

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Trends of blood pressure, raised blood pressure, hypertension and its control among Italian adults: CUORE Project cross-sectional health examination surveys 1998/2008/2018
<b>AUTHORS</b>	Donfrancesco, Chiara; Di Lonardo, Anna; Lo Noce, Cinzia; Buttari, Brigitta; Profumo, Elisabetta; Vespasiano, Francesca; Vannucchi, Serena; Galletti, Ferruccio; Onder, Graziano; Gulizia, Michele; Galeone, Daniela; Bellisario, Paolo; Palmieri, Luigi

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Flack , John M Southern Illinois University School of Medicine
<b>REVIEW RETURNED</b>	23-May-2022

<b>GENERAL COMMENTS</b>	The manuscript is very well done. The main concern that I struggled with is the voluminous number of tables and the small print. One specific comment has to do with the last sentence of the abstract where the presentation of 2018/2019 data where hypertensive men and women with uncontrolled BP were 73% and 59%. I do not understand these high percentages - please clarify.
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<b>REVIEWER</b>	Aekplakorn, Wichai Faculty of medicine, mahidol university, Community medicine
<b>REVIEW RETURNED</b>	12-Jun-2022

<b>GENERAL COMMENTS</b>	<p>Comment</p> <p>This paper is interesting in looking at the trends of BP, hypertension and its coverage of diagnosis, treatment and control in the Italians.</p> <p>There are few points that need to be clarified.</p> <ol style="list-style-type: none"><li>1. Introduction is quite too long that the paper put too much about the integrated NCD program, eg. gaining health in Italy, about the factors (sodium, behavior etc.) related to the program were not covered in the paper. At the same time, some relevant previous studies and statistics regarding raised blood pressure, hypertension and coverage were not stated in the introduction.</li><li>2. Methods: sampling methods is not elucidated adequately, probability weighted for sampling method was not accounted for the analysis which is important to provide weighted mean and prevalence.</li><li>3. The paper does not mention about the question of previously diagnosis in the survey, otherwise the categories of “undiagnosed” but no treatment should not be possible, how do you define those with “undiagnosed”, and diagnosis but untreated.</li></ol>
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	<p>4. Table 1 and other tables in supplement, the overall trend of 3 periods should be evaluated?</p> <p>5. Table1 and other should present the relative reduction instead of absolute reduction?</p> <p>6. The discussion does not give explanation regarding differences of BP, prevalence of raised BP and hypertension by men and women and also differences by education levels?</p> <p>7. The discussion, one point mentions about the favorable results of hypertension due to the reduction of salt content on processed food and weight reduction, are there any evidence to support that the trends of reduction of sodium intake /weight change among the population in Italy during these peroid, please elaborate more.</p>
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<b>REVIEWER</b>	Dias, Carlos National Institute of Health Ricardo Jorge, Department of Epidemiology
<b>REVIEW RETURNED</b>	14-Jun-2022

<b>GENERAL COMMENTS</b>	<p>The paper you submitted deals with an important topic in cardiovascular epidemiology at population level. In my oppinion the text describes very well all the work done and the great value of the results obtained. I think that the submitted text only deserves minor corrections to clarify the comparisons that have been made. Specifically I suggest that the abstract is revised to clarify which comparisons were made and which trend analysis was used. In the materials and methods section, clarification is made on the statistical methds used for analysing the trend between the three periods, and the comparisons made in Table 1 and suplementar material. Given the sample design used statistical methods for comparison need to be clarified. Given the low response rates of the three HES, it would be useful to know if characteristics of non-respondents were studied or not in all three survey periods. I hope you can find these minor suggestions useful for improving the excelent paper you submitted.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1  
John M Flack , Southern Illinois University School of Medicine

#### Comments to the Author:

The manuscript is very well done. The main concern that I struggled with is the voluminous number of tables and the small print. One specific comment has to do with the last sentence of the abstract where the presentation of 2018/2019 data where hypertensive men and women with uncontrolled BP were 73% and 59%. I do not understand these high percentages - please clarify.

R. Thank you for the suggestion. The last sentence of abstract results referred to the sum of undiagnosed, diagnosed but untreated, and uncontrolled percentages. According to suggestion, for clarity, the last sentence of abstract results has been changed as follows: "In 2018/2019, hypertensive men and women with controlled BP were only 27% and 41%, but a significant favorable trend was observed".

Reviewer: 2

Dr. Wichai Aekplakorn, Faculty of medicine, mahidol university

Comments to the Author:

This paper is interesting in looking at the trends of BP, hypertension and its coverage of diagnosis, treatment and control in the Italian adults.

There are few points that need to be clarified.

1. Introduction is quite too long that the paper put too much about the integrated NCD program, eg. gaining health in Italy, about the factors (sodium, behavior etc.) related to the program were not covered in the paper. At the same time, some relevant previous studies and statistics regarding raised blood pressure, hypertension and coverage were not stated in the introduction.

R. Thank you for the comment and suggestion. In the introduction, the part dedicated to the programs conducted in Italy for NCDs prevention has been reduced, and references that could contextualize the Italian situation in relation to raised blood pressure since the 1970s have been cited.

2. Methods: sampling methods is not elucidated adequately, probability weighted for sampling method was not accounted for the analysis which is important to provide weighted mean and prevalence.

R. Thank you for the comment. Details about probability samples were added in the Methods paragraph.

3. The paper does not mention about the question of previously diagnosis in the survey, otherwise the categories of “undiagnosed” but no treatment should not be possible, how do you define those with “undiagnosed”, and diagnosis but untreated.

R. Thank you for the comment. Description of the method used to investigate previous diagnosis of hypertension was added in the Study procedures and methods paragraph.

4. Table 1 and other tables in supplement, the overall trend of 3 periods should be evaluated?

R. The statistical significance of tests used to compare multiple measurements over time does not give an account of the fluctuations in the several points observed and is often unusable to comment because it is misleading in describing the changes that have occurred over time. For this reason, it was preferred to highlight the most recent situation (2018-2019) in comparison to the previous ones, so as to be able to evaluate the 10 and 20-year trend. However, in Figures 1 and 2 the trend lines of the main indicators by gender, age group and level of education were displayed, also showing the confidence intervals, so that the trend in the three periods can be assessed at a glance.

5. Table1 and other should present the relative reduction instead of absolute reduction?

R. The presentation of the absolute difference between the means was preferred because the test statistic used in the t-test report the difference in the means of surveys to the numerator and also for this reason the statistical significance is closely linked to the difference between the means, making this indicator more consistent with the t-test significance reported in the tables and with related comments in the text. With regard to the difference between percentages, it was chosen to present the absolute difference, mainly because the absolute difference gives immediate knowledge of the proportion of the population involved, giving the possibility of calculating the number of persons affected by the change starting from the resident population. However, the relative percentage difference has been reported in the text for the main indicators.

6. The discussion does not give explanation regarding differences of BP, prevalence of raised BP and hypertension by men and women and also differences by education levels?

R. In the discussion paragraph was reported an epidemiological explanation about higher level of blood pressure and raised blood pressure/hypertension in men than in women and more severe values in people with lower education level, underlying that they are in line with higher level of excess of weight and salt consumption in men than in women and in those with lower education than in higher educated persons (the references were cited). It was also reported that such results are consistent with other Italian and European studies showing a consistent epidemiological basis (the references were cited).

7. The discussion, one point mentions about the favorable results of hypertension due to the reduction of salt content on processed food and weight reduction, are there any evidence to support that the trends of reduction of sodium intake /weight change among the population in Italy during these period, please elaborate more.

R. The increase in the normal weight prevalence and the reduction of the daily consumption of salt in the Italian general adult population were documented through the following publications (cited now in the text with numbers 16 and 17):

- Donfrancesco C, Profumo E, Lo Noce C, Minutoli D, Di Lonardo A, Buttari B, et al. Trends of overweight, obesity and anthropometric measurements among the adult population in Italy: The CUORE Project health examination surveys 1998, 2008, and 2018. PLoS One. 2022 Mar 1;17(3):e0264778.

- Donfrancesco C, Lo Noce C, Russo O, Minutoli D, Di Lonardo A, Profumo E, et al. Trend of salt intake measured by 24-h urine collection in the Italian adult population between the 2008 and 2018 CUORE project surveys. Nutr Metab Cardiovasc Dis. 2021 Mar 10;31(3):802-813.

Reviewer 3

Dr. Carlos Dias, National Institute of Health Ricardo Jorge, National Institute of Health Doctor Ricardo Jorge

Comments to the Author:

Dear Dr. Donfrancesco

The paper you submitted deals with an important topic in cardiovascular epidemiology at population level. In my opinion the text describes very well all the work done and the great value of the results obtained. I think that the submitted text only deserves minor corrections to clarify the comparisons that have been made. Specifically I suggest that the abstract is revised to clarify which comparisons were made and which trend analysis was used. In the materials and methods section, clarification is made on the statistical methods used for analysing the trend between the three periods, and the comparisons made in Table 1 and supplemental material. Given the sample design used statistical methods for comparison need to be clarified. Given the low response rates of the three HES, it would be useful to know if characteristics of non-respondents were studied or not in all three survey periods. I hope you can find these minor suggestions useful for improving the excellent paper you submitted. Best regards.

R. Thank you for your comments and suggestions. According to comments, the abstract was revised including all indicators and subgroups compared and the way as trends were considered. In accordance with the suggestions, in the text the statistical analysis paragraph has been revised to clarify the methodologies used for the comparisons. Unfortunately, the characteristics of the non-respondents cannot be studied for privacy reasons as they are not participants of the study and not having signed the informed consent.

**VERSION 2 – REVIEW**

<b>REVIEWER</b>	Aekplakorn, Wichai Faculty of medicine, mahidol university, Community medicine
<b>REVIEW RETURNED</b>	24-Sep-2022
<b>GENERAL COMMENTS</b>	I have no further comments.