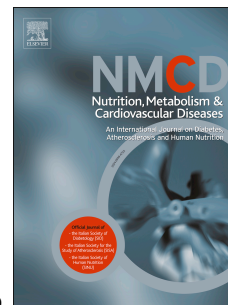# Journal Pre-proof

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Trend of salt intake measured by 24-h urine collection
in the Italian adult population between the 2008 and 2018 CUORE Project surveys

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ABSTRACT

Background and aims: The WHO Global Action Plan for the Prevention of NCDs recommends a 30% relative reduction in mean population salt/sodium intake. The Study assessed the trend in the habitual salt intake of the Italian adult population from 2008-2012 to 2018-2019 based on 24-hour urinary sodium excretion, 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 distributed in North, Centre and South of the Country. Urinary sodium and creatinine measurements were carried out 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. The age-standardized mean daily population salt (sodium chloride) intake was 10.8 g (95% CI 10.5-11.1) in men and 8.3 g (8.1-8.5) in women in 2008-2012 and respectively 9.5 g (9.3-9.8) and 7.2 g (7.0-7.4) in 2018-19. A statistically significant (p<0.0001) salt intake reduction was thus observed over 10 years for both genders, and all age, BMI and educational classes.

Conclusions: The average daily salt intake of the Italian general adult population remains higher than the WHO recommended level but a significant reduction of 12% in men and 13% in women has occurred in the past ten years. These results encourage the initiatives undertaken by the Italian Ministry of Health aimed at the reduction of salt intake at the population level.

Abstract word count: 249 words

Keywords: epidemiology; salt intake; non-communicable diseases.

INTRODUCTION

Non-communicable diseases (NCDs) are the main cause of death in all industrially developed countries.[1] Unhealthy life styles such as tobacco use, physical inactivity, inadequate diets and harmful use of alcohol all increase the risk of NCDs.[1] Creating environmental conditions that favour sustainable healthy habits is a fundamental tool to prevent and control NCDs. The WHO Global NCDs Action Plan 2013-2020 focused on nine global targets and indicated a roadmap of policies and interventions useful to meet the commitments on NCDs prevention made at the United Nations General Assembly in 2011 and 2014 and included in the 2030 Agenda for Sustainable Development.[1]

The Global Burden of Disease Risk Factors Collaboration estimated that 4.1 million annual deaths are attributable to excess salt/sodium intake mainly because of its impact on the incidence of hypertension, coronary heart disease and stroke.[2] Decreasing sodium intake has been shown to reduce blood pressure and the risk of associated cardiovascular disease [3,4,5,6,7] and has been identified as one of the most cost-effective measures countries can take to improve population health. A 30% relative reduction in the mean population salt intake by 2025 was indicated as one of the nine NCD-related global targets.[1]

In Italy, since 2008, the Ministry of Health, within the framework of the "Gaining Health: making healthy choices easy" strategic Programme for NCDs prevention, has launched specific initiatives, with the collaboration of the Interdisciplinary Working group for Salt Reduction in Italy (GIRCSI), aimed at the reduction excess salt intake.[8,9] Furthermore, the reduction of excessive salt consumption is one of the main objectives of the National Preventive Plan (NPP) 2014-2018, extended to 2019, pursued at the Regional and local level.

An assessment of the habitual salt intake was carried out in 2008-2012 in the Italian general population aged 35-74 years 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.[10] In order to evaluate the effectiveness of the salt reduction population strategy implemented by the Italian Ministry of Health in collaboration with non-governmental organizations, a further assessment of the adult population salt intake has been made in 2018-2019 (HES 2018-2019 – CUORE Project) to evaluate the trend in salt intake over the past ten years. Both studies were promoted and supported by the Italian Ministry of Health.

METHODS

Study population

 Habitual salt intake comparison between OEC/HES 2008-2012 and HES 2018-2019 data for the purpose of the present analysis included persons aged 35-74 years, residents in 10 Regions involved in both surveys: Lombardy, Piedmont, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

From March 2008 to July 2012, the OEC/HES, within the CUORE Project, investigated randomlyselected 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%.[10] In this framework, for the assessment of

the population 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 aged 35-74 years, 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-hour urine collection.[11]

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 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 100 men and 100 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. [12]

Study procedures and methods

Both surveys included a 24-hour urine collection, a physical examination and the administration of a common face to face questionnaire to collect information on demographic characteristics, educational level, lifestyles (physical activity, smoking, alcohol consumption, salt consumption), pathological history, family history and drug treatments. Standardized methods were used in the collection and measurement following EHES recommendations [10, 12] 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.

For the assessment of dietary salt 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 -80oC in the biological bank of the ISS for future determinations; during the HES 2018-2019, one at -30 ^{o}C and two at -80°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.

The measurement of sodium and creatinine was performed for both surveys at Federico II

University of Naples by the central laboratory of Department of Clinical and Experimental Medicine (later become Department of Clinical Medicine and Surgery). In each survey, both urinary sodium and creatinine concentrations were measured using an ABX Pentra 400 apparatus (HORIBA ABX, Rome, Italy) with an integrated ion-selective electrode (ISE) module. Sodium was 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 the 2008-2012 survey were: accuracy -0.1% for sodium and -1.95% for creatinine, inter-assay variation coefficient 2.2% for sodium and 1.5% for creatinine and intra- assay variation coefficient 0.7% for sodium and 1.1% for creatinine. The respective data for the 2018-2019 survey were: accuracy -0.0% for sodium and -0.7% for creatinine, inter-assay variation coefficient 1.4% for sodium and 2.7% for creatinine and intra-assay variation coefficient 1.3% for sodium and 3.8 % for creatinine. 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.

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.[10] Similar procedures and methods were used for data collection in the HES 2018-2019 survey.

Statistical analysis

Sodium was expressed in mmol as 24-hour urinary excretion and was translated to salt intake in g/day (1 mmol= 23 mg of sodium), following the WHO suggestion to deliver, as salt intake indicator, the age-standardized mean population intakes of salt expressed as g/day in order to allow comparisons among studies.[1] Sodium excretion (mmol) was multiplied by 23 to obtain sodium intake (g/day) which was further multiplied by 2.5 to obtain salt intake (g/day). 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.[13, 14] According to the WHO recommendation, the EFSA scientific opinion for sodium and the Standard Dietary Target for prevention in Italy [15, 16, 17] the prevalence of 24-hour sodium excretion lower than 85 mmol (corresponding to 5 g of salt) per day was calculated.

Salt intake 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.

Similar mean levels of 24-hour urine volume as well as crude and weight adjusted creatinine were found in the two surveys by age class and gender (Table S1). Mean level of crude urinary creatinine excretion was higher in men than in women within both periods in each age class (p-value<0.0001). Also, in both periods, a progressively lower crude and weight adjusted creatinine excretion rate was found with age (p-value<0.0001). A trend was also observed towards a higher urine volume with age (Table S1).

In the 2008-2012 survey, mean 24-hour urinary sodium excretion was 186 mmol (95% CI 181-190) in men and 143 mmol (139-146) in women; in the 2018-2019 survey, the respective values were 164 (160-168) and 124 (121-127) (Figure 1). Mean sodium excretion was significantly reduced from 2008-2012 to 2018-2019 in both men (-12%) and women (-13%) (p-value<0.0001); the reduction was statistically significant in all age classes (Table 1).

The age-standardized mean population salt intake was 10.8 g (standard deviation 4.1; 95% CI 10.5-11.1) in men and 8.3 g (3.2; 8.1-8.5) in women in the 2008-2012 survey and 9.5 g (3.6; 9.3-9.8) in men and 7.2 g (2.8; 7.0-7.4) in women in the 2018-2019 survey; the reduction by period was equal to 1.3 g in men and 1.1 g in women (p<0.0001 for both).

Frequency distributions of 24-hour urinary sodium excretion are shown in Figure 1. Sodium excretion was consistently higher in men than in women, with a difference of 23% (p-value< 0.0001) in 2008-2012 and 24% in 2018-2019 (p-value<0.0001). Within period, no statistically significant differences were found for the mean of 24-hour urinary sodium excretion across age classes (ANOVA, Table 1).

In the 2008-2012 survey, 24-hour sodium excretion was lower than 85 mmol per day, in 4% (95% CI 3-5%) of men and 15% (13-17%) of women; in the 2018-2019 survey significantly higher values of 9% (7-11%) and 23% (20-26%) were found for men and women (p-value<0.0001).

In both periods and genders, 24-hour sodium excretion was significantly and directly associated with BMI classes and inversely associated with educational levels, independently of age (ANOVA within period – Table 2).

The statistically significant reduction of 24-hour sodium excretion between 2008-2012 and 2018-19 was consistent across BMI classes and educational levels, considered singly (t-test –Table 2) or together independently of age (period significance of ANOVA between periods – Table 2).

In both periods, some geographical differences were found for 24-hour sodium excretion independently of age, BMI and educational classes (Table S2); no Region had mean levels within those recommended (lower than 85 mmol) (Table S2 and Figure 2) but a trend to reduction was observed between the two surveys in all Regions (except for men in the Abruzzo Region) (Table S2).

A trend to an increased prevalence of healthy salt related habits was also observed between 2008-2012 and 2018-2019: in the second survey there was a higher proportion of men and women who reportedly never or rarely add salt at table, who eat always or very often bread without salt and who taste as more salty the food consumed out of home (Figure 3). Nevertheless, in the 2018-2019 survey as many as 80% of men and 77% of women declared to be not influenced from the salt content information on food labels while shopping (data not available in the 2008-2012 survey) (Figure 3).

DISCUSSION

The main finding of the present study is the observation of a significant reduction of the habitual salt intake in randomly selected samples of general adult population recruited in ten Italian Regions approximately ten years apart. The reduction was detected to different extents in almost all Regions and was consistent with respect to sex, age, BMI category and education level.

The second important finding however was that the average daily salt intake remains largely higher as compared with the level recommended by WHO and taken as the Standard Dietary Target for the Italian population: this is also true in all the surveyed Regions, for both men and women, and all age classes, education levels and BMI categories.

A significant trend of habitual salt intake reduction had never been observed in Italy: previously available information on dietary salt intake from several local studies such as the 1976 study of households, the 1985-1987 Intersalt (Gubbio, Bassiano, Mirano, Naples), the 1991 and the 2002-2004 Olivetti Heart Study showed approximately similar levels, not far from those observed within the OEC/HES 2008-2012 survey, considering similar geographical areas. [8, 18, 19, 20, 21]

The average reduction in salt intake observed in adults within the HES 2018-2019 survey compared to the previous one (12% in men and 13% in women) is more than one third of the 2025 WHO global target of a 30% relative reduction. The trend observed in our study is consistent with the trend to salt intake reductions recently reported for other countries, albeit with different methodologies for salt intake assessment. Thus, Slovenia (from 2007 to 2012), Turkey (from 2008 to 2012) and UK (from 2001 to 2011) reported salt intake reductions of 9%, 17% and 15% respectively, based on 24-hour urinary excretion. [22, 23, 24] Finland monitored population salt intake through both 24-hour urine collection and dietary surveys and reported a 36% reduction from 1979 to 2007.[24] Using spot urine collections, Denmark reported a 7% decrease from 2006 to 2010.[25, 26] Dietary surveys were used by France (1999.2007), Iceland (1999-2007) and Ireland (2001-2011) which reported reductions of 5%, 6% and 14%, respectively.[28- 30] Among non-European countries, China (from 1991 to 2009), Japan (from 1997 to 2012), Korea (from 2005 to 2012) and South Korea (from 2010 to 2014) reported reductions of 29%, 23%, 14% and 20%, respectively.[31, 22, 32]

On the other hand, a few countries have reported increases in the population habitual salt intake, such as Iran, U.S.A. and India.[33-35]

Additional findings of the present study are the sex related difference in salt intake and the statistical associations of salt intake with BMI and educational level. All these findings are confirmatory of previous evidence. The gender difference is likely explained by differences in food and energy intake between men and women. The association between sodium excretion and BMI was also found in the preliminary report on the MINISAL Study [8] and is also consistent with previous evidence from the Olivetti Heart Study [36] and with data from many other countries [36-44]. A possible explanation in this case is that foods with high sodium content are also usually high in energy, such as fatty and highly processed foods [45, 46], leading to weight gain.[47]

The inverse association between salt intake and educational level was already reported by the OEC/HES 2008-2012 survey on 20 Italian Regions, showing that social inequalities, including disparities in the educational level, explained the geographical variation in salt intake in our country.[48] This finding was consistent with evidence from a recent systematic review and meta-analysis that included cohorts from high income countries of East Asia, Australia, North America, Europe, and Latin America.[49] In this case too it is conceivable that less educated people consume relatively greater amounts of possibly cheaper fatty and highly processed foods with high sodium content and high caloric density.[50-54] It is also possible that the educational level impacts on the way people are responsive to health information with a greater propensity of more educated individuals to comply with nutritional advice. It is to be noted however that in our study the reduction in salt intake over the past 10 years was similar for higher and lower educational levels, with only a minor difference in men. These results may suggest that salt consumption among Italian adults benefited from preventive actions that have reached the population across the board, such as agreements between the Italian Ministry of Health and associations of artisan bakers and companies in the food industry aimed at reducing salt content in artisan and industrial bread and in some industrial products (pasta, rice, soups) and the actions developed by all the Italian Regions with the National Prevention Plan 2014-2019, recently renewed and strengthened for 2020-2025.[9] The agreements provided for a relative reduction of the salt content of 10-15%, depending on products and association/manufactures. Initiatives included in the National Prevention Plan, such as local intersectoral agreements and information activities for the population and training for operators related to the food sector, were followed by specific monitoring systems of the Regional Prevention Plans. These preventive programmes have been supported by the advocacy actions and the educational campaigns promoted at regular intervals by scientific societies.

In accordance with the trend in salt intake, the findings of the questionnaire on the population's life style habits related to salt intake showed an overall substantial improvement, although it is a matter of concern the modest attention paid to food labels concerning the salt content of foods when shopping.

Strengths and limitations

Major strengths of our study are the following: the use of the gold standard method for the assessment of salt 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] and anyway within the WHO recommended sample size for this kind of epidemiological investigations [11]. 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 salt intake due to the well-known large day to day variation in sodium excretion: however, it is sufficient for the assessment of salt 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. Nerveless, these differences cannot have affected our major findings because, both in men and women, the amount of salt reduction was similar by BMI classes and educational levels. Moreover, the reduction of mean salt intake between periods was statistically significant when adjusted by BMI class and educational level. Finally, the salt intake monitoring was not extended to the younger age classes.

Conclusions

In conclusion, this comparison of 24-hour urinary sodium excretion in two independent samples of Italian adult population, carried out in 10 Regions approximately 10 years apart from each other, showed a significant and substantial reduction in salt intake. This reduction was independent of gender, age, BMI category and educational level and met more than one third of the 30% reduction target indicated in the WHO Global Action Plan 2013-2020.

This notwithstanding, the study indicated that the average salt intake in Italy remains definitely higher than the level recommended by WHO for both genders, all Regions and every class of age, BMI and educational level. Mean levels of salt intake were higher in men than in women, in those with overweight and obesity compared with normal weight people, and in less educated compared with more educated individuals, confirming the important role of social inequalities.

Although these results need confirmation through further systematic and periodic monitoring, they have major public health implications in as much as they encourage the initiatives undertaken by the Italian Ministry of Health in collaboration with non-governmental organizations and in particular with the scientific societies in order to reduce salt intake at the population level through the "Gaining Health: making healthy choices easy" Programme and the National Prevention Plan. The attainment of this initial success in the contrast to a major causal factor of NCDs should prompt further actions to lower the amount of salt in the food supply, to generate knowledge and improve

people behaviours through educational campaigns targeting also children and adolescents, to change the food environment and promote social norms so that people demand and gain greater control over their salt consumption. As suggested by the WHO and in accordance with the Italian Ministry of Health population strategy developed since 2008, 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 of 24-hour urinary sodium 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 sodium 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.

Figure 3 Prevalence (%) of self-reported salt related habits by gender and period 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 creatinine excretion and urine volume by sex, age class 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 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.

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Author contributions

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, MMG, 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.

Competing Interests: Authors have nothing to disclose.

References

1. WHO. Global Action Plan for the prevention and control of Noncommunicable Diseases 2013-2020. World Health Organization 2013.

2. GBD 2015 Risk Factors Collaborators. Global, Regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*, 2016; 388(10053):1659-1724.

3. WHO. Prevention of Cardiovascular Disease. Guidelines for assessment and management of cardiovascular risk. World Health Organization 2007.

4. WHO. Prevention of recurrent heart attacks and strokes in low and middle income populations: Evidence-based recommendations for policy makers and health professionals. Geneva, World Health Organization (WHO), 2003.

5. Bibbins-Domingo K, Chertow GM, Coxson PG et al. Projected effect of dietary salt reductions on future cardiovascular disease. *N Engl J Med*, 2010, 362(7):590–599.

6. Cohen HW et al. Sodium intake and mortality in the NHANES II follow-up study. *Am J Med*. 2006;119(3): 275, e7–14. 177.

7. Cutler JA, Follmann D, Allender PS. Randomized trials of sodium reduction: an overview. *Am J Clin Nutr*. 1997;65(2 Suppl):643S–651S.

8. Donfrancesco C, Ippolito R, Lo Noce C, et al. Excess dietary sodium and inadequate potassium intake in Italy: results of the MINISAL study. *Nutr Metab Cardiovasc Dis*. 2013 Sep;23(9):850-6.

9. Strazzullo P, Cairella G, Campanozzi A, et al for the GIRCSI Working Group. Population based strategy for dietary salt intake reduction: Italian initiatives in the European framework. *Nutr Metab Cardiovasc Dis*. 2012 Mar;22(3):161-6.

10. Giampaoli S, Palmieri L, Donfrancesco C, et al for the Osservatorio Epidemiologico Cardiovascolare/Health Examination Survey Research Group. Cardiovascular health in Italy. Ten-year surveillance of cardiovascular diseases and risk factors: Osservatorio Epidemiologico Cardiovascolare/Health Examination Survey 1998-2012. *Eur J Prev Cardiol*. 2015 Sep;22(2 Suppl):9-37.

11. WHO. Reducing salt intake in populations: report of a WHO forum and technical meeting. World Health Organization 2007.

12. European Health Examination Survey (EHES) – Measuring the Health of Europeans. http://www.ehes.info/national/national_hes_status.htm (accessed 19 September 2020)

13. National Institute of Statistics. Resident population 2010. http://dati.istat.it/Index.aspx?DataSetCode=DCIS_RICPOPRES2011 (accessed 19 September 2020)

14. National Institute of Statistics. Resident population 2019. http://demo.istat.it/index_e.html (accessed 19 September 2020)

15. WHO. Guideline: Sodium intake for adults and children. World Health Organization 2012, reprinted 2014.

16. European Food Safety Authority. Dietary reference values for sodium. Adopted: 3 July 2019. https://www.efsa.europa.eu/en/efsajournal/pub/5778 (accessed 9 October 2020)

17. SINU, the Italian Society of Human Nutrition. Recommended intake levels of energy and nutrients for the Italian population. 4th Revision, Milan: SICS editore 2014.

18. Strazzullo P, Trevisan M, Farinaro E, Cappuccio FP, Ferrara LA, Mancini M. Characteristics of the association between salt intake and blood pressure in a sample of male working population in southern Italy. *Eur Heart J* 1983;4:608e13.

19. Intersalt Cooperative Research Group. Intersalt: an interna- tional study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. *BMJ* 1988;297:319e28.

20. Leclercq C, Ferro-Luzzi A. Total domestic consumption of salt and their determinants in three Regions of Italy. *Eur J Clin Nutr* 1991;45:151e9.

21. Venezia A, Barba G, Russo O, et al. Dietary sodium intake in a sample of adult male population in southern Italy: results of the Olivetti heart study. *Eur J Clin Nutr* 2010;64:518e24.

22. Kathy T, Bruce N, Corinna H, et al. Salt Reduction Initiatives around the World – A Systematic Review of Progress towards the Global Target. PLoS One. 2015 Jul 22;10(7).

23. World Health Organization. Progress in reducing salt consumption in Turkey. World Health Organization; 2013 http://www.euro.who.int/en/countries/turkey/news/news/2013/04/progress-in-reducing-salt-consumption-in-turkey. (accessed 19 September 2020)

24. Sadler K, Nicholson S, Steer T, Gill V, Bates B, Tipping S, et al. National Diet & Nutrition Survey—Assessment of dietary sodium in adults (aged 19 to 64 years) in England, 2011. Department of Health; 2011 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213420/Sodium-Survey-England-2011_Text_to-DH_FINAL1.pdf. (accessed 19 September 2020)

25. Pietinen P, Paturi M, Reinivuo H, Tapanainen H, Valsta LM. FINDIET 2007 Survey: energy and nutrient intakes. *Public Health Nutr*. 2010 Jun;13(6A):920–4.

26. European Commission. National Salt Initiatives: Implementing the EU Framework for Salt Reduction Activities. European Commission,; 2009 http://ec.europa.eu/health/ph_determinants/life_style/nutrition/documents/national_salt_en.pdf. (accessed 19 September 2020)

27. Thuesen HB, Toft U, Buhelt LP et al Estimated daily salt intake in relation to blood pressure and blood lipids: the role of obesity. Europ J Preventive Cardiology 2015, 22: 1567-1574

28. European Commission. Collated information on salt reduction in the EU. European Commission, 2008. http://ec.europa.eu/health/ph_determinants/life_style/nutrition/documents/compilation_salt_en.pdf. (accessed 19 September 2020)

29. World Health Organization. Mapping salt reduction initiatives in the WHO European Region. Copenhagen: WHO Regional Office for Europe; 2013

http://www.euro.who.int/en/health-topics/diseaseprevention/nutrition/publications/2013/mapping-salt-reduction-initiatives-in-the-who-european-Region. (accessed 19 September 2020)

30. Walton J. Salt Intakes in the Irish Population: Estimates and Trends. 2013 https://www.fsai.ie/uploadedFiles/Science_and_Health/Salt_and_Health/SRP_2013_Janette%20Walton_IUNA.pdf. (accessed 19 September 2020)

31. Du S, Batis C, Wang H, Zhang B, et al. Understanding the patterns and trends of sodium intake, potassium intake, and sodium to potassium ratio and their effect on hypertension in China. *Am J Clin Nutr*. 2014 Feb;99(2):334–43.

32. Hye-Kyung P, Yoonna L, Baeg-Won K et al. Progress on sodium reduction in South Korea. *BMJ Glob Health*. 2020; 5(5): e002028.

33. Mohammadifard N, Khosravi A, Salas-Salvadó J, et al.. Trend of salt intake measured by 24-hour urine collection samples among Iranian adults population between 1998 and 2013: The Isfahan salt study. *Nutr Metab Cardiovasc Dis*. 2019 Dec;29(12):1323-1329.

34. Pfeiffer CM, Hughes JP, Cogswell ME, et al. Urine sodium excretion increased slightly among U.S. adults between 1988 and 2010. *J Nutr*. 2014 May;144(5):698-705.

35. Johnson C, Praveen D, Pope A, et al. Mean population salt consumption in India: a systematic review. *J Hypertens*. 2017 Jan;35(1):3-9.

36. Venezia A, Barba G, Russo O, et al. Dietary sodium intake in a sample of adult male population in southern Italy: results of the Olivetti heart study. *Eur J Clin Nutr* 2010;64:518e24.

37. Ortega RM, Lopez-Sobaler AM, Ballesteros JM, et al. Estimation of salt intake by 24 h urinary sodium excretion in a representative sample of Spanish adults. Br J Nutr; 2010.

38. Oh SW, Koo HS, Han KH, et al. Associations of sodium intake with obesity, metabolic disorder, and albuminuria according to age. *PLoS One*. 2017 Dec 15;12(12).

39. Lee J, Hwang Y, Kim KN, et al. Associations of urinary sodium levels with overweight and central obesity in a population with a sodium intake. *BMC Nutr*. 2018 Nov 21;4:47

40. Khosravi A, Toghianifar N , Sarrafzadegan N, Gharipour M, Azadbakht L. Salt intake, obesity, and pre-hypertension among Iranian adults: A cross-sectional study. *Pak J Med Sci*. 2012; 28: 297 – 302

41. Haghighatdoost F, Sarrafzadegan N, Khosravi A, Noori F, Boshtam M, Mohammadifard N, Abdollhi Z, Azadbakht L. Is the association between salt intake and blood pressure mediated by body mass index and central adiposity? *Arch Iran Med*. 2013 Mar;16(3):167-71.

42. Yi SS, Firestone MJ, Beasley JM. Independent associations of sodium intake with measures of body size and predictive body fatness. *Obesity* (Silver Spring). 2015 Jan;23(1):20-3.

43. Zhang X, Wang J, Li J, Yu Y, Song Y A positive association between dietary sodium intake and obesity and central obesity: results from the National Health and Nutrition Examination Survey 1999-2006. *Nutr Res*. 2018 Jul;55:33-44..

44. Lydon, R., McAnena, L., Livingstone, M., & Kerr, M. (2016). The association between salt intake and obesity in UK adults aged 19–64 years. *Proceedings of the Nutrition Society*, 75(OCE3).

45. Bolhuis DP, Lakemond CM, de Wijk RA, et al . Effect of salt intensity in soup on ad libitum

intake and onsubsequent food choice. *Appetite* 2012;58:48-55.

46. Mejean C, Deglaire A, Kesse-Guyot E, et al. Association between intake of nutrients and food groups and liking for fat (The Nutrinet-Sante Study). *Appetite* 2014;78:147-55

47. Keskitalo K, Tuorila H, Spector TD, et al. The Three-Factor Eating Questionnaire, bodymass index, and responses to sweet and salty fatty foods: atwin study of genetic and environmental associations. *Am JClin Nutr* 2008;88:263-71.

48. Cappuccio FP, Ji C, Donfrancesco C, et al Geographic and socioeconomic variation of sodium and potassium intake in Italy: results from the MINISAL-GIRCSI programme. *BMJ Open*. 2015 Sep 10;5(9)

49. de Mestral C, Mayén AL, Petrovic D, Marques-Vidal P, Bochud M, Stringhini S. Socioeconomic Determinants of Sodium Intake in Adult Populations of High-Income Countries: A Systematic Review and Meta-Analysis. *Am J Public Health*. 2017 Apr;107(4):e1-e12.

50. Darmon N, Drewnowski A. Does social class predict diet quality? Am J Clin Nutr. 2008;87(5):1107–1117. [Comment in: Social class and diet quality. *Am J Clin Nutr*. 2008.]

51. Novakovi´c R, Cavelaars A, Geelen A, et al. Socioeconomic determinants of micronutrient intake and status in Europe: a systematic review. *Public Health Nutr*. 2014; 17(5):1031–1045.

52. Wang DD, Leung CW, Li Y, et al. Trends in dietary quality among adults in the United States, 1999 through 2010. *JAMA Intern Med*. 2014;174(10):1587–1595.

53. Nikoli´c M, Glibeti´c M, Gurinovi´c M, et al. Identifying critical nutrient intake in groups at risk of poverty in Europe: the CHANCE project approach. *Nutrients*. 2014; 6(4):1374–1393.

54. WHO. (2016). A global brief on hypertension: Silent killer, global public health crisis. Geneva: World Health Organization.

55. Mindell JS, Giampaoli S, Goesswald A, et al. Sample selection, recruitment and participation rates in health examination surveys in Europe--experience from seven national surveys. BMC Med Res Methodol. 2015;15:78.

56. Italian National Institute of Statistics. Population education levels and occupational returns: the main indicators. ISTAT 2017. https://www.istat.it/it/files/2018/07/Indicatori-dellistruzione.pdf] (accessed 19 September 2020)

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

MEN

Age class (years)	2008-2012					ANOVA p-value	2018-2019					ANOVA p-value	% mean diff	t-test p-value
	n	mean	std	95% CI			n	mean	std	95% CI				
						0,4599						0,7640		
35-44	235	185	72	176	194		228	162	66	154	171		-12	0,0004
45-54	238	191	68	182	199		232	167	63	159	176		-12	0,0001
55-64	240	187	75	178	197		266	163	60	156	170		-13	0,0001
65-74	229	180	68	172	189		241	162	59	155	170		-10	0,0023

WOMEN

Age class (years)	2008-2012					ANOVA p-value	2018-2019					ANOVA p-value	% mean diff	t-test p-value
	n	mean	std	95% CI			n	mean	std	95% CI				
						0,1899						0,0936		
35-44	220	143	56	135	150		213	121	47	115	127		-15	<0.0001
45-54	223	149	62	141	157		252	123	47	117	129		-17	<0.0001
55-64	241	141	50	135	148		275	130	55	124	137		-8	0,0156
65-74	232	138	54	131	145		270	121	46	115	126		-12	0,0002

t-test: normal standardize t-test for comparison between periods.

ANOVA: ANOVA to compare 24 h sodium excretion among age classes within the period.

Italian regions: Lombardy, Piedmont, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table 2. 24-hour sodium excretion (mmol) 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.

	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
						<0.0001						<0.0001			
Normal weight	235	170	64	*162*	*178*		314	147	54	*141*	*153*		-14	<0.0001	
Overweight	454	182	67	*176*	*189*		458	168	63	*163*	*174*		-8	0,0013	
Obese	246	209	79	*199*	*219*		191	182	63	*173*	*191*		-13	0,0001	
Education						0,0195						0,0003			<0.0001
Higher education	497	181	72	*175*	*187*		685	159	58	*155*	*164*		-12	<0.0001	
Lower education	436	191	69	*185*	*198*		279	175	70	*167*	*183*		-9	0,0020	
Period														<0.0001

	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						<0.0001						<0.0001			<0.0001
Normal weight	361	129	49	*124*	*134*		443	114	45	*110*	*119*		-12	<0.0001	
Overweight	299	143	51	*138*	*149*		299	130	52	*124*	*136*		-9	0,0017	
Obese	246	161	64	*153*	*169*		250	135	50	*129*	*141*		-16	<0.0001	
Education						0,0053						0,0063			<0.0001
Higher education	455	137	55	*132*	*143*		685	121	47	*117*	*124*		-12	<0.0001	
Lower education	447	147	55	*142*	*152*		323	130	52	*124*	*136*		-11	<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 1010 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 sodium 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 sodium 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 performed among those with BMI>=18.5 kg/m^2.

Normal weight - body mass index-BMI within 18.5-24.9 kg/m^2, 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.
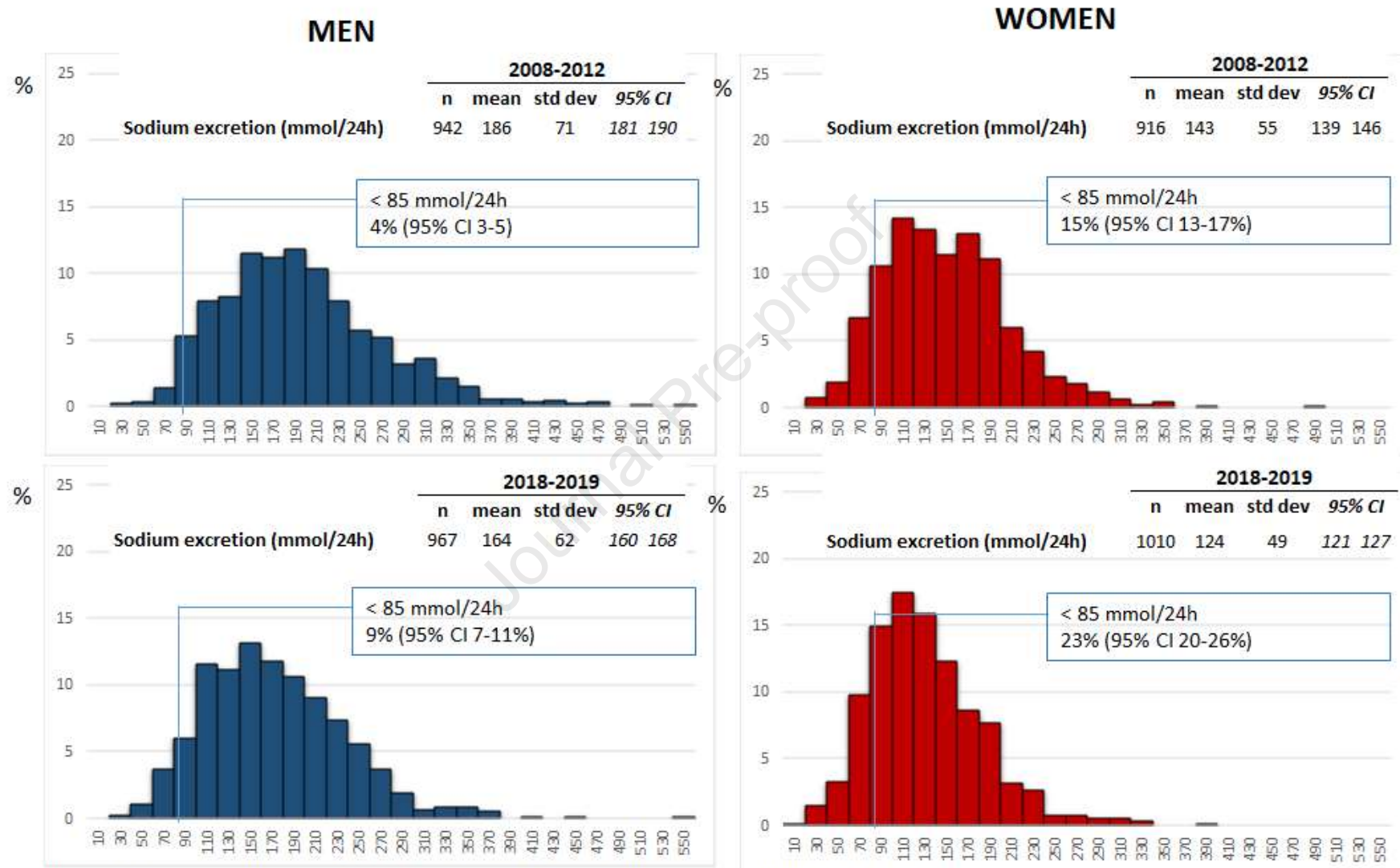
Figure 1.

Italian regions: Lombardy, Piedmont, Liguria, Emilia Romagna, Tuscany, Abruzzo, Lazio, Calabria, Basilicata and Sicily
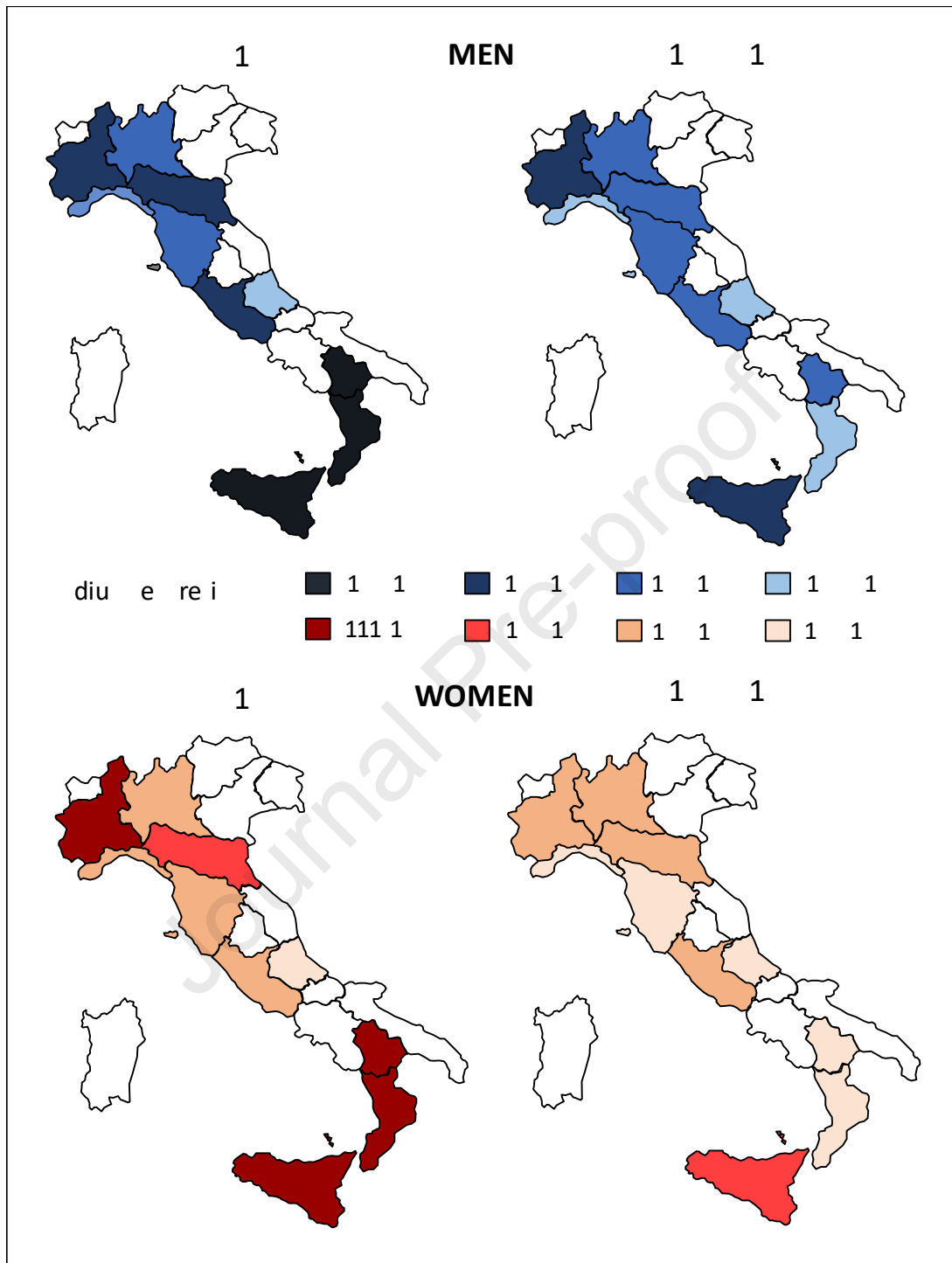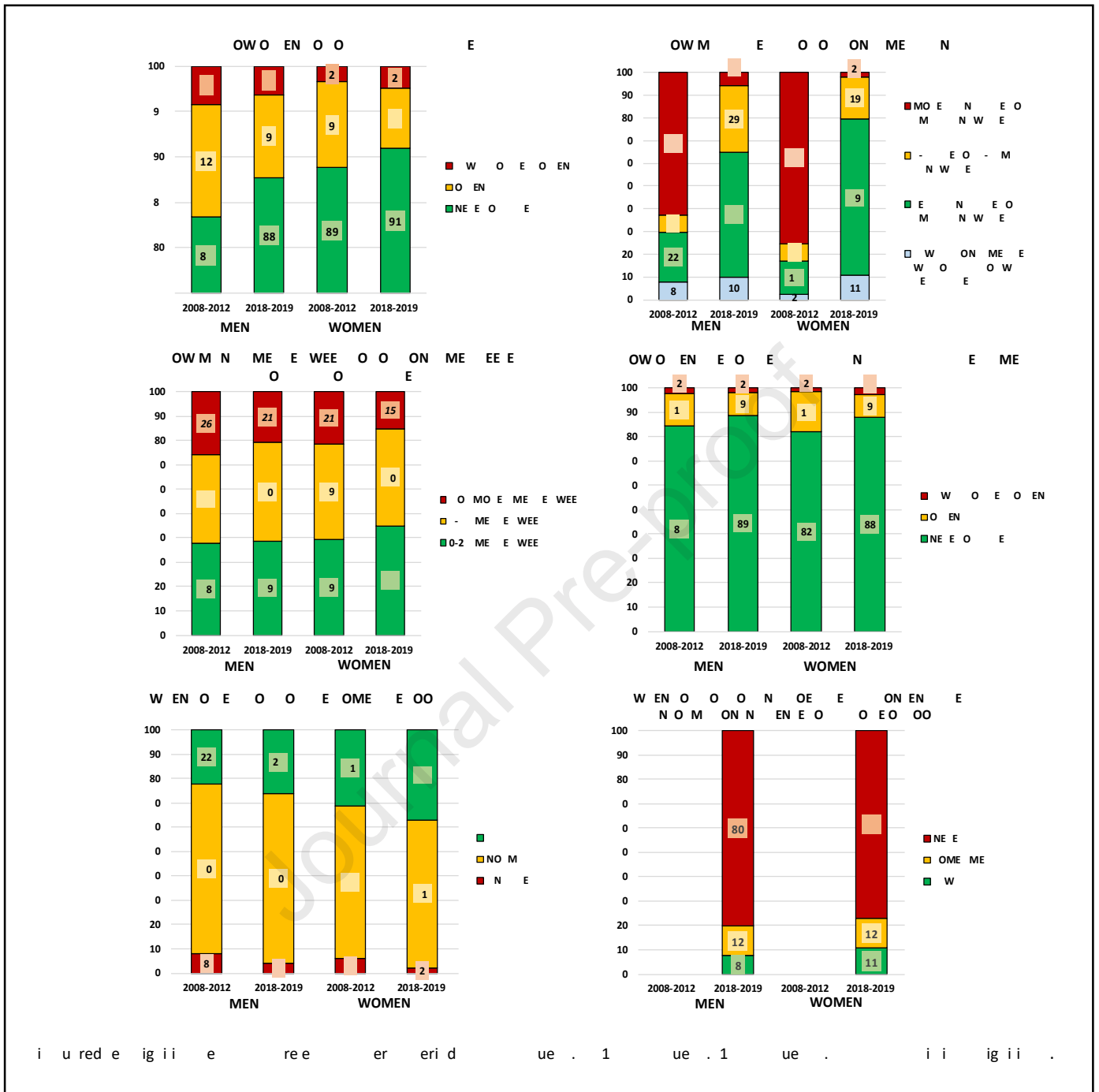St dev: standard deviation. CI: confidence interval.

Figure .

Figure .

Highlights

- In Italian adults a significant reduction in salt intake has occurred over 10 years.

- This reduction was independent of gender, age, BMI category and educational level.

- The salt intake in Italy remains definitely higher than recommended by WHO.

- Salt intake remains higher in men, in overweight/obese and less education persons.