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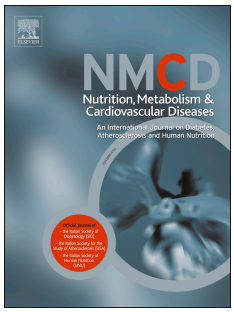

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Trend in potassium intake and Na/K ratio in the Italian adult population between the 2008 and 2018 CUORE Project surveys

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ABSTRACT

Background and aims: Low potassium intake, in addition to high sodium, has been associated with higher risk of hypertension and CVD. The Study assessed habitual potassium intake and sodium/potassium ratio of the Italian adult population from 2008-2012 to 2018-2019 based on 24-hour urine collection, in the framework of the CUORE Project/MINISAL-GIRCSI/MENO SALE PIU' SALUTE national surveys.

Methods and results: Data were from cross-sectional surveys of randomly selected age-and-sex stratified samples of resident persons aged 35-74 years in 10 (out of 20) Italian regions. Urinary electrolyte and creatinine measurements were performed in a central laboratory. Analyses considered 942 men and 916 women, examined in 2008-2012, and 967 men and 1,010 women, examined in 2018-2019.

In 2008-2012, the age-standardized mean of potassium intake (urinary potassium accounts for 70% of potassium intake) was 3147 mg (95% CI 3086-3208) in men and 2784 mg (2727-2841) in women, whereas in 2018-2019, it was 3043 mg (2968-3118) and 2561 mg (2508-2614) respectively. In 2008-2012, age-adjusted prevalence of persons with an adequate potassium intake (i.e. ≥ 3510 mg/day) was 31% (95% CI 28-34%) for men and 18% (16-21%) for women; in 2018-2019, it was 26% (23-29%) and 12% (10-14%) respectively. The sodium/potassium ratio significantly decreased both in men and women.

Conclusions: The average daily potassium intake of the Italian general adult population remains lower than the WHO and EFSA recommended level. These results suggest the need of a revision to strengthen initiatives for the promotion of an adequate potassium intake at the population level.

Abstract word count: 247 words

Keywords: epidemiology; nutrition; public health.

INTRODUCTION

Low potassium intake has been associated with several non-communicable diseases (NCDs), including cardiovascular disease, chronic kidney stone formation and low bone-mineral density.[1] In particular, there is consistent randomized controlled trial evidence that increased potassium intake may reduce both systolic and diastolic blood pressure and in prospective studies a higher potassium intake is associated with reduced risk of stroke [2-8]. Thus the interest in dietary potassium intake and its potential impact on public health has grown in the last decades due to the increasing burden of cardiovascular diseases and the need of cost-effective and feasible actions to contain the epidemic of NCDs.[9]

Based on a meta-analysis of the available intervention studies showing that the largest significant reduction in blood pressure was attained when potassium intake was increased to between 3510 and 4680 mg/day (approximatively equivalent to a 24-hour urinary potassium excretion of 70-90 mmol accounting for about 30% of extra-urinary losses), [1, 10], the World Health Organization (WHO suggested a potassium intake of at least (3510 mg/day) for all individuals aged 16 years or more; this recommended level of intake is a conditional recommendation because there is limited evidence regarding the precise level that will result in maximum health benefits.[1, 10, 11]. Also the European Food Safety Authority (EFSA) has set an adequate potassium intake of 3510 mg/day for men and women over 14 years old. [12, 13]

WHO recommended taking potassium through food. Key dietary sources of potassium are fruits and vegetables—with potatoes being the highest source of potassium from all foods.[14, 15]

Due to safety of increased potassium intake by food, no upper limit has been recommended.[1]

Potassium and sodium are closely interrelated but have opposite effects on BP [8, 16, 17]; actually, it has been suggested that the sodium to potassium intake ratio may be an even better predictor of hypertension and cardiovascular events than sodium or potassium intake *per sé* [18-20]. Although the WHO guidelines do not focus on an optimal sodium to potassium ratio, assuming that the recommendations for potassium and sodium consumption are achieved, the target molar ratio of sodium to potassium should be approximately 1.

In line with the objectives of the "Gaining health: making healthy choices easy" strategic Programme for non-communicable diseases prevention, and within the National Preventive Plan (NPP) 2014-2018, extended to 2019, in Italy, the Ministry of Health has launched initiatives to support a larger intake of fruits and vegetables, for their general benefits on health, also aiming to support an adequate level of potassium intake.

An assessment of the habitual potassium intake was carried out in 2008-2012 in the Italian general adult population using 24-hour urine collections obtained from the participants of the Osservatorio Epidemiologico Cardiovascolare/Health Examination Survey (OEC/HES 2008-2012) within the CUORE Project.[21, 22]

The aim of the present study was to evaluate the trend in potassium intake and sodium to potassium ratio over the past ten years considering data of a further assessment of the adult population salt intake made in 2018-2019 (HES 2018-2019 – CUORE Project). Surveys of 2008-2012 and 2018-2019 were promoted and supported by the Italian Ministry of Health.

METHODS

Study design

From March 2008 to July 2012, the Osservatorio Epidemiologico Cardiovascolare/Health Examination Survey (OEC/HES), within the CUORE Project, investigated randomly selected age and sex stratified samples of 220 men and women aged 35-79 years per every 1.5 million residents in all Italian Regions. The participation rate of OEC/HES 2008-2012, defined as the number of persons who participated in the survey after receiving the invitation divided by the size of the eligible sample, was 53%.[21] In this framework, for the assessment of the population potassium and salt intake, the MINISAL-GIRCSI Study and MENO SALE PIU' SALUTE Study used for each Region a randomly selected subsample of 100 men and 100 women stratified by age and sex, based on the WHO recommendation that a sample of 100-200 individuals is required to estimate sodium intake with a 95% confidence interval (CI) about the mean of consumption of ±12 mmol/day using a single 24 hours collection.[23]

The OEC/HES 2008-2012 was conducted by the Italian National Institute of Health (Istituto Superiore di Sanità-ISS) in collaboration with a national scientific association of cardiologists (ANMCO–Associazione Nazionale Medici Cardiologi Ospedalieri) and its foundation [Fondazione per il Tuo Cuore – Heart Care Foundation (HCF)]. The MINISAL-GIRCSI and MENO SALE PIU' SALUTE studies were conducted by the ISS for the part referring to the adult population that is included in the present analysis, in collaboration with the Federico II University of Naples Department of Clinical and Experimental Medicine, which had the responsibility of the overall MINISAL-GIRCSI Study.

From April 2018 to December 2019, a new HES has been conducted by the ISS which has included the assessment of the Italian general adult population potassium and salt intake carried out in collaboration with Federico II University of Naples Department of Clinical Medicine and Surgery. The new survey investigated randomly selected age and sex specific samples of 200 men and women aged 35-74 years resident in 10 Regions (out of 20) chosen in the North, Centre and South of Italy. The participation rate of HES 2018-2019 was 40%.

The 2008-2012 and 2018-2019 surveys were approved by the Ethical Committee of the ISS respectively on 11 November 2009 and 14 March 2018, and are recognized within the European Health Examination Survey collaboration [24].

Study procedures and methods

The measurement of urinary potassium excretion has been adopted in both surveys in order to estimate the population average potassium intake since 24-hour potassium excretion represents over 70% of the electrolyte intake based on several studies considered in the recent EFSA report on Dietary Reference Values .[12] Thus, both surveys included a 24-hour urine collection in addition to a physical examination and the administration of a face to face questionnaire. Persons were invited to enrol by postal letter and an information notice of the project made the participant informed about the research purposes and able to consciously sign an informed consent to participate. The following categories of people were considered ineligible and removed from the original sample: the dead, the emigrants, those working outside the residence area for

the full survey period, and those whose undelivered letters were returned with the notation 'unknown'.

For the assessment of dietary salt and potassium intake, participants were asked to collect all urines they passed during a 24-hour period starting from the second morning urine pass and ending with the first urine passed the following morning. They were provided with a SARSTED plastic container of 3 L with the addition of thymol to prevent bacterial growth. Once the collection was returned, the total volume of urine was recorded and urine specimens were extracted after shaking. The specimens were immediately frozen: during the HES 2008-2012, three of them were kept at -30^{o}C for measurement of sodium and creatinine whereas another one was maintained at -80^{o}C in the biological bank of the ISS for future determinations; during the HES 2018-2019, one at -30^{o}C and two at -80^{o}C respectively. The response rates to the request to provide 24-hour urines among those who participated to the surveys were 92% in 2008-2012 and 99% in 2018-2019 (Appendix).

The measurement of sodium, potassium and creatinine was performed for both surveys at Federico II University of Naples by the Central Laboratory of the Department of Clinical and Experimental Medicine (later become Department of Clinical Medicine and Surgery).

In both surveys, urinary sodium, potassium and creatinine concentrations were measured using an ABX Pentra 400 apparatus (HORIBA ABX, Rome, Italy) with an integrated ion-selective electrode (ISE) module. Sodium and potassium were measured by ion selective electrode potentiometry using as urine specific reference the Urichem Gold Bio Dev (Milan, Italy). Urinary creatinine was measured by a kinetic Jaffe´ reaction using as urine reference the Urichem Gold Bio Dev (Milan, Italy) in the 2008-2012 survey and the Low-and-High Control ABX (Montpellier, France) in the 2018-2019 survey. Quality control data for sodium and creatinine has been provided apart.[25]

Quality control data for potassium assessed in the 2008-2012 survey were: accuracy 0.02%, inter-assay variation coefficient 1.7% and intra- assay variation coefficient 0.7%; the respective data for the 2018-2019 survey were: accuracy 0.8%, inter-assay variation coefficient 1.2% and intra-assay variation coefficient 1.3%. Pre-defined criteria for a high likelihood of incomplete urine collection were set as a 24-hour urine volume below 500 ml or a creatinine content referred to body weight outside the range given by the population mean ± 2 standard deviations: based on these criteria, 122 participants were excluded from the analysis for the 2008-2012 and 104 participants for the 2018-2019 survey. In both surveys an overall good quality of the urine collections was found as indicated by the large mean urinary volume and by the finding of the expected mean values for urinary creatinine with the physiological differences related to sex, age and body weight. [25]

The persons' weight and height were measured while they were clothed only in their underwear. A balance beam scale was used for weight measurements, and height was measured with a height rule. Educational level and salt related habits were investigated through a face to face standardized questionnaire. A complete description of standardized methods and procedures of the OEC/HES 2008-2012 has been provided apart.[21] Similar procedures and methods were used for data collection in the HES 2018-2019 survey.

Statistical analysis

The statistical comparison of OEC/HES 2008-2012 and HES 2018-2019 data for the purpose of the present analysis included the residents aged 35-74 years resident in 10 Regions involved in both surveys: Lombardy, Piedmont, Liguria Emilia RomagnaTuscany, Lazio Abruzzo , Basilicata, Calabria, and Sicily.

Urinary sodium intake has been provided apart. [25] Urinary potassium was expressed in mmol per 24-hour. In order to provide an indicator directly comparable with the data from other countries, urinary potassium (mmol/24h) was converted to potassium intake (g/day) (1 mmol corresponding to 39 mg of potassium) multipling by 39 and then again by 1.30 according to WHO and EFSA indications. [10-13] This coefficient was based on the ratio of potassium dietary intake to urinary excretion reported in two studies which used chemical analysis of the diet and 24-h urinary collection. [26, 27] For the assessment of this indicator, age-standardization was performed using the direct method referring to the age sex-specific distributions of Italian adult population 2010 and 2019, respectively for OEC/HES 2008-2012 and HES 2018-2019.[28, 29]

The prevalence of adequate potassium intake was calculated with reference to the value of at least 3510 mg/day , according to WHO and EFSA. [10-13]

Urinary molar sodium to potassium were calculated for each participant as mmol/day ratio. Potassium intake and sodium to potassium ratio was also assessed by four classes of age (35-44, 45-54, 55-64 and 65-74 years) and, for those with available information, by three classes of body mass index (BMI; weight in kg divided by height in m^2) (normal weight - BMI within 18.5-24.9 kg/m^2, overweight BMI within 25.0-29.9 kg/m^2 and obesity BMI≥30 kg/m^2) and two classes of educational level (higher education- high school or college, lower education - primary or middle school). Results are expressed as means and standard deviations for quantitative variables and prevalence for qualitative ones; the related 95% CIs are reported. T-test for unpaired samples (for equal or unequal variance as appropriate) or analysis of variance (ANOVA) were used to assess differences between group means. The chi-squared test was used to compare prevalence. Two sided p-values less than 0.05 were considered statistically significant. Statistical analyses were performed using SAS software, release 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

After the exclusions reported above due to possibly incomplete urine collections, 942 men and 916 women (mean age ± std.: men 54 ± 11 and women 55 ± 11) and 967 men and 1,010 women (mean age ± std.: men 55 ± 11 and women 56 ± 11) were included in the analysis relative to the 2008-12 and the 2018-19 survey, respectively.

Potassium intake

In the 2008-2012 survey, mean 24-hour urinary potassium excretion was 62 mmol (95% CI 61-64) in men and 55 mmol (54-56) in women; in the 2018-2019 survey, the respective values were 60 (59-62) and 51 (50-52) (Figure 1). Mean potassium excretion was significantly reduced from 2008-2012 to 2018-2019 in both men (-4%) (p-value=0.0202) and women (-8%) (p-value<0.0001); when

compared by age classes, in men the reduction was not statistically significant in any age class whereas in women it was significant starting from 45 years old (Table 1).

In 2008-2012, the age-standardized mean of potassium intake was 3147 mg (standard deviation 951; 95% CI 3086-3208) in men and 2784 mg (882; 2727-2841) in women, whereas in 2018-2019, it was 3043 mg (1182; 2968-3118) and 2561 mg (860; 2508-2614) respectively. The reduction by period was equal to 104 mg for men (p-value 0.0344) and 223 mg for women (p<0.0001). Potassium intake was consistently higher in men than in women, with a difference of 12% (p-value< 0.0001) in 2008-2012 and 16% in 2018-2019 (p-value<0.0001).

The frequency distributions of 24-hour urinary potassium/potassium intake in men and women are shown in Figure 1.

In the 2008-2012 survey, 24-hour potassium excretion was of at least 70 mmol/day (corresponding to a potassium intake of at least 3510 mg/day) in 30% (95% CI 27-33%) of men and 18% (15-20%) of women; in the 2018-2019 survey values of 25% (22-28%) and 11% (9-13%) were found for men and women respectively; in men the difference between periods did not reach statistical significance (p-value=0.0783 for men, p-value=0.0004 for women).

In the 2008-2012 survey, the age-adjusted prevalence of persons with at least 3510 mg/day of potassium intake (corresponding to an urinary excretion of at least 70 mmol/day) was 31% (95% CI 28-34%) for men and 18% (16-21%) for women; in the 2018-2019 survey values of 26% (23-29%) and 12% (10-14%) were found for men and women respectively; in men, the difference between periods did not reach statistical significance (p-value=0.1105 for men, p-value=0.0005 for women).

Within period, a trend was observed towards a higher 24-hour urinary potassium excretion with age, which reached statistical significance in 2008-2012 but not in 2018-2019 (ANOVA, Table 1).

In both periods and both genders, 24-hour potassium excretion was significantly and directly associated with BMI classes independently of age (ANOVA within period – Table2); no significant association was found with educational levels, except for men in 2008-2012 (ANOVA within period – Table2).

In men, the statistically significant reduction of 24-hour potassium excretion between 2008-2012 and 2018-2019 was seen even uponadjustment for age class, BMI class and educational level (period significance of ANOVA between periods – Table 2), but it was consistent only among overweight and obese individuals and among those with lower education (t-test –Table 2). In women, the statistically significant reduction of 24-hour potassium excretion between periods was consistent across BMI classes and educational levels, considered singly (t-test –Table 2) or together and independently of age (period significance of ANOVA between periods – Table 2). Both in men and women the educational level lost its significant association with potassium intake when considered together with BMI class (educational level significance of ANOVA between periods – Table 2).

In both periods, some geographical differences were found for 24-hour potassium excretion independently of age, BMI and educational classes (Table S1); (Table S1 and Figure 2); in men, only in five Regions was observed a trend to reduction (for four at significance level), while in women it was observed for eight Regions (for four at significance level) (Table S1).

Sodium to potassium ratio

In the 2008-2012 survey, mean 24-hour urinary sodium to potassium excretion ratio was 3.2 (95% CI 3.0-3.3) in men and 2.7 (2.7-2.8) in women; in the 2018-2019 survey, the respective values were 2.9 (2.8-3.0) and 2.6 (2.5-2.6). Mean sodium to potassium excretion ratio was significantly higher than 1 ($p<0.0001$) in both genders and periods, but it was significantly reduced from 2008-2012 to 2018-2019 in both men (-8%) (p-value=0.0008) and women (-6%) (p-value=0.0011).

The sodium to potassium excretion ratio was higher in men than in women, with a difference of 14% (p-value< 0.0001) in 2008-2012 and 12% in 2018-2019 (p-value<0.0001); within period, no statistically significant differences were found for the ratio across age classes except for women in 2008-2012 (ANOVA, Table 3). The reduction in the sodium to potassium excretion ratio was detected in all age classes, but it was statistically significant only in men and women aged 35-54 years (Table 3).

The sodium to potassium excretion ratio was significantly and directly associated with BMI class and educational level independently of age (ANOVA within period – Table S2), except in men examined in 2008-2012. The statistically significant reduction of sodium to potassium excretion ratio between 2008-2012 and 2018-19 wassignificant even when adjusted for age class, BMI class and educational level (period significance of ANOVA between periods – Table S2) but it was consistent only among normal weight men and obese women and among those with higher educational level (t-test – Table S2).

Reflecting the variability of sodium and potassium, in both periods, some geographical differences were found for sodium to potassium excretion ratio independently of age, BMI and educational classes (Table S3); in both periods and genders, all Regions had a mean ratio higher than 1.

DISCUSSION

Potassium intake

The main finding of the present study is the observation that, in randomly selected samples of Italian general adult population from ten Italian Regions, the average estimated daily potassium intake is still definitely lower than the level recommended by the major health institutions. This is true in all the surveyed Regions, for both men and women, and all age classes, education levels and BMI categories. Actually, potassium intake was slightly reduced ten years after the previous national survey. This reduction was very limited in men and not significant in any age class, was observed only in half of the Regions and mostly apparent in the lower educated and obese categories. The potassium intake reduction in women was instead consistent in most Regions, significant in those aged 45-74 years, and independent from BMI and educational class. Due to the limited reduction, in men the proportion of participants with a potassium intake attaining the WHO and EFSA recommended level was not significantly changed from the first to the second survey.

Similarly to our surveys and using the same tool of 24h urine collection,the Italian section of the INTERSALT study in the late eighties reported a potassium excretion between 56 and 60 mmol in

population samples from Northern, Central and Southern Italy (Bassiano, Gubbio, Mirano and Naples) .[30]

In the late 1980s and 1990s, the adult population average potassium intake was found inadequate in many European and extra-European countries, as evidenced by the INTERSALT and INTERMAP Studies.[30,31] More recently, again based on 24h urine collection, an inadequate potassium intake was reported in many countries worldwide, including among Irish women, in Greece, Republic of Moldova, South Africa, New Zealand, Japan, USA, New York City and Australia.[30-40]. An adequate intake was recently found among Irish men. [33]

Based on 24-hour dietary recall, an inadequate potassium intake was also reported in UK, France, China and South Korea.[43-46]

Few studies were carried out to assess temporal trends in potassium intake. Data from the China Health and Nutrition Survey based on 3 consecutive 24-hour recalls showed a 12% potassium intake decrease between 1991 and 2015.[45] By contrast, data from the Korean National Health and Nutrition Examination Surveys based on 24-hour dietary recall evidenced a 12% increase of potassium intake from 1998 to 2009.[46]

Additional findings of the present study are the sex related difference in potassium intake and the statistical positive associations of potassium intake with BMI classes. Other surveys reported higher levels of potassium intake in men than in women: this difference is probably secondary to higher food and energy intake in men. The association between potassium intake and BMI is also consistent with previous evidence from other countries.[38, 39]

The main sources of potassium in the Italian diet are vegetables and fruits [47] providing together approximately 34% of the total potassium intake, followed by potatoes (10%) and cereals (14%). Other sources are given by meats (12%), dairy products (10%) and fish (5%). Thus, the insufficient potassium intake in the Italian adult population points to an inadequate consumption of fruits and vegetable foods, including also legumes, once a major component of the traditional Mediterranean diet. This interpretation is supported by data on widespread inadequate consumption of fruit or vegetables in Italian adult and in adolescents living in Italy and in Western countries. [21, 48, 49-51] It is very likely that unfavourable dietary habit tracks into adulthood for a majority of individuals. Indeed, several programs of nutritional education have been implemented in the Italian school system to try and overcome this problem.

Reaching 5-a-day fruit and vegetable consumption has proved difficult in low income population groups [52] and even in an Italian study population a substantial reduction in the consumption of plant derived foods was demonstrated at the time of economical crisis. [53].

Although the risk of hyperkalaemia following the high potassium intake of food is definitely unlikely, periodic monitoring of serum potassium levels is indicated in patients with chronic kidney disease and/or under treatment with potassium sparing medications. [54]

Sodium to potassium ratio

Within the present study, a 24-hour sodium to potassium excretion ratio higher than the desirable value of approximately 1 was found both in men and women, all classes of age, BMI and educational level: this notwithstanding, due to the salt intake reduction, a significantly lower ratio was observed between the first and the second survey among participants aged 35-54 years.

A significant trend to a reduction of the of average daily sodium to potassium excretion ratio had never been observed in Italy: available information from the previously cited Italian section of the INTERSALT population study indicated a sodium:potassium ratio between 2.9 and 3.3, similar to the levels observed within the OEC/HES 2008-2012 survey.[30]
In the late 1980s INTERSALT reported sodium:potassium ratios ranging between 0.01 (Brazil) to 7.58 (China), with the mean ratio of Western populations estimated to be 2.98.[30]
More recently, cross-sectional studies have reported a mean sodium to potassium ratio ranging from 1.9 to 3.8 in the general adult population of Ireland, Greece, South Africa, New Zeland, Japan, USA, New York City, Australia.[33, 34, 37-42]

Strengths and limitations

Major strengths of our study are the following: the use of 24 hours urine collection, an objective and reliable method for the assessment of potassium intake at the population level; the good national coverage with enrolment of the study participants through random age and sex stratification in half of the Italian Regions distributed in Northern, Central and Southern Italy; the excellent compliance with the request to provide 24-hour urines; the overall good quality of the urine collections as indicated by the large mean urinary volume and by the finding of the expected mean values for urinary creatinine with the physiological differences related to sex, age and body weight.
On the other hand, we acknowledge some study limitations which should be taken into account when interpreting our results. First, because of the choice of urban districts for the random selection of the study participants in both surveys, the results may not be representative of the habits of populations living in rural areas. The participation rates to the surveys were lower than desirable, yet consistent with lower contact rates occuring in more highly urbanized areas and with the decreasing trend of participation observed in health examination surveys in other European countries [55]; anyway surveys are within the WHO recommended sample size for this kind of epidemiological investigations [23].
The cross-sectional design of the study does not allow to assess causality of the associations between salt intake and BMI or educational level. The use of a single 24-hour urine collection does not allow to accurately assess the individual potassium intake due to the well- known large day to day variation in potassium excretion: however, it is sufficient for the assessment of potassium intake in adequately sized population groups.
There were differences in the educational level distribution between the two surveys which is consistent with the increase of secondary and tertiary education assessed in adults from 2008 to 2017 by the Italian National Institute of Statistics [56]. There was also some difference in the BMI distribution. Nevertheless, these differences cannot have affected our major finding because, both in men and women, potassium intake is definitely lower than recommended in all classes of BMI and educational level. The increase of normal weight, albeit not statistically significant, and of participants with a higher level of education observed between the 2008-2012 and the 2018-2019 survey, might have affected the overall potassium reduction observed in men since a lower reduction was seen among normal weight and better educated compared to obese and less

educated male participants. In women, the amount of potassium reduction was similar by BMI classes and educational levels. However, both in men and women, the reduction of potassium intake between periods was statistically significant when adjusted by BMI class and educational level.

A further limitation was that potassium intake monitoring was not extended to the younger age classes.

A final critical point deserving mention is the conversion of 24h urinary potassium excretion to potassium intake. 24-hour urinary excretion is considered the most reliable biomarker of dietary potassium intake in adults on a population basis and a more objective indicator than dietary recall surveys that indeed depend on the memory, awareness and reliability of participants in the survey, and do not consider the incomplete dietary potassium absorption in the gut [12, 27, 57-60]. However, due to partial elimination of potassium through other physiological ways such as faeces and, to a lesser extent, sweat, recovery rates of between 77% and 92% of dietary potassium in the urine have been reported in different studies [12, 26, 27, 35, 57, 58, 61]. According to the EFSA document on Dietary reference Values for potassium [12], we made the choice to use a conversion factor of 1.30 which was based on the ratio of potassium dietary intake to urinary excretion reported in the only two studies in which both chemical analysis of the diet and 24-h urine collection were performed. [26, 27] Our choice was further supported by the fact that this factor has also been applied by other authors. [1, 2, 34]

Conclusions and Perspectives

In conclusion, this study indicated that 24-hour urinary potassium/potassium intake, in two independent samples of Italian adult population carried out in 10 Regions approximately 10 years apart from each other, was definitely lower than the level recommended by WHO and ESFA for both genders, all Regions and every class of age, BMI and educational level. Mean levels of potassium excretion/intake were higher in men than in women and in those with overweight and obesity compared with normal weight people. Some decrease in the daily average potassium excretion/intake was detected mainly among those aged 45-74 years, and especially among women and obese and less educated men. The prevalence of participants with a potassium intake reaching the WHO and EFSA recommended level somewhat decreased, albeit to a significant extent only in women, in the approximately ten years from the first to the second survey.

As a consequence of the high sodium and insufficient potassium intake, in the Italian adult population the sodium to potassium ratio has been found well higher than 1, despite a significant small reduction between the first and the second survey.

Although these results need confirmation through further systematic and periodic monitoring, they have major public health implications as much as they justify the strengthening of initiatives timely undertaken by the Italian Ministry of Health to promote a healthy diet, i.e. the “Gaining Health: making healthy choices easy” Programme and the National Prevention Plan. Key elements in this regard have been so far the promotion of fruit and vegetable consumption and the implementation of larger legume consumption at the population level starting from childhood and adolescence, in accordance with WHO recommendations. In spite of these efforts, a large gap still remains between the recommended and the actual intakes of potassium, not only in Italy but all

around the world. This suggests the need for an in-depth evaluation by the scientific community and the public health institutions, of the reasons underlying this major problem, which in Italy and in other Mediterranean countries must be read in the context of the progressive decline in the adherence to the traditional Mediterranean diet in favor of a 'westernisation' of food habits leading to reduced consumption of potassium rich plant foods. [52, 62, 63]

Among the factors that explain these negative changes in the population dietary habits are global industrialization and commerce, massive movements of people from rural to urban areas and increasing costs of plant foods but also due to their substitution by less wealthy people with more energy dense lower quality foods. [53, 64-66]

Educational campaigns aiming to enhance population awareness in this regard are important but may not be sufficient, at least in the short term, and the assessment of the utility and safety of additional measures specifically aiming to increase potassium intake at the population level is warranted: in particular, the partial substitution of sodium with potassium salts in the foods, e.g. bread and bakery products, identified as major sources of sodium chloride, may deserves attention given results shown by studies conducted in other countries.[67-70]

These options should be evaluated in due time because the successful implementation of specific action plans would have an important public health impact through reductions in morbidity and mortality, improvement in the quality of life for millions of people, and substantial reductions in health-care costs.[2, 16, 17, 71-74]

Regular surveillance is needed to make sure that strategies are appropriately targeted and changes can be measured over time.

Figures captions

Figure 1. Frequency distribution, mean and standard deviation of 24-hour urinary potassium excretion by gender and period in Italy. Men and women aged 35-74 years, CUORE Project health examination surveys 2008-2012 and 2018-2019.

Figure 2. Mean of 24-hour urinary potassium excretion by gender, period and Region in Italy. Men and women aged 35-74 years, CUORE Project health examination surveys 2008-2012 and 2018-2019.

Supplemental tables captions

Table S1. 24-hour potassium excretion (mmol) by sex, region and period in Italy. Men and women aged 35-74 years, CUORE Project health examination surveys 2008-2012 and 2018-2019.

Table S2. 24-hour sodium (mmol) to potassium excretion (mmol) ratio by sex, body mass index class, educational level and period in Italy. Men and women aged 35-74 years, CUORE Project health examination surveys 2008-2012 and 2018-2019.

Table S3. 24-hour sodium (mmol) to potassium excretion (mmol) ratio by sex, region and period in Italy. Men and women aged 35-74 years, CUORE Project health examination surveys 2008-2012 and 2018-2019.

Appendix caption

Information of participants did not collect 24-hour urine

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Authors contribution

CD participated in the study conception and design, managed the data collection and quality control, performed data analysis, interpreted results, drafted the manuscript and contributed to the management and storage of urine samples; CL contributed to the data collection, to quality control, to the management and the storage of urine samples and critically revised the manuscript; OR and RI performed the laboratory measurements, contributed to the data quality control and critically revised the manuscript; DM performed information technology services, contributed to the data collection and quality control and critically revised the manuscript; ADL contributed to data collection and quality control and critically revised the manuscript; EP contributed to data collection and critically revised; BB contributed to data collection and critically revised; FV contributed to information technology services and critically revised the manuscript; SV, FG, AndDL, GO critically revised the manuscript; DG participated in the study conception, scientifically supported the studies and critically revised the manuscript; PB scientifically supported the studies and critically revised the manuscript; SG participated in the study conception and design, managed the data collection and quality control, contributed to the management and storage of urine samples and critically revised the manuscript; LP contributed to the storage of urine samples and critically revised the manuscript; PS participated in the study conception and design, was responsible of the laboratory measurements and data quality control, interpreted results and critically revised the manuscript. All authors have read and approved the final version of this manuscript for submission.

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Table 1. 24 hours potassium excretion (mmol) by sex, age class and period. Men and women aged 35-74 years, The CUORE Project health examination surveys 2008-2012 and 2018-2019.

	MEN												
	2008-2012						2018-2019						
Age class (years)	n	mean	std	*95% CI*		ANOVA p-value	n	mean	std	*95% CI*		ANOVA p-value	% mean diff	t-test p-value
						0.0018						0.2446		
35-44	235	59	16	*57*	*61*		228	59	34	*54*	*63*		0	0.9437
45-54	238	62	20	*60*	*65*		232	59	18	*57*	*62*		-5	0.1142
55-64	240	65	21	*62*	*68*		266	62	21	*59*	*64*		-5	0.0828
65-74	229	64	19	*61*	*66*		241	61	18	*58*	*63*		-5	0.0604
	WOMEN												
	2008-2012						2018-2019						
Age class (years)	n	mean	std	*95% CI*		ANOVA p-value	n	mean	std	*95% CI*		ANOVA p-value	% mean diff	t-test p-value
						0.0455						0.3996		
35-44	220	52	17	*50*	*55*		213	50	20	*47*	*52*		-5	0.1407
45-54	223	56	18	*53*	*58*		252	50	17	*47*	*52*		-11	0.0001
55-64	241	57	17	*54*	*59*		275	52	16	*50*	*54*		-8	0.0030
65-74	232	56	18	*53*	*58*		270	51	16	*49*	*53*		-9	0.0015

t-test: normal standardize t-test for comparison between periods.
ANOVA: ANOVA model to compare 24 h potassium excretion among age classes within the period.
Italian regions: Lombardy, Piedmont, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Tab … od.
Men and women aged 35-74 years, The CUORE Project health hxamination surveys 2008-2012 and 2018-2019.

	MEN											
	2008-2012					2018-2019						
	n	mean	std	95% CI	ANOVA within period p-value	n	mean	std	95% CI	ANOVA within period p-value	% mean diff	t-test p-value	ANOVA between periods p-value
Body mass index					<0.0001					0.0511			<0.0001
Normal weight	235	58	17	56 60		314	59	30	56 63		3	0.4552	
Overweight	454	62	19	60 64		458	60	19	58 61		-4	0.0483	
Obese	246	68	20	67 70		191	63	21	60 66		-7	0.0261	
Education					0.0382					0.6389			0.1519
Higher education	497	61	19	60 63		685	60	25	59 62		-1	0.4850	
Lower education	436	64	19	62 66		279	60	20	57 62		-7	0.0045	
Period													0.0194

	WOMEN											
	2008-2012					2018-2019						
	n	mean	std	95% CI	ANOVA within period p-value	n	mean	std	95% CI	ANOVA within period p-value	% mean diff	t-test p-value	ANOVA between periods p-value
Body mass index					0.0151					0.0434			0.0004
Normal weight	361	53	17	52 55		443	49	18	48 51		-7	0.0014	
Overweight	299	55	17	54 57		299	51	16	50 53		-7	0.0027	
Obese	246	58	19	55 60		250	52	17	50 54		-9	0.0013	
Education					0.7292					0.1643			0.7237
Higher education	455	55	18	53 57		685	51	18	50 52		-7	0.0006	
Lower education	447	55	17	54 57		323	50	15	48 51		-10	<0.0001	
Period													<0.0001

Body mass index was available in 941 men and 916 women for the 2008-2012 survey and 967 men and 1016 women for 2018-2019 survey.
Educational level was available in 933 men and 902 women for the 2008-2012 survey and 964 men and 1008 women for 2018-2019 survey.
t-test: normal standardize t-test for comparison between periods.
ANOVA within period: ANOVA p-value of the corresponding variable to compare 24 h potassium excretion among age classes (35-44, 45-54, 55-64 and 65-74 years), body mass index classes and educational levels.
ANOVA between periods: ANOVA p-value of the corresponding variable to compare 24 h potassium excretion among periods, age classes (35-44, 45-54, 55-64 and 65-74 years), body mass index classes and educational levels.
ANOVA analyses were permormed among those with BMI>=18.5 kg/m2.
Normal weight - body mass index-BMI within 18.5-24.9 kg/m2, overweight BMI within 25.0-29.9 kg/m2 and obesity BMI≥30 kg/m^2.
Higher education - high school or college; lower education - primary or middle school.
Italian regions: Lombardy, Piedmont, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table 3. 24 hours sodium to potassium excretion (mmol) ratio by sex, age class and period.
Men and women aged 35-74 years, The CUORE Project health examination surveys 2008-2012 and 2018-2019.

MEN

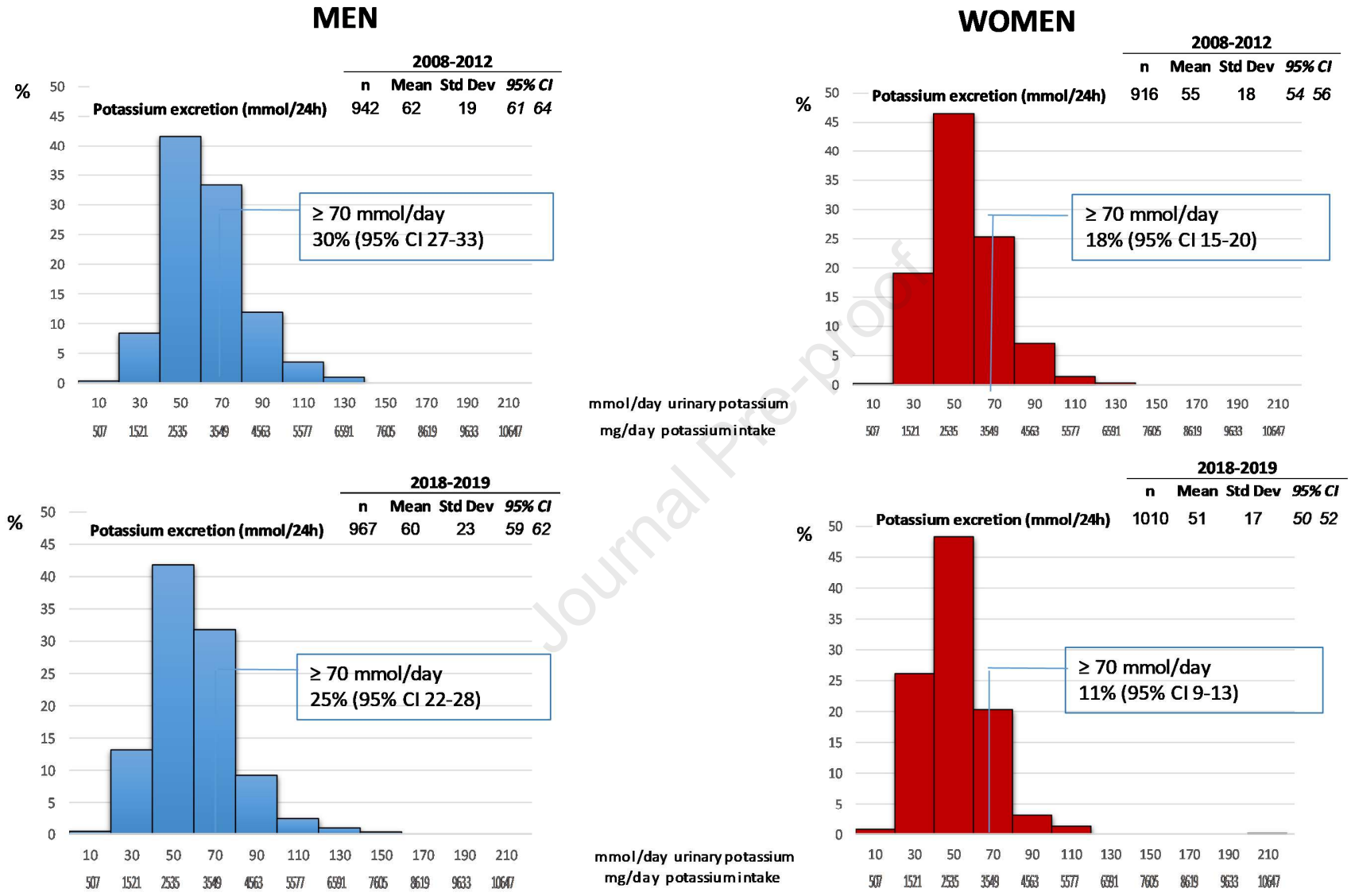
Age class (years)	2008-2012						2018-2019						% mean diff	t-test p-value
	n	mean	std	*95% CI*		ANOVA p-value	n	mean	std	*95% CI*		ANOVA p-value		
						0.3438						0.1304		
35-44	235	3.3	1.3	*3.1*	*3.4*		228	3.0	1.2	*2.8*	*3.2*		-8	0.0276
45-54	238	3.3	1.3	*3.1*	*3.4*		232	3.0	1.2	*2.8*	*3.2*		-8	0.0247
55-64	240	3.2	3.7	*2.7*	*3.7*		266	2.8	1.2	*2.7*	*3.0*		-12	0.1324
65-74	229	2.9	1.1	*2.8*	*3.1*		241	2.8	1.0	*2.7*	*2.9*		-5	0.1366

WOMEN

Age class (years)	2008-2012						2018-2019						% mean diff	t-test p-value
	n	mean	std	*95% CI*		ANOVA p-value	n	mean	std	*95% CI*		ANOVA p-value		
						0.0255						0.4624		
35-44	220	2.9	1.1	*2.7*	*3.0*		213	2.6	1.1	*2.5*	*2.8*		-9	0.0132
45-54	223	2.8	1.2	*2.6*	*3.0*		252	2.6	0.9	*2.5*	*2.7*		-7	0.0376
55-64	241	2.6	1.0	*2.5*	*2.8*		275	2.6	1.1	*2.5*	*2.7*		-2	0.6363
65-74	232	2.6	1.0	*2.5*	*2.7*		270	2.5	0.9	*2.4*	*2.6*		-5	0.1678

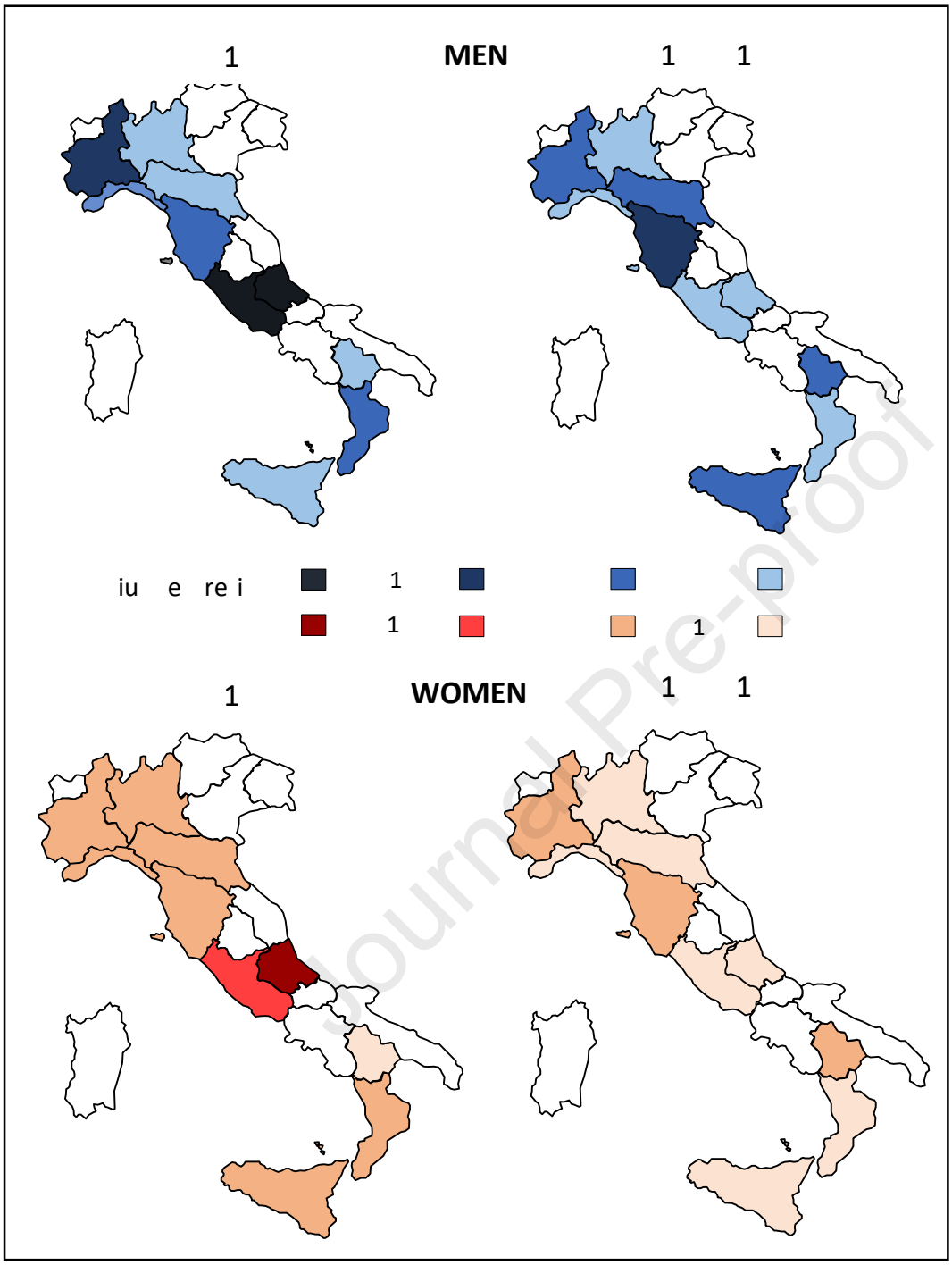
t-test: normal standardize t-test for comparison between periods.
ANOVA: ANOVA to compare 24 h sodium to potassium excretion ratio among age classes within the period.
Italian regions: Lombardy, Piedmont, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Figure 1.



Italian regions: Lombardy, Piedmont, Liguria, Emilia Romagna, Tuscany, Abruzzo, Lazio, Calabria, Basilicata and Sicily
St dev: standard deviation. CI: confidence interval.
Mg potassium intake: mmol of urinary potassium multiplied by 39 and then again by 1.30. [10-13]
Adequate urinary potassium: ≥ 70 mmol/24h (approximatively equivalent to 3510 mg/day of potassium intake).

Figure .



Highlights

- Italian adult potassium intake remains lower than the WHO recommended level.
- Potassium intake was low independently of gender, age, BMI and educational level.
- Potassium intake was higher in men and in those with overweight and obesity.
- The sodium to potassium ratio decreased over 10 years in both men and women.