letters (A,B) indicate statistically significant difference between intervention groups for the same exposure, outcome, and adjustment level at the $p < 0.05$ level.

[//] ANCOVA Phosphorus type by intervention $P < 0.05$ indicates a statistically significant difference in the association between phosphorus intake and blood pressure by intervention and/or phosphorus type at the same adjustment level.

[‡] ANCOVA Intervention $P < 0.05$ indicates a statistically significant difference in the association between phosphorus intake and blood pressure by intervention at the same adjustment level. Only performed if the ANCOVA Phosphorus type by intervention had a $P < 0.05$.

[§] ANOVA Phosphorus type. $P < 0.05$ indicates a statistically significant difference in the association between phosphorus intake and blood pressure by phosphorus type within the same intervention and at the same adjustment level. Only performed if the ANCOVA Phosphorus type by intervention had a $P < 0.05$.

Table 5.

‘What is known about topic’
A recent systematic review of randomized trials and prospective observational studies did not find a consistent association of total dietary phosphorus intake with blood pressure
Dietary phosphorus exists in a variety of forms, with some suggesting that specific types of phosphorus may be associated with either positive or negative health outcomes.
‘What this study adds’.
We found that increases in total dietary phosphorus intake were not associated with changes in blood pressure.
The type of phosphorus (plant, animal, or added) significantly modified the crude association between phosphorus intake and blood pressure.
These findings suggest that the type of phosphorus may modify the association between phosphorus intake and blood pressure.