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# Rising Trend of Hypokalemia Prevalence in the US Population and Possible Food Causes

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**ABSTRACT**

**Background:** Potassium intake deficiency is a chronic issue in the US and many other countries. Possible causes of the deficiency are understudied.
**Objective:** This study examined potassium deficiency in the US population and possible causes for the new trend.
**Methods:** Serum potassium data of 28,379 men and 29,617 women between ages 12 and 80 years old who participated in the US National Health and Nutrition Examination Survey (NHANES) between 1999 and 2016 were examined. Blood samples were collected by NHANES and blood biochemistry data were measured in designed laboratories. The data were released bi-annually. Possible causes of low potassium intakes were explored.
**Results:** There was an apparent decline of serum potassium in the US population between ages 12 and 80 years from 1999 to 2016. Annual average serum potassium concentrations changed from 4.14 ± 0.01 to 3.97 ± 0.01 mmol/l during this period. Hypokalemia prevalence in the US rose from 3.78%±0.68% to 11.06%±1.08% during this period with a higher hypokalemia prevalence in non-Hispanic black than in non-Hispanic white persons. It is possible that declining potassium concentration in food sources in the US contributed to lower potassium intake and increasing potassium deficiency.
**Conclusion:** The rising trend of hypokalemia prevalence in the US population between 1999 and 2016 is alarming. Renewed efforts to reduce potassium intake deficiency in the US at population level are needed. The impact of possible decreasing crop available potassium levels and increasing consumption of processed food on the potassium deficit trend in the US are possible explanations for the rise in hypokalemia prevalence and require further study.

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**KEYWORDS**
Serum potassium; potassium deficit; hypokalemia; crop available potassium

## Introduction

Potassium (K) is the most abundant cation in the intracellular fluid of human body, and plays a critical role in maintaining cell function (1). Potassium intake deficits in the US population has long been recognized (2,3). Average K intake from food for Americans (adults aged 20 and over) was 2633 mg/day for men and 2323 mg/day for women according to the 2015-2016 National Health and Nutrition Examination Survey (NHANES) (4). These intakes are significantly lower than the recently established Adequate Intake levels of 3400 mg/day for adult men and 2600 mg/day for adult women reflecting the highest dietary intakes of that age group of North Americans by the US National Academies of Sciences, Engineering, and Medicine (5). An earlier study on the 2003-2008 NHANES data estimated that only 3% of the US adults and 10% of children under the age of five (2003-2010) met the Adequate Intake at that time of 4700 mg/day for K which reflected an intake recommended to help maintain normal blood pressure (2,3). Low dietary K intake and hypokalemia have been associated with high blood pressure, increased risk of cardiovascular diseases, overall mortality and progression of renal disease (6–8). It is also associated with the increase of urinary calcium excretion and risk of osteoporosis, and is detrimental for the management of hypercalciuria and kidney stones (9,10). Given the significant health impact of K deficiency on people, it is essential that severity of K deficiency in the US population be properly recognized and possible causes be identified. Because food and beverage supply in the US is mostly domestic (87.3% in 2016 according to the USDA report) (11), a possible contribution of lowered K level in food sources to the K deficiency in the US population is also examined.

This study intends to examine how trends of serum K level and percentage of people with hypokalemia (will be referred as hypokalemia prevalence in this paper) in the US population changed from 1999 to 2016 using data from NHANES. It will attempt to examine whether a possible decline of K stores in the US food produces could be part of the cause for the epidemic of K deficiency and hypokalemia patterns in the US.

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## Material and methods

### Data

Serum K data in mmol/liter were obtained from the Standard Biochemistry Profile files of the NHANES measured between 1999 and 2016 of 28,379 men and 29,617 women (12). The data contained measurements of nine NHANES sampling cycles between 1999 and 2016 because NHANES data are released in 2-year cycles. Age, gender, race, and MEC (mobile examination center) sample weight data were obtained from the demographic files in NHANES database. Only the records that have serum K data were selected. NHANES is a program of studies intended for assessing the health and nutritional status of adults and children in the US, administered by the National Center for Health Statistics (NCHS) of the US Centers for Diseases Control and Prevention (CDC). The population was sampled with a complex, stratified, multistage probability cluster sampling design to provide data that are nationally representative of the civilian, noninstitutionalized US population. Approximately 6,000 participants across the country in each bi-annual cycle, were examined in the NHANES MEC. Participants provided written informed consent before participation. Blood samples were collected from these participants and standard biochemistry profile data, including potassium ion concentration were determined in NAHNES designated laboratories. Detailed descriptions of the survey design and data collection procedures are available in NHANES documents (12). NHANES data collection was reviewed and approved by the NCHS ethics review board (13).

Changes of soil K median in ammonium acetate extractable K (ppm) for farms in the US from 2010 to 2015 were obtained from the report of the International Plant Nutrition Institute (14). The data reflect the crop available soil K which were measured by the cation exchange method (14). The data included only the states with more than 2000 test results from farm soil samples. Amounts of K fertilizer applied in the US were obtained from Economic Research Service, US Department of Agriculture (15).

### Statistical analyses

Because of the significant variation in individual's serum K levels, age grouped averages were used to extract the underlying trend pattern (Figure 1). Potassium data of seven age groups (12–20, 21–30, 31–40, …,71–80 etc., therefore, adults and adolescents) for men and women were analyzed independently. Given the large dataset, a "low passing filter" of age stratification allows the trend in underlying patterns to be uncovered in an otherwise highly fluctuated data series (16). Respective MEC sample weights in the demographic files of the nine cycles were used to account for differential nonresponse and/or noncoverage, to adjust for planned oversampling of some groups, and to adjust for uneven representation of days of the week. Weighted means, standard errors and their 95% confidence levels of serum K of 27,826 men and 28,975 women grouped by age, sex, and race were calculated. All statistical analyses (including weighted means, proportion, standard errors, 95% confidence interval and linear regression trend) were conducted in Stata (SE/14) using its Survey Data Analysis tool.

Hypokalemia (potassium deficiency) is defined as blood serum K level being less than 3.6 mmol/l (17). Hypokalemia proportions (prevalence) of men, women, non-Hispanic black and non-Hispanic white were the quotients of number of individuals with blood serum level $<3.6$ mmol/l (as numerator) and total population of corresponding category (as denominator) after samples were weighted. The choropleth map of changes of crop available soil K using ArcGIS 10.4 (ESRI software) was plotted to illustrate the change of crop-available soil K levels from 2011 to 2015 in the US agricultural regions.

## Results

### Trends of serum K levels and hypokalemia prevalence in the US population

Average serum K levels decreased significantly during the seventeen years between 1999 and 2016 (Figure 1) in the US population across all stratified age groups. Men's K levels were consistently higher than women's, though the gap narrows after approximately age 55. Annual average potassium levels for all races and sexes between ages of 12 and 80 years old (adolescents and adults) changed from $4.14 \pm 0.01$ to $3.97 \pm 0.01$ mmol/l (number after ± denotes the 95% confidence range) during this period. Average prevalence of hypokalemia for all races and sexes between ages of 12 and 80 years old rose from 3.78%±0.68% to 11.06%±1.08%. Average hypokalemia prevalence increased from 2.39%± 0.83% and 5.1%±1.11% in 1999-2000 to 7.52%±1.38% and 14.42%±1.69% in 2015-2016 for men and women respectively. Average serum K level of all ages and sexes between 12 and 80 years was lower in non-Hispanic black than in non-Hispanic white ($3.95 \pm 0.007$ vs. $4.03 \pm 0.005$ mmol/l); average hypokalemia prevalence was higher in non-Hispanic black than in non-Hispanic white adults as well (10.39%±0.58% vs. 6.56%±0.37%) during this period (Figure 2). Based on the linear regression model of hypokalemia between 1999 and 2016, by year 2050, the projected average hypokalemia prevalence in the US population will increase to about 20.3%±9.6% for non-Hispanic white and $21.7 \pm 12.98$% for non-Hispanic black if the current trend continues.

### Decrease of crop available soil K in most farming states

The decline of crop available soil K in the majority of the US farming states in the recent past years based on data gathered by the International Plant Nutrition Institute is apparent (Figure 3) (14). There has been a long-term reduction in the application of K fertilizers in the US accompanying the increasing crop yield per acre (14,15) and the subject deserves more in-depth study. The proportion of K as the total amount of nutrient applications (total of

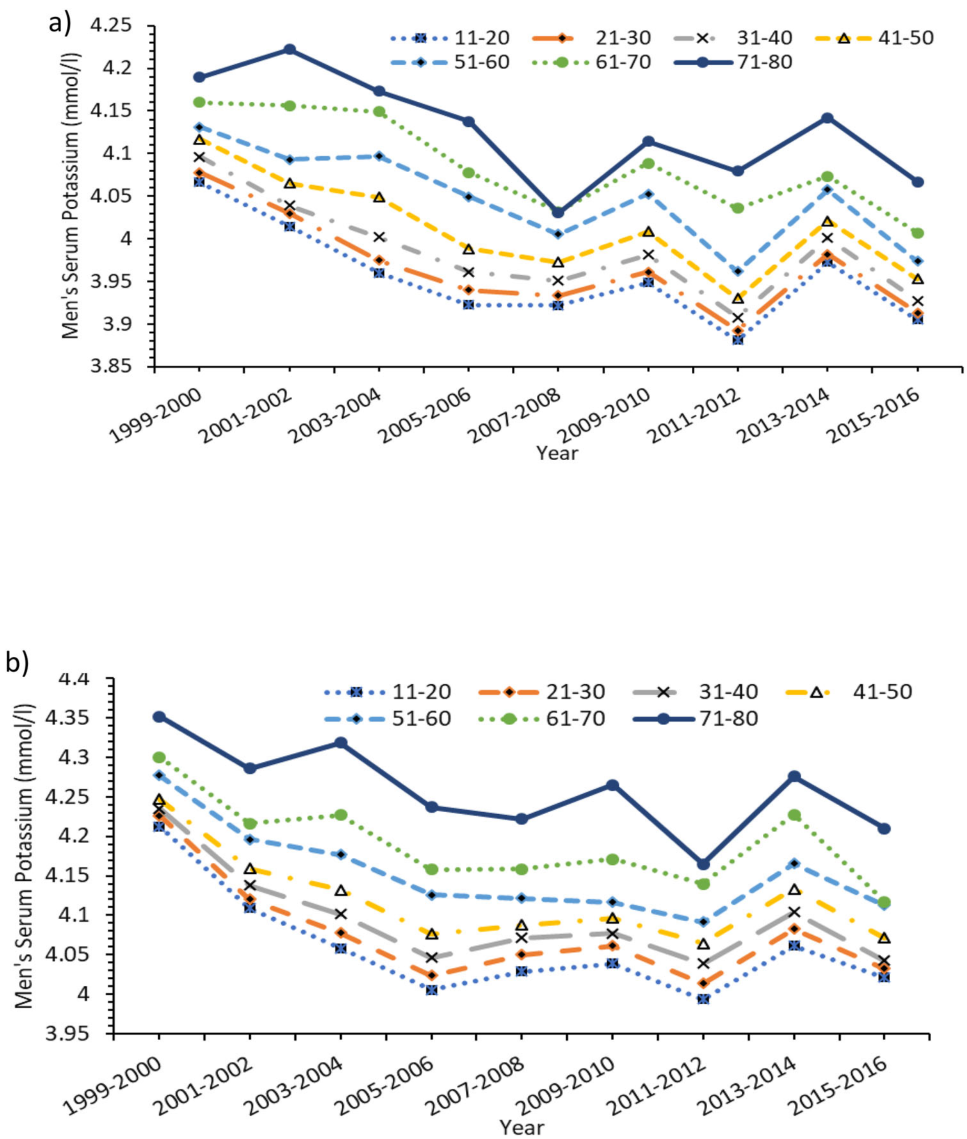


**Figure 1.** Serum potassium levels of a), 28,379 men and b), 29,617 women between ages of 12 and 80 years old in the US between 1999 and 2016. Numbers in legends show the age range.

nitrogen, phosphate and potash) in the US farms declined even more during the past 50 years (Figure 3) (15).

## Discussion

### *Declining serum K level and increasing hypokalemia prevalence in the US population between 1999 and 2016 and possible causes*

Previous studies suggested that higher hypokalemia prevalence in non-Hispanic black than in non-Hispanic white might be related to lower consumption of potassium-rich vegetables in blacks compared to whites (18). Because hypokalemia is defined as a serum K level being less than 3.6 mmol/l for both men and women (16), the rate of hypokalemia was more prevalent in women than in men because of their overall lower K intake. The difference of serum K level between men and women is reported to be largely related to their physiological sex difference (19,20). Broad causes for the increase of hypokalemia prevalence in the US population from 3.78%±0.68% to 11.06%±1.06% between 1999 and 2016 (Figure 2) may be multiple.

Some have suggested that increasing consumption of processed food, which has some K removed during skin removal, boiling, and cooking, combined with a reduction in the consumption of fruits and vegetables, as a cause for K intake deficiency (1, 6). Varied dietary preferences have also been suggested as causes for higher potassium deficiency in some population groups (18). A common cause for low serum K at individual level might has been attributed to the excessive loss of K in urine from the kidney induced by metabolic alkalosis or from the GI tract in stool induced by diarrhea (21). The uniform decline of serum K level across all age groups from 1999 to 2016 in this study and lower potassium intake reported for year 2003-2008 than that of year 1988-1999 in the US adult population (2) might suggest a possible broad decline of potassium levels in the US food supply. The temporal decline of potassium concentration in the food supply has not been considered in most previous studies (22). There have been declines of crop available soil

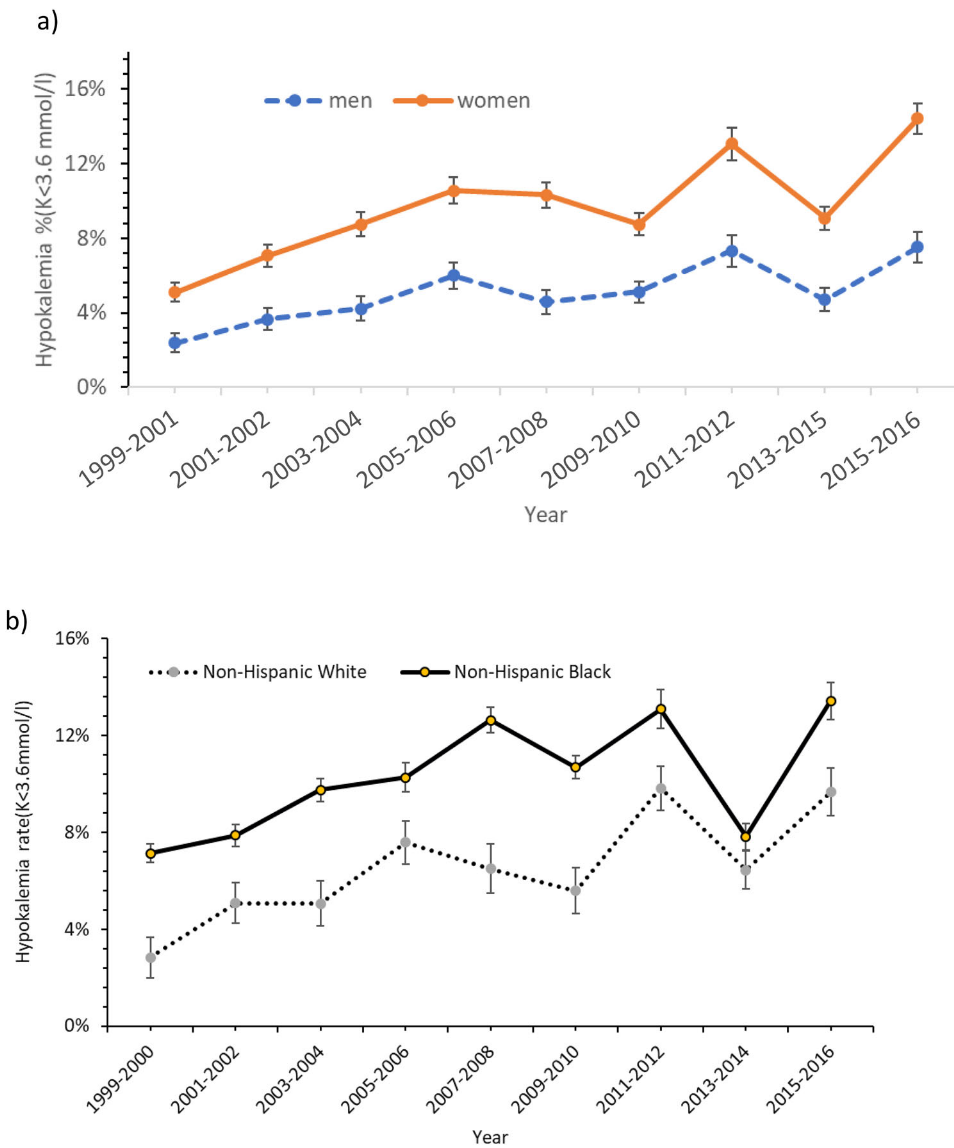


**Figure 2.** Hypokalemia (serum potassium level <3.6 mmol/l) prevalence in the US between 1999 and 2016 for a), 28379 men and 29,617 women, b), 23,771 non-Hispanic white and 12,795 non-Hispanic black between ages of 12 and 80 years old. Vertical bars show standard errors.

K in the majority of US agricultural states and a steady reduction in the K fertilizer application in the US over the last 50 years (14,15, 23). K fertilizer application has declined in the US primarily due to its low yield benefit compared to nitrogen and phosphate fertilizers (24). Excess application of K fertilizers can compete with available soil calcium (24). Low crop available K in soil will likely result in an overall reduction of K in crop produce in the US, including both forage and grains (25). Given that most of the US food supply (USDA estimated about 87.3% of food and beverage being domestic in 2016) (11) is domestic, declining K levels in the US agricultural produce is, therefore, suspected to have contributed to the increased hypokalemia prevalence across all age groups of people in the US.

Because the gradient of cell K concentration is one of the key factors in determining the cell's membrane potential, abnormal serum K levels can lead to severe muscle dysfunction, resulting in respiratory failure and cardiac arrest (9, 26,27). Deficiencies in K intake are related to hypertension, diabetes, and increased risks of cardiovascular diseases and stroke (1, 28). Even mild hypokalemia can increase morbidity and mortality in some patient populations (9,10). Therefore, current trends of declining serum K level and increasing hypokalemia prevalence in the US population is alarming.

### *Measures for combating K deficiency are needed*

The worsening serum K levels and rising hypokalemia prevalence in the US population show that past efforts to encourage food intake of high K diet have not been effective in alleviating the K deficiency in the US at the population level (2, 9, 29). Most potassium supplements in the US contain only up to 99 mg (which is about 2% of the recommended daily value) of K. K in supplements above that level are considered unsafe by US Food and Drug Administration

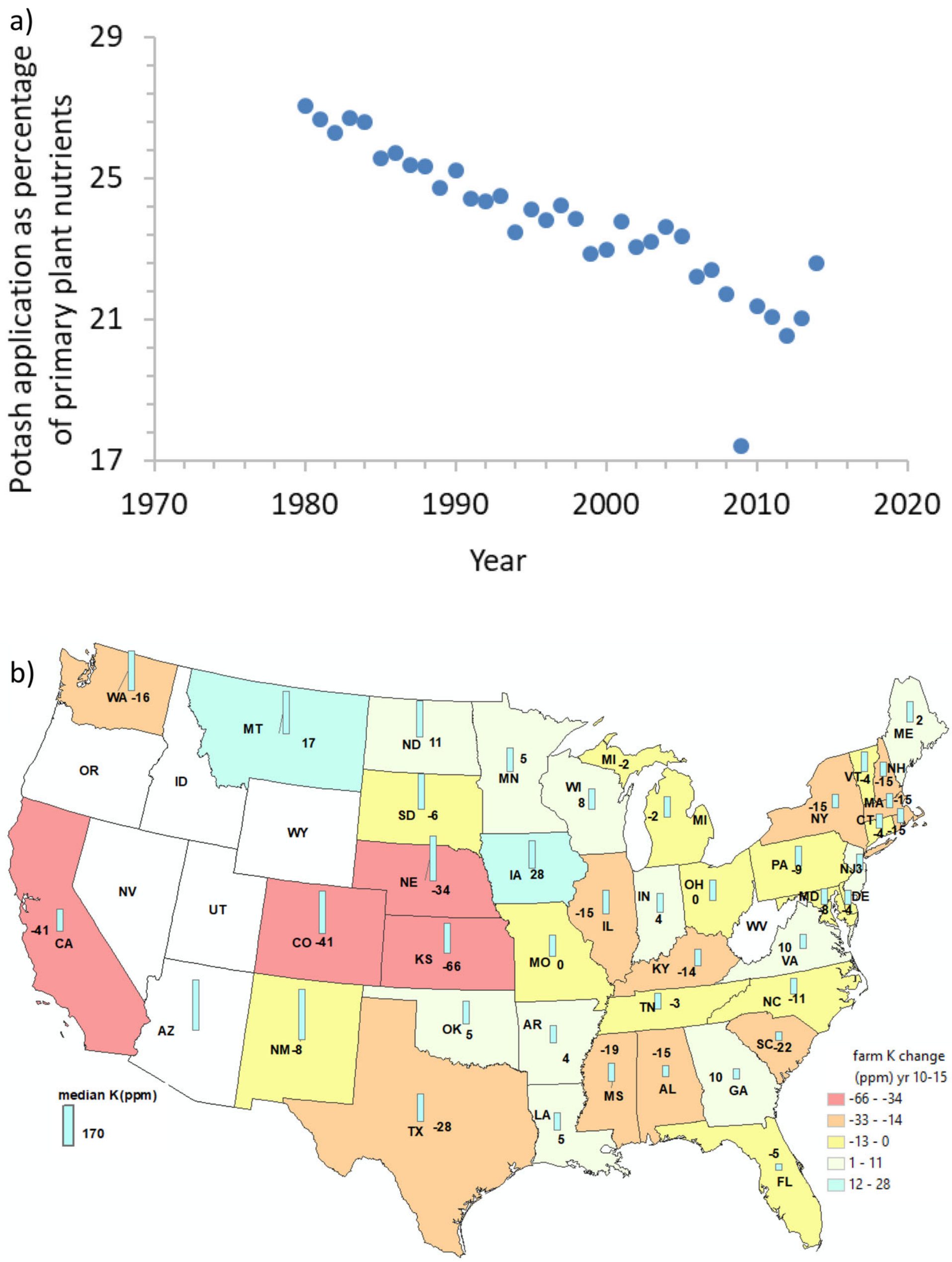


**Figure 3.** a), trend of potassium fertilizer ($K_2O$) usage as a percentage of the primary plant nutrients (nitrogen, phosphate, and potash) in the US between 1980 and 2014, b), state median plant available potassium in 2015 (bar symbol) and changes of crop available soil potassium (number units in ppm) in farming states from 2010-2015.

(30,31) because of risk of small-bowel lesions (4, 31,32). Given the possibility of the hypokalemia prevalence reaching above 20% by year 2050 if the current trend continues, new measures combating K deficiency need to be examined. Strategies to more effectively increase the consumption of high K diet in the US population are needed from medical communities. The declining crop available soil K in the US, resulting in lower uptake by US food produce, also suggests that agricultural policies encouraging application of K fertilizer for restoring soil K level should be initiated. Other than potassium leaching during the precipitation-runoff process, K removal through crop harvesting is probably the most consequential K removal in US soil. K fertilizer could help restore crop available K in soil and, therefore, increase K stores in crops and overall K intake in the US population. However, the rate of optimal K fertilizer application is beyond the scope of this study (33).

## Limitation of the study

Cross-sectional data used in the current study, and therefore, causal inferences are not possible. Another limitation is the inconsistency of some serum K data in the NHANES database and resulting uncertainty in predicting the future hypokalemia prevalence. Also, serum K levels in the NHANES database were from a one-time measurement. Though low potassium intakes at a population level contribute to hypokalemia prevalence, hypokalemia diagnosis of a person often is not a reflection of an individual's low potassium intake, rather, an excessive potassium loss in urinary excretion or stool (22). The impact of declining K levels in the US food supply resulting from the reduced crop available K and declining application of K fertilizers in the US soil, on the K deficit in the US population needs to be further studied.

## Conclusions

Despite long recognition of K intake deficiency, the problem became significantly worse between 1999 and 2016. Serum K levels, which is a better reflection of potassium status in the body than that of urinary excretion, decreased during this period across all age groups in the US population. Hypokalemia prevalence in the US population between ages 12 and 80 years old more than doubled from 1999 to 2016 and was significantly higher in non-Hispanic black than in non-Hispanic white. Decreases of K in the US agricultural products (through decreases in crop-available soil K and reduction in application of K fertilizer) likely contributed significantly to the decline in the K intake in the US population. Increasing consumption of processed food might have contributed to the decreasing serum K level in the US population as well. Low serum K level and hypokalemia are related to higher risks of hypertension, cardiovascular, and renal diseases etc. The worsening trend of the hypokalemia prevalence in the US calls for renewed efforts in the medical community to encourage high K diets for people with normal renal function and policy initiatives to increase K stores in the US agricultural produces.

## Disclosure statement

The authors declare that there is no conflict of interest regarding the publication of this paper. There is no external funding source for the project.

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