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Trends of blood pressure, raised blood pressure, hypertension and its control among Italian adults: CUORE Project health examination surveys 1998/2008/2018

Trends of blood pressure in Italian adults

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Abstract

Objectives: To assess in the Italian adults trends of blood pressure (BP) and prevalence of raised blood pressure (RBP), hypertension and its control in order to evaluate population health and care, and the achievement of a RBP 25% relative reduction as recommended by the WHO at population level.

Design: Results comparison of three cross-sectional surveys based on randomly selected age and sex stratified samples of resident persons aged 35-74 years.

Setting: Health examination surveys conducted in Italy within the CUORE Project following standardized methodologies.

Participants: 2985 men and 2955 women examined in 1998/2002, 2218 men and 2204 women examined in 2008/2012, 1031 men and 1066 women examined in 2018/2019.

Primary and secondary outcome measures: Age-standardized mean of BP and prevalence of RBP (systolic BP and/or diastolic BP >= 140/90 mmHg) and hypertension (presenting or being treated for RBP).

Results: In 2018/2019, a significant reduction was observed in systolic BP and diastolic BP in men (136/86, 132/84, 132/78 mmHg) and women (132/82, 126/78, 122/73 mmHg), and in the prevalence of RBP (50%, 40% and 30% in men, 39%, 25%, and 16% in women) and of hypertension (54%, 49% and 44% in men, 45%, 35% and 32% in women). Trends were consistent by age and education attainment. In 2018/2019, hypertensive men and women with uncontrolled BP were 73% and 59%, but a significant favorable trend was observed.

Conclusions: Data from 2018/2019 underlined that RBP is still commonly observed in the Italian population aged 35-74 years, however, the WHO RBP target at that time may be considered met.

Word count: 255

Keywords: epidemiology, blood pressure, raised blood pressure, hypertension, health examination survey.

Strengths and limitations of this study

- Use of blood pressure measurements to estimate mean of blood pressure and the prevalence of raised blood pressure and hypertension.
- Recruitment of randomly selected age and sex specific samples of residents in 10 Italian Regions with coverage of the Northern, Central and Southern Italian territory.
- Adoption of standardized procedures and methods to collect data in the three health examination surveys.
- Assessment of blood pressure indicators by sex, age-classes and educational levels.
- Inadequacy of blood pressure measurement in a single day for the diagnosis of raised blood pressure and hypertension.

INTRODUCTION

Raised blood pressure (BP) is a condition constituting a leading cause of premature death and disability worldwide, since it significantly increases the risk of heart attack, stroke, kidney failure, dementia and blindness [1]. The main contributors to raised BP are unhealthy eating behaviours – among which sodium excess – physical inactivity, excess of weight, smoking habit, harmful use of alcohol and exposure to persistent stress [2].

The value of blood pressure, in particular of systolic blood pressure (SBP), is included in the risk charts for estimating the probability of incurring or dying from a cardiovascular event, both for the strong etiological significance and for its simplicity and low cost [3-5].

To combat global mortality from non-communicable diseases (NCDs), at the Sixtysixth World Health Assembly in 2013 Member States developed a Global Plan of Action, for 2013-2020 setting global targets that include achieving a 25% relative reduction in the prevalence of raised BP or contain the prevalence of raised BP, according to national circumstances by 2025, proposed to leading a 33% of relative reduction by 2030, using 2010 as a baseline [6,7]. The World Health Organization (WHO) is supporting countries to meet this global target and to reduce hypertension as part of WHO's Thirteenth General Programme of Work (2019–2023), which focuses on measurable impacts on people's health at country level.

Integrated NCDs programmes implemented through a primary health care approach are an affordable and sustainable way for countries to tackle hypertension. In Italy, the prevention of NCDs is supported by the "Gaining Health: making healthy choices easy" Programme and the National Preventive Plans (NPPs), which were implemented in a context in which NCDs were estimated to account for 91% of all deaths in the period 2000-2016 [8], with a decreasing trend of premature death since 2000 to 2016 for both men and women aged between 30 and 70 years. "Gaining Health" aims to intervene on the four main modifiable risk factors of NCDs (tobacco consumption, sedentary lifestyle/low physical activity, risky and harmful alcohol consumption, poor diet), through policies and actions adopting an intersectoral vision that have also been incorporated over the years by the NPPs.

WHO recommended improving country-level surveillance and monitoring as a top priority in the fight against NCDs, also providing data disaggregated by age, gender, and socioeconomic groups [9, 10]. Monitoring should provide internationally comparable assessments of the trends in NCDs and related risk factors over time, help to benchmark the situation in individual countries versus others in the same region or development category, provide a foundation for advocacy, policy development and coordinated action [9]. Age-standardized prevalence of raised BP among adults and mean systolic BP are among the 25 indicators suggested by the WHO in order to monitor global and national progress in the prevention and control of NCDs. [10]

This study aimed to assess temporal trends for mean values of BP and heart rate measurements, and for prevalence of raised BP, hypertension, awareness and control of hypertension in the Italian population aged 35–74 years, according to sex, age class, educational level, and Region using data measured within the CUORE Project national health examination surveys (HESs) 1998–2002, 2008–2012, and 2018–2019.

METHODS

Study design

Three HESs were conducted in Italy within the CUORE Project. The first survey was conducted from May 1998 to December 2002 in all Italian Regions, enrolling a random sample of 100 men and 100 women aged 35–74 years for every 1.5 million inhabitants (participation rate 50%). The second survey was conducted from March 2008 to July 2012, investigating a sample of 110 men and 110 women aged 35–79 years for every 1.5 million residents in all Italian Regions (participation rate 53%). The third survey was conducted from April 2018 to December 2019, in 10 Regions (out of 20) chosen in the North, Central, and South Italy, using a sample of 100 men and 100 women aged 35–74 years in each examined Region (participation rate 40%).

The three HESs were conducted by the Italian National Institute of Health (Istituto Superiore di Sanità-ISS); the first and second surveys in collaboration with the national scientific association of hospital cardiologists (ANMCO–Associazione Nazionale Medici Cardiologi Ospedalieri) and its foundation (Fondazione per il Tuo cuore - Heart Care Foundation). Surveys details were published elsewhere [11-14]. The three HESs were approved by the Ethical Committee of the ISS; all participants received an informative note and signed an informed consent. The three HESs are recognized within the Italian National Statistical Program. The second and third surveys were also recognized within the European HES collaboration [15, 16].

Study procedures and methods

The CUORE Project HESs used international standardized procedures and methods for the data collection and measurements [11-14].

BP measurements were performed applying the appropriate cuff to the right arm, while the participant was in a sitting position after 5 minutes at rest. During the 1998-2002 and 2008-2012 HES, SBP and DBP were identified at the beginning of the first and fifth phase of the Korotkoff sounds using a mercury sphygmomanometer; during the 2018-2019 HES an oscillometric device (Omron HEM-907) was used. Two consecutive readings were recorded in the first survey and three consecutive readings were recorded in the second and third survey, one minute apart. Heart rate was measured at the wrist between the first and the second measurements; it was measured at the right wrist by placing the middle fingers of the left hand on it to locate the radial artery - when a pulse was found, the number of beats felt within a one-minute period was counted using a stop watch as a time references. Information on pharmacological treatment were recorded by a standardized questionnaire and by checking the boxes of the drugs being used.

Patient and Public Involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Statistical analysis

The statistical comparison of the 1998–2002, 2008–2012, and 2018–2019 CUORE Project HESs data included 35- to 74-year-old residents in 10 Regions, distributed in north, central, and south Italy, involved in all the surveys: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

The average of the first and second BP measurement was used for the statistical analysis. As suggested by the WHO, raised blood pressure was defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg [6, 10]. Hypertensives were defined as those with SBP≥140 mmHg and/or DBP≥90 mmHg or under specific pharmacological treatment and were divided into groups of "undiagnosed", "diagnosed but untreated", "uncontrolled" (treated and SBP≥ 140 mmHg and/or DBP≥ 90 mmHg) and "controlled" (treated and SBP<140 mmHg and DBP<90 mmHg). The European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) also consider these cut off values of RBP and hypertension [17].

Educational level was selected as a proxy of socio-economic level; social class was dichotomized as those with primary/middle school attainment (≤8 years, lower education) and high school/university degree (>8 years, higher education).

Mean, standard deviation (SD), and 95% confidence interval of SBP, DBP, SBP and DBP in those not under treatment for hypertension and heart rate, and prevalence of raised blood pressure, hypertension and awareness and control of hypertension were assessed by sex, age group (35–44, 45–54, 55–64, and 65–74 years), and periods and, for those with available information, by educational level.

Following the suggestion reported in the WHO Global NCDs Action Plan 2013–2020 [6, 10], indicators, where appropriate, were age standardized using the direct method, referring to the age- and sex-specific distributions of the Italian adult population in 2000, 2010, and 2019 (Italian National Institute of Statistics-ISTAT), for the 1998–2002, 2008–2012, and 2018–2019 HESs respectively [18]. Data were also age standardized using the European Standard Population (EuStPop) 2013 for international comparisons [19].

Indicators assessed in the most recent period, 2018–2019, were compared with those of previous periods, 1998–2002 and 2008–2012, through statistical tests and regression models. Associations of the indicators with age and educational level were also determined within those periods. Regarding continuous indicators, a t-test was used to assess differences between periods and analysis of variance was used to assess association with age and educational level. Regarding categorical indicators, the chi-square test was used to assess differences between periods and association with age and educational classes. Comparisons between periods were also conducted, adjusting by age and educational level, using linear (continuous indicators) and logistic (categorical indicators) regression models, considering indicators as dependent variables, and period (2018–2019/1998–2002 or 2018–2019/2008–2012), age (35–54/55–74 years) and educational level (high/low) as independent variables; the statistical significance of the period was reported. Two-sided p-values <0.05 were considered statistically significant. Statistical analyses were performed using SAS software, release 9.4.

RESULTS

After the exclusions of persons with missing data for SBP or DBP or use of specific drug treatments (8 persons in 1998, 18 in 2008 and 9 in 2018), 2985 men and 2955 women (mean age ± SD: men 55 ± 11, women 54 ± 11), 2218 men and 2204 women (mean age ± SD: men 55 ± 11, women 55 ± 11),

and 1031 men and 1066 women (mean age ± SD: men 55 ± 11, women 55 ± 11) were included in the analysis of the 1998–2002, 2008–2012, and 2018–2019 HESs, respectively (S1 Table).

Blood pressure and heart rate measurements

The evaluation of the temporal trend of the mean BP shows in the period 2018-2019 as compared to twenty years before a significant reduction in SBP and DBP in both men (132/78 mmHg in 2018-2019 with a 3% of reduction for SBP, 10% for DBP) and women (122/73 mmHg, with a reduction of 7% and 11% respectively), while in the period 2018-2019 compared to ten years earlier, a reduction in mean SBP is observed only in women (3%), being stable in men, and in mean DBP both in men and women (7%) (Table 1). Similar trends are also observed for those not under antihypertensive drugs, and by age groups and education level (Tables 1, S2, S3, S4 and S5, Figures 1 and 2).
Within the 1998, 2008, and 2018 periods, mean SBP and DBP was higher in men than in women, regardless of antihypertensive drug treatment use, class of age and educational level, although not always statistically significant, especially in the 1998-2002 period considering that the difference increased progressively over time, passing from 3% in 1998-2002 to 4% in 2008-2012 until it reached 8% in 2018-2019 (Tables 1, S2, S3, S4, and S5, Figures 1 and 2). Within those periods, in both men and women, mean SBP and DBP, regardless of antihypertensive drug treatment use, progressively increased by age group and was tendentially higher in those with a lower level of education, except DBP in men (Tables S2, S3, S4, and S5). The mean SBP difference between educational levels increased progressively in the 1998, 2008, and 2018 periods in both men and women (men: 2%, 3%, and 4%; women: 7%, 8%, and 12%) (Table S4 and S5, Figures 1 and 2).
The mean heart rate was progressively increasing in the three surveys periods, both in men and women, in all age groups and education levels, remaining between 66 and 74 beats per minute. Within the 1998, 2008, and 2018 periods, no significant differences are observed in the mean heart rate by age group, with the exception of women in 1998-2002 for whom it decreases starting from 55 years; there are no differences between levels of education with the exception of men in 2018-2019 for whom there is an average level of heart rate higher in the lowest level of education.

Table1. Age-standardized blood pressure and heart rate measurements and prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control by sex and period. Men and women residing in Italy aged 35-74 years, The CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

	MEN															
	1998-2002 n=2985				2008-2012 n=2218				2018-2019 n=1031				2018-2019 vs 1998-2002			2018-2019 vs 2008-2012		
	mean	SD	95% CI		mean	SD	95% CI		mean	SD	95% CI		Diff	t-test sign^	Regression sign^^	Diff	t-test sign^	Regression sign^^
Systolic blood pressure - SBP (mmHg)	**136**	18	*135*	*136*	**132**	16	*131*	*132*	**132**	14	*131*	*132*	**-4**	***	***	**-0,3**	ns	ns
Diastolic blood pressure - DBP (mmHg)	**86**	11	*86*	*87*	**84**	10	*83*	*84*	**78**	10	*77*	*78*	**-9**	***	***	**-6**	***	***
SBP not under drug treatment (mmHg)	**134**	17	*133*	*134*	**130**	15	*129*	*131*	**131**	14	*130*	*132*	**-3**	***	**	**1**	ns	ns
DBP not under drug treatment (mmHg)	**85**	10	*85*	*86*	**83**	10	*83*	*84*	**77**	10	*76*	*78*	**-9**	***	***	**-6**	***	***
Heart rate (beats per minute)	**66**	11	*66*	*66*	**68**	10	*68*	*69*	**72**	12	*71*	*72*	**6**	***	***	**3**	***	***
	%	95% CI			%	95% CI			%	95% CI			Diff	chi-squared sign^	Logistic sign^^	Diff	chi-squared sign^	Logistic sign^^
Blood pressure drug treatment	**19**	*17*	*20*		**24**	*22*	*26*		**25**	*23*	*28*		**7**	***	***	**1**	ns	ns
Raised blood pressure	**50**	*48*	*52*		**40**	*38*	*42*		**30**	*27*	*32*		**-20**	***	***	**-10**	***	***
Hypertension	**54**	*52*	*55*		**49**	*47*	*52*		**44**	*41*	*47*		**-9**	***	***	**-5**	**	**
Hypertension																		
Undiagnosed	**53**	*51*	*56*		**40**	*37*	*42*		**36**	*32*	*41*		**-17**	***	***	**-3**	ns	ns
Diagnosed but untreated	**15**	*14*	*17*		**19**	*16*	*21*		**14**	*11*	*18*		**-1**	ns	ns	**-4**	*	ns
Uncontrolled	**25**	*23*	*27*		**25**	*22*	*27*		**22**	*19*	*26*		**-2**	ns	**	**-2**	ns	*
Controlled	**6**	*5*	*8*		**17**	*15*	*19*		**27**	*23*	*31*		**20**	***	***	**10**	***	***

	WOMEN															
	1998-2002 n=2955			2008-2012 n=2204			2018-2019 n=1066			2018-2019 vs 1998-2002			2018-2019 vs 2008-2012		
	mean	SD	95% CI	mean	SD	95% CI	mean	SD	95% CI	Diff	t-test sign^	Regression sign^^	Diff	t-test sign^	Regression sign^^
Systolic blood pressure - SBP (mmHg)	**132**	18	131 132	**126**	16	125 127	**122**	16	121 123	**-10**	***	***	**-4**	***	***
Diastolic blood pressure - DBP (mmHg)	**82**	10	82 82	**78**	9	78 79	**73**	11	72 74	**-9**	***	***	**-6**	***	***
SBP not under drug treatment (mmHg)	**129**	16	128 129	**124**	15	123 124	**120**	15	119 121	**-9**	***	***	**-4**	***	***
DBP not under drug treatment (mmHg)	**81**	10	80 81	**78**	9	77 78	**72**	10	71 73	**-9**	***	***	**-6**	***	***
Heart rate (beats per minute)	**70**	11	69 70	**71**	9	71 71	**73**	10	72 73	**3**	***	***	**2**	***	***
	%	95% CI		%	95% CI		%	95% CI		Diff	chi-squared sign^	Logistic sign^^	Diff	chi-squared sign^	Logistic sign^^
Blood pressure drug treatment	**22**	20	23	**22**	20	24	**23**	20	25	**1**	ns	**	**1**	ns	ns
Raised blood pressure	**39**	38	41	**25**	24	27	**16**	14	19	**-23**	***	***	**-9**	***	***
Hypertension	**45**	43	46	**35**	33	37	**32**	29	34	**-13**	***	***	**-4**	*	ns
Hypertension															
Undiagnosed	**44**	42	47	**32**	28	35	**28**	23	32	**-17**	***	***	**-4**	ns	**
Diagnosed but untreated	**16**	14	18	**16**	13	18	**15**	12	19	**-0,4**	ns	**	**-0,4**	ns	ns
Uncontrolled	**30**	27	32	**26**	23	29	**16**	13	20	**-13**	***	***	**-10**	**	**
Controlled	**10**	9	12	**27**	24	30	**41**	36	46	**31**	***	***	**14**	***	***

SD: standard deviation; CI: confidence interval; Diff: mean or percentage difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means or prevalence. Means, standard deviations, and prevalence were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. ^ t-test to compare mean values between periods; chi-square test to compare prevalence between periods. ^^ Linear regression and logistic models were assessed considering indicators as dependent variable and period (2018–2019/1998–2002 or 2018–2019/2008–2012), age (35–54/55–74 years), and educational level (high/low) as independent variables; the statistical significance of the period was reported. *** p < 0.0001; ** p < 0.01; *p < 0.05; ns not significant p-value. Raised blood pressure: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Hypertension drug treatment, raised blood pressure and hypertension

The prevalence of antihypertensive drug treatment use in men showed a significant increase by 7% in 2018-2019 compared to twenty years earlier, it remained stable for men compared to ten years earlier and for women in the three survey periods (Table 1), however a significant increase was observed in 2018-2019 compared to twenty years earlier in men aged 55 years and over and women aged 65 years and over (Tables S6 and S7). The general increase in the use of antihypertensive drug treatment in men was especially observed among those with higher education level; in women, a generally stable prevalence was observed regardless of education level (Tables S8 and S9). Antihypertensive drug treatment use, was higher in men than in women, in 1998-2002, and reached, in 2018-2019, more similar values between men (25%) and women (23%).

The prevalence of raised BP was 30% in men and 16% in women in 2018-2019, significantly decreased compared to twenty and ten years earlier: in men it decreased by 20% and 10% respectively and in women 23% and 9% respectively (Table 1). The decreasing trend of raised BP was progressively higher by age classes, reaching, in 2018-2019 compared to 1998-2002, the 27% in men and 38% in women aged 65-74 years, while it was similar between educational levels both in men and women (Tables S6, S7, S8, S9, Figures 1 and 2).

The prevalence of hypertension was 44% in men and 32% in women in the 2018-2019, significantly decreased compared to twenty and ten years earlier: in men it decreased by 9% and 5% respectively and in women 13% and 4% respectively (Table 1); in men the decrease was observed among those aged 35 to 54 years both compared to twenty and ten years earlier, in women in all age groups compared to twenty years earlier, while from 55 to 74 years of age compared to the previous ten years; similar decreasing trend was observed between educational levels with a more favourable trend among more educated women (Tables S6, S7, S8 and S9, Figures 1 and 2).

As expected, within periods, both in men and women, prevalence of raised BP and hypertension significantly increased by age group and was tendentially higher in those with a lower level of education (Tables S6, S7, S8, S9, Figures 1 and 2). Prevalence of raised BP and hypertension decreased or remained stable in all Italian Regions both in men and women (Figures 3 and 4, and Table S10).

Awareness and control of hypertension

In 2018-2019, prevalence of undiagnosed hypertension resulted in 36% and 28% of hypertensive men and women, with a decreasing trend of 17% in comparison with twenty years earlier both in men and women and 3-4 % in comparison with ten years earlier (Table 1); these trends were found in particular in those aged 45 years and over and were similar by educational level, with some advantage in women with higher education (Tables S6, S7, S8 and S9). Within periods, both in men and women, prevalence of undiagnosed hypertension was higher among younger men and women but similar between educational levels (Tables S6, S7, S8 and S9).

Prevalence of not controlled hypertension was found to be halved in women, from 30% of 1998-2002 to 16% in 2018-2019 (Table 1); favorable, but much more contained, trend was found in men with a reduction of 2% (Table 1). Within periods, both in men and women, prevalence of uncontrolled hypertension was found increasing by age classes and tendentially higher in those with lower educational level (Tables S6, S7, S8 and S9).

Although in 2018-2019 only 27% of hypertensive men and 41% of hypertensive women had their blood pressure under control, a positive growth trend of hypertension under control was observed both in men and women, with an increase in 2018-2019, compared to 20 years earlier, of 20% in men and 31% in women (10% and 14 % respectively compared to ten years earlier) (Table 1). An

important increase was observed in men from the age of 55 years and in women in all age groups; similar trend for more or less educated men, while a more favorable trend is observed among more educated women (Tables S6, S7, S8 and S9, Figures 1 and 2). In 2008-2012 and 2018-2019, in men, prevalence of controlled hypertension increases by age classes (in women only in the last survey), and in the latter two surveys it is higher in men with higher education level (Tables S6, S7, S8 and S9).

Results, age standardized according to the European standard population 2013, are available in Tables S11, S12, S13, S14 and S15.

DISCUSSION

Data of measured BP in random samples of the general Italian population aged 35–74 years during three HESs conducted in 1998–2002, 2008–2012, and 2018–2019, showed a significant reduction, in 2018-2019 compared to twenty years earlier, of SBP and DBP mean levels and prevalence of raised BP and hypertension. The reductions were consistent with respect to sex, age classes and education level and were detected to different extents in almost all Italian Regions. This favorable decline in mean blood pressure and in the prevalence of raised BP and hypertension was observed in 2018-2019 even when compared with ten years earlier, except for mean SBP in men which was stable. Although around 7 out of 10 men and 6 out of 10 women with raised BP still in 2018-2019 did not have their blood pressure under control (because it is not diagnosed, diagnosed but not treated or treated but not under control), an important increase in raised BP control was observed in 2018-2019 compared to twenty years earlier, for men mostly due to a decrease in the prevalence of undiagnosed high blood pressure and for women also due to a reduction in the prevalence of uncontrolled RBP.

These results, which to our knowledge are based on the most recent national measured data on Italian general adult population, responds to the WHO's request to provide information on effectiveness of national policies and strategies, showing, in relation to the objective indicated in the Global Action Plan 2013-2020 (25% relative reduction in the prevalence of raised BP or containment of the prevalence of raised BP by 2025, proposed leading to a 33% of relative reduction by 2030), a significant decline from 1998-2020 to 2018-2019 in the prevalence of raised BP, from 50% to 30% in men and from 39% to 16% in women, equal to a relative reduction of 41% and 58% respectively, and also a significant decline from 2008-2012 to 2018-2019, from 40% to 30% in men and from 25% to 16% in women, equal to a relative reduction of 25% and 36% respectively [6].

Mean values of SBP and DBP, as well as prevalence of raised blood pressure trends are consistent with those of other studies conducted in the Italian adult population. NCD Risk Factor Collaboration, that pooled data of population-based studies with measured blood pressure in adults aged 18 years and older from 200 countries, showed that within the 36 Italian surveys (at community, subnational, and national levels, including the CUORE Project surveys 1998–2002 and 2008–2012), mean values of SBP and DBP, as well as prevalence of RBP decreased during 1995–2015 period [20, 21].

In some other European countries, such as United Kingdom, Switzerland, Spain, Sweden, Norway, Netherlands, Luxemburg, Ireland, Germany, France, Finland, Belgium and Austria, a decline of blood pressure levels was also observed with various intensities both in men and women, while in other countries, mainly from Eastern Europe, such as Slovenia, Slovakia, Serbia, Romania, Poland, Lithuania, Hungary, Greece, Czech Republic and Portugal, a trend of decline was observed in women and a stable or slightly increasing trend in men; in other countries, such as Moldova, Croatia, Bosnia

and Herzegovina and Albania, a stable or an increasing trend is still ongoing both in men and women [20, 21].

High-income countries have begun to reduce hypertension in their populations through strong public health policies such as the reduction of salt content in processed food and widely available early diagnosis and treatment that tackle hypertension and other risk factors together [2, 22]. Also in Italy, an explanation of the reasons why a decrease in mean blood pressure and in the prevalence of raised blood pressure is observed in the general adult population might be on the one hand the enhancement of its early detection, treatment and control and on the other hand successful national programmes of primary prevention which have led to an increase in the normal weight prevalence and to the reduction of the daily consumption of salt in the general adult population, despite the average levels of daily potassium consumption being not yet adequate [11-13]. In the last past two decades, the "Gaining Health" Programme and NPPs in Italy were oriented to reduce risk factors associated to the increase of blood pressure, such as physical inactivity, excess of weight and salt consumption, as well as the smoking habit, through intersectional strategies at both population (e.g., facilitating the choice of correct lifestyles) and individual levels (e.g., motivational counselling and specific therapeutic groups), promoting, and supporting national surveillance systems and monitoring studies, and through voluntary agreements for salt reduction in food products, school and workplace programs, and public awareness campaigns [23]. As an example, aimed directly at the diagnosis and control of raised BP, in the NPP 2005-2008 the promotion of a multifactorial cardiovascular diseases (CVD) risk assessment, based also on BP measurements, and its monitoring over time in clinical practice has been explicitly included. As well as, NPP 2014-2019 also focused on the early identification and integrated assessment of persons with NCDs risk factors, to be directed towards an adequate systemic management, able to enhance personal resources for the conscious adoption of correct life, or when necessary, towards suitable multidisciplinary therapeutic and assistance paths.

Additional findings of the study, including higher level of blood pressure and raised BP/hypertension in men than in women and more severe values in the southern Italy Regions and tendentially in people with lower education levels, are consistent with results from other Italian and European Studies [20,21,24], and are in line with the association of excess of weight and salt consumption with gender, education level and Italian macro-area [11, 12,14, 25, 26].

As far as, the favourable trend of increase in hypertension awareness, treatment, and control is concerned, it could be due to the greater diffusion and compliance with the guidelines for hypertension in clinical practice that include simplified recommendations. In Italy, over the period of our analysis, the antihypertensive treatment was based on the guidelines drawn up by the ESC/ESH [17, 27-29] which indicated as threshold for immediate treatment BP ≥180/110 or BP of 140-179/90-109 (depending on CVD risk stratification) after lifestyle modifications, with a treatment target that has changed over time (2003: BP<140/90 mmHg; 2007: BP<140/90 mmHg and BP<130/80 mmHg in high CVD risk; 2013: BP<140/90 mmHg; 2018: DBP<80 mmHg for all and SBP 120-129 mmHg for persons aged<65 years or SBP 130-139 mmHg for persons aged≥65 years). The progressively lower thresholds for diagnosing hypertension and the beginning of treatment also may have contributed to this favourable trend based on the threshold of 140/90 mm Hg. In addition, over time, treatment efficacy and control for some patients suffering from smaller side-effects of the earliest generations of drugs improved thanks to the availability of newer drugs [30].

Early detection and treatment of raised BP and other risk factors, as well as public health policies that reduce exposure to behavioural risk factors, have contributed to the gradual decline in mortality due to heart disease and stroke in Italy and other high-income countries over the last three decades [31, 32].

Strengths and limitations

Major strengths of this study are the following: the use of standardized procedures and methods to assess blood pressure measurements, allowing objective and reliable estimates of SBP, DBP and raised blood pressure; the checking of drug boxes to assess the use of specific pharmacological treatments; a good national coverage with the enrolment of study participants from half of the Italian regions distributed in northern, central, and southern Italy; the random selection and the sex and age classes stratification of samples from the general population.

Conversely, we acknowledge some study limitations, which should be taken in consideration when interpreting results. First, because of the choice of urban districts for the random selection of the study participants within the surveys, the results may not be representative of the habits of the population living in rural areas. The participation rates in the surveys were lower than desirable, yet consistent, with lower contact rates occurring in more highly urbanized areas and with a decreasing trend of participation observed in HESs in other European countries [33]. The cross-sectional design of the study does not allow to assess causality of the associations between SBP, DBP and raised blood pressure and educational level. There were differences in the educational level distribution between the three 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 [34]. The use of mercury sphygmomanometer in the 1998-2002 and 2008-2012 surveys and of an oscillometric device in the 2018-2019 survey (due to the EU regulation 847/2012 that banned the sale of mercury sphygmomanometers from 10 April 2014 onwards [35]) may affect comparison among surveys [36]; however, the oscillometric device used in HES 2018-2019 was certified according to international validation protocol to ensure that the device measures accurately in comparison with the mercury sphygmomanometer; in addition it should prevent the observer's error due to the use of a mercury sphygmomanometer, and the common standardized protocol based on aspects such as room temperature, disturbing noises, lighting, adequacy of the table and chair for the measurement, interaction between the survey participant and the measurer, availability of different cuffs may minimize variation due to measurement technique [16, 37, 38]. Anyway, with all device types, mercury and aneroid sphygmomanometers, and oscillometric devices, calibration error may bias the results [39]. Hypertension diagnosis should be based on several BP readings taken on several occasions (at least two), as recommended by international guidelines [17]; however, epidemiological studies are based on BP measurement in a single visit, possibly with two or more measurements repeated during the same visit [16, 40].

Conclusions

BP assessment in three independent surveys on the Italian population aged 35-74 years, carried out in 10 Regions approximately 10 years apart from each other, showed a significant reduction of BP mean values and prevalence of raised BP and hypertension in 2018-2019 compared to twenty years earlier, with a favourable trend also observed compared to ten years earlier. This reduction was independent of gender, age and educational level and met the 25% target for reduction/containment of the RBP prevalence indicated in the WHO Global Action Plan 2013-2020 by 2025 with baseline 2010. Albeit in 2018-2019 underdiagnoses and non-control of elevated blood pressure was still largely prevalent in Italy, a favourable trend in the control of raised BP has been observed.

Although systematic and periodic monitoring are necessary to observe the trend and control of blood pressure in the coming years, also in relation to the direct and indirect effects of the COVID-19 pandemic, these results have major public health implications in so much as they encourage the

initiatives undertaken by the Italian Ministry of Health in order to contain risk factors associated to the onset of raised BP at individual and population level through the "Gaining Health: making healthy choices easy" Programme and the NPPs. In continuity with the NPP 2014-2019, the NPP 2020-2025 renewed the commitment to the health promotion and the prevention of NCDs by providing preventive and protective interventions according to a life-course approach and aiming at the early identification and management of persons with risk factors.

Prevention and control of raised BP involve multi-stakeholder collaboration, such as governments, academia, the food and beverage industry and civil society. In view of the enormous public health benefits of BP control, some concerted action has been implemented and data demonstrate that the prevention of raised BP is today an attainable goal.

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FIGURES

Figure 1. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident men aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

Bars refer to 95% confidence intervals. Statistics by educational level were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Higher education—high school or college; lower education—primary or middle school. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: under drug treatment for hypertension with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Figure 2. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

Bars refer to 95% confidence intervals. Statistics by educational level were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Higher education—high school or college; lower education—primary or middle school. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: under drug treatment for hypertension with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Figure 3. Prevalence of raised blood pressure based on measurements, by sex, Regions, and period. Italian resident men and women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.

Figure 4. Prevalence of hypertension based on measurements, by sex, Regions, and period. Italian resident men and women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment.

FIG 1

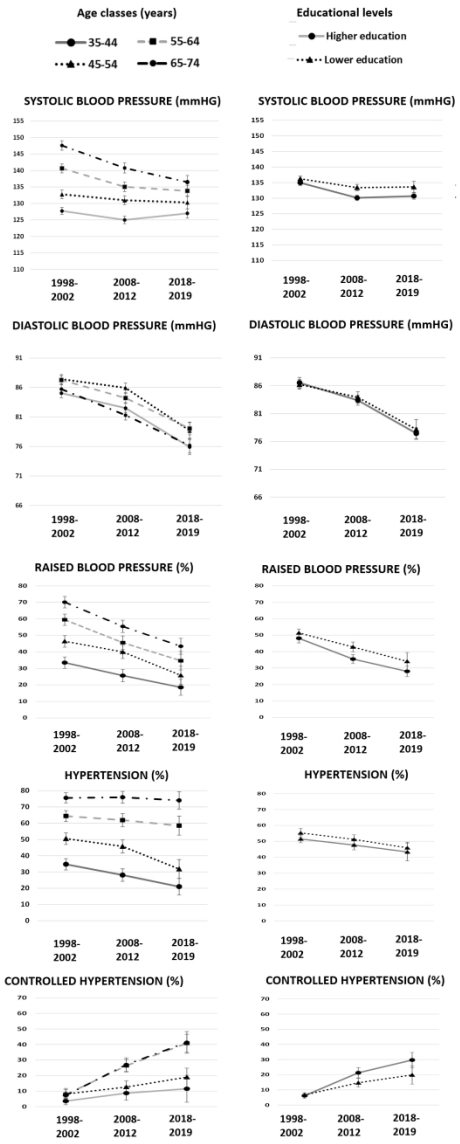

Figure 1. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident men aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.
Bars refer to 95% confidence intervals. Statistics by educational level were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Higher education—high school or college; lower education—primary or middle school. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: under drug treatment for hypertension with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

322x586mm (150 x 150 DPI)

FIG 2

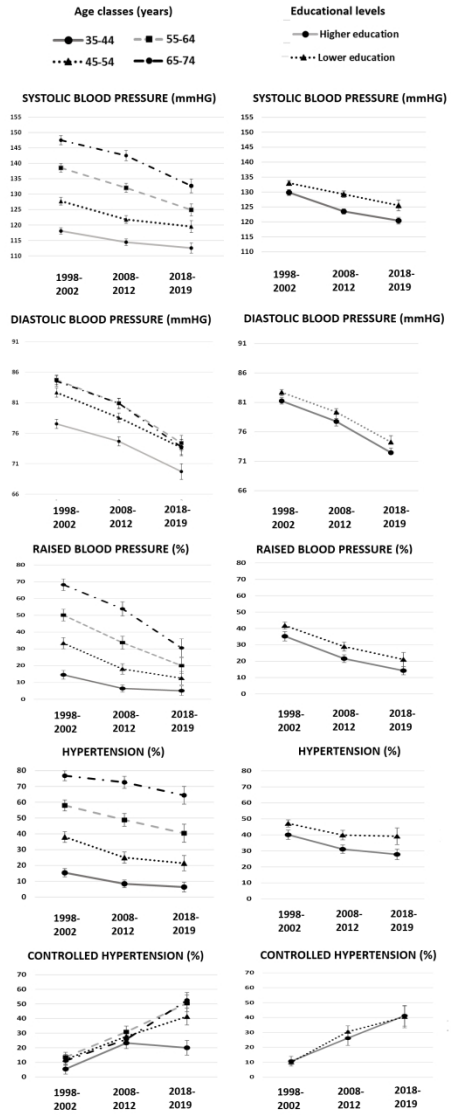

Figure 2. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.
Bars refer to 95% confidence intervals. Statistics by educational level were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Higher education—high school or college; lower education—primary or middle school. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: under drug treatment for hypertension with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

366x594mm (150 x 150 DPI)

Fig 3

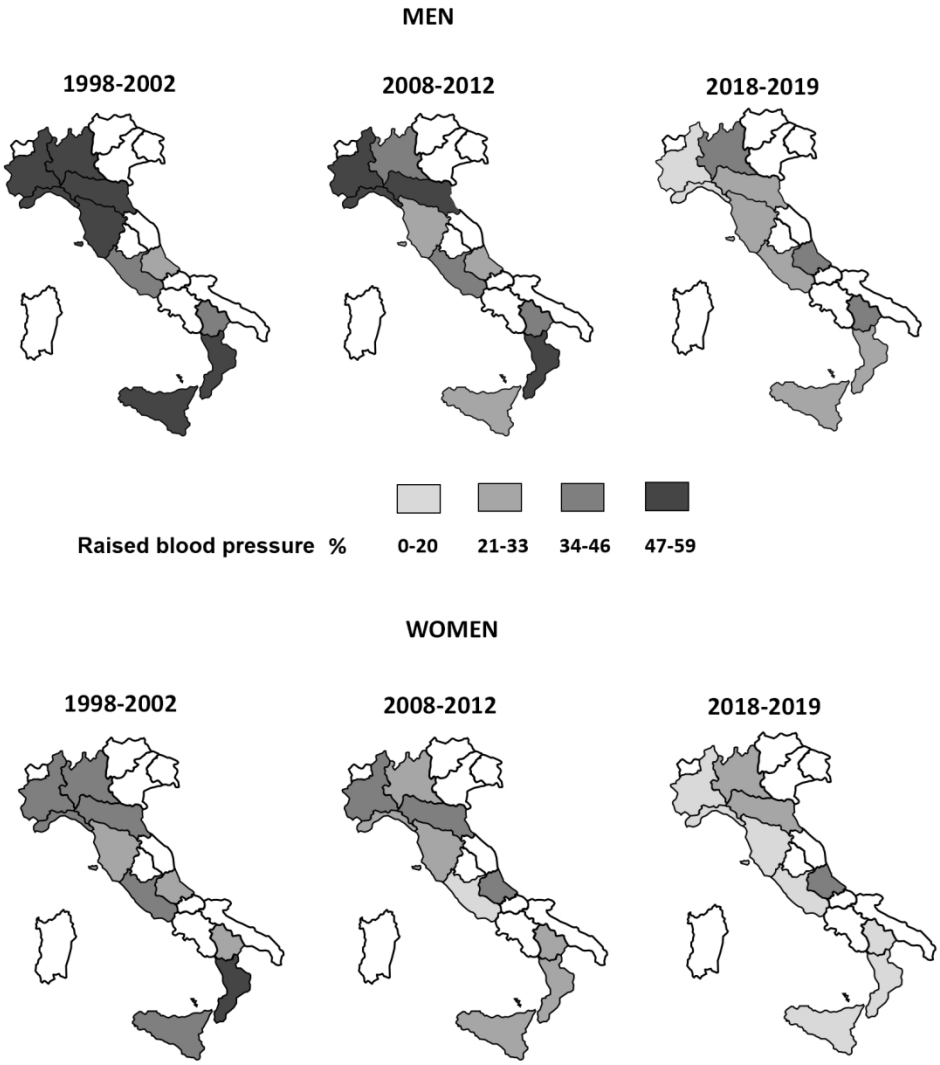

Figure 3. Prevalence of raised blood pressure based on measurements, by sex, Regions, and period. Italian resident men and women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.
Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.

287x345mm (150 x 150 DPI)

Fig 4

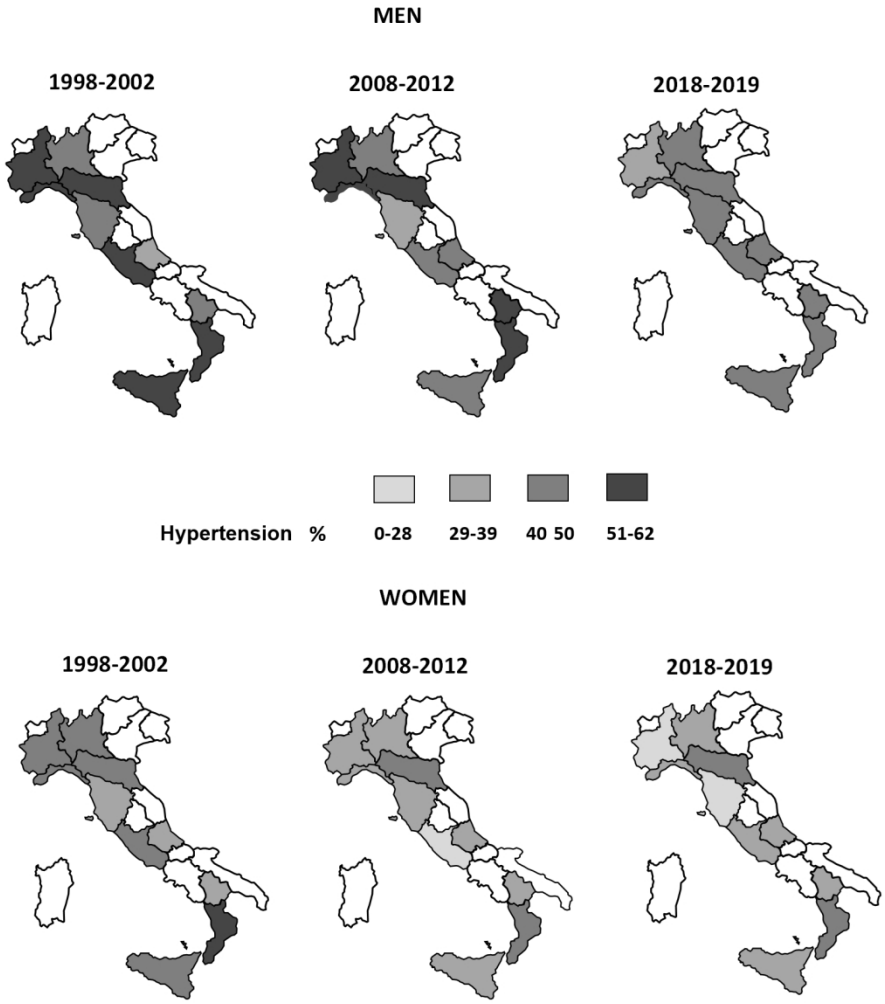

Figure 4. Prevalence of hypertension based on measurements, by sex, Regions, and period. Italian resident men and women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019. Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment.

287x367mm (150 x 150 DPI)

Table S1. Demographic characteristics of men and women with available blood pressure measurements and information on the use of specific drug treatment within the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

	MEN					
	1998-2002		2008-2012		2018-2019	
Age class (years)						
	n	**%**	**n**	**%**	**n**	**%**
35-44	717	24	530	24	248	24
45-54	752	25	588	27	248	24
55-64	784	26	564	25	277	27
65-74	732	25	536	24	258	25
Educational level						
	n	**%**	**n**	**%**	**n**	**%**
Higher education	1249	42	1183	54	725	71
Lower education	1730	58	1018	46	303	29
	WOMEN					
	1998-2002		2008-2012		2018-2019	
Age class (years)						
	n	**%**	**n**	**%**	**n**	**%**
35-44	715	24	514	23	237	22
45-54	769	26	577	26	271	25
55-64	778	26	584	27	280	26
65-74	693	23	529	24	278	26
Educational level						
	n	%	n	%	n	%
Higher education	1052	36	1167	53	725	68
Lower education	1887	64	1017	47	339	32

Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Higher education - high school or college; lower education - primary or middle school.

Table S2. Blood pressure and heart rate measurements mean levels by age class and period. Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Systolic blood pressure (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						***				
35-44	717	**128**	15	127	129		530	**125**	13	124	126		248	**127**	11	126	128		**-1**	ns	**2**	*
45-54	752	**133**	18	131	134		588	**131**	16	130	132		248	**130**	16	128	132		**-2**	*	**-1**	ns
55-64	784	**141**	20	139	142		564	**135**	17	134	136		277	**134**	14	132	135		**-7**	***	**-1**	ns
65-74	732	**148**	20	146	149		536	**141**	18	139	142		258	**136**	17	134	138		**-11**	***	**-4**	**

Diastolic blood pressure (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						**				
35-44	717	**85**	11	84	86		530	**83**	10	82	83		248	**76**	10	75	77		**-9**	***	**-7**	***
45-54	752	**87**	11	87	88		588	**86**	10	85	87		248	**79**	11	77	80		**-9**	***	**-7**	***
55-64	784	**87**	11	87	88		564	**84**	10	83	85		277	**79**	9	78	80		**-8**	***	**-5**	***
65-74	732	**86**	10	85	86		536	**81**	10	80	82		258	**76**	10	75	77		**-10**	***	**-5**	***

Systolic blood pressure not under drug treatment (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						***				
35-44	682	**127**	14	126	128		504	**125**	13	123	126		237	**127**	11	125	128		**-0.2**	ns	**2**	*
45-54	640	**131**	17	130	132		481	**129**	16	127	130		212	**128**	14	126	130		**-3**	*	**-1**	ns
55-64	581	**137**	19	136	139		370	**133**	17	131	135		170	**133**	14	131	135		**-4**	**	**-0.2**	ns
65-74	454	**143**	20	142	145		252	**138**	18	136	140		125	**138**	18	134	141		**-6**	**	**-1**	ns

Diastolic blood pressure not under drug treatment (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						**						***						ns				
35-44	682	**85**	10	84	85		504	**82**	10	81	83		237	**75**	10	74	77		**-9**	***	**-7**	***
45-54	640	**86**	11	86	87		481	**85**	10	84	86		212	**77**	10	76	78		**-9**	***	**-8**	***
55-64	581	**86**	10	85	87		370	**84**	10	83	85		170	**78**	9	77	79		**-8**	***	**-6**	***
65-74	454	**84**	10	83	85		252	**81**	10	80	82		125	**77**	11	75	79		**-8**	***	**-4**	**

Heart rate (beats per minute)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						ns						ns						ns				
35-44	715	**66**	10	65	67		530	**68**	9	67	69		248	**72**	12	70	73		**6**	***	**4**	***
45-54	750	**66**	11	65	67		588	**69**	10	68	70		248	**72**	11	71	74		**6**	***	**3**	***
55-64	783	**66**	11	65	67		564	**68**	10	68	69		277	**72**	12	70	73		**6**	***	**3**	***
65-74	732	**66**	11	65	67		536	**69**	10	68	69		258	**70**	12	69	72		**4**	***	**2**	ns

SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S3. Blood pressure and heart rate measurements mean levels by age class and period. Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Systolic blood pressure (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
35-44	715	**118**	14	117	119	***	514	**114**	13	113	116	***	237	**113**	13	111	114	***	**-6**	***	**-2**	ns
45-54	769	**128**	18	126	129		577	**122**	15	121	123		271	**120**	16	118	121		**-8**	***	**-2**	*
55-64	778	**139**	20	137	140		584	**132**	18	131	134		280	**125**	16	123	127		**-14**	***	**-7**	***
65-74	693	**147**	20	146	149		529	**143**	20	141	144		278	**133**	19	130	135		**-15**	***	**-10**	***

Diastolic blood pressure (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
35-44	715	**78**	10	77	78	***	514	**75**	9	74	75	***	237	**70**	10	68	71	***	**-8**	***	**-5**	***
45-54	769	**83**	11	82	83		577	**79**	9	78	79		271	**74**	11	72	75		**-9**	***	**-5**	***
55-64	778	**85**	10	84	85		584	**81**	10	80	82		280	**74**	11	73	76		**-10**	***	**-7**	***
65-74	693	**85**	10	84	85		529	**81**	10	80	82		278	**74**	11	72	75		**-11**	***	**-7**	***

Systolic blood pressure not under drug treatment (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
35-44	698	**118**	14	116	119	***	499	**114**	12	113	115	***	234	**112**	13	111	114	***	**-5**	***	**-1**	ns
45-54	657	**125**	17	124	126		510	**120**	15	119	122		238	**118**	15	116	120		**-7**	***	**-2**	*
55-64	539	**134**	18	132	135		401	**128**	17	126	130		203	**123**	17	121	126		**-10**	***	**-4**	**
65-74	374	**142**	18	140	144		244	**138**	20	135	140		122	**127**	16	124	130		**-15**	***	**-10**	***

Diastolic blood pressure not under drug treatment (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
35-44	698	**77**	10	76	78	***	499	**74**	8	74	75	***	234	**70**	10	68	71	**	**-8**	***	**-5**	***
45-54	657	**81**	10	81	82		510	**78**	9	77	79		238	**73**	11	71	74		**-9**	***	**-5**	***
55-64	539	**83**	10	82	83		401	**79**	9	79	80		203	**73**	11	72	75		**-9**	***	**-6**	***
65-74	374	**83**	9	82	83		244	**80**	9	79	81		122	**71**	9	70	73		**-11**	***	**-9**	***

Heart rate (beats per minute)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
35-44	711	**71**	11	70	72	**	514	**72**	9	71	72	*ns*	237	**74**	11	73	75	*ns*	**3**	**	**2**	**
45-54	769	**70**	10	69	71		577	**71**	9	70	71		271	**73**	10	72	74		**3**	***	**3**	**
55-64	776	**69**	10	68	70		584	**71**	9	70	72		280	**72**	10	71	73		**3**	***	**1**	ns
65-74	690	**69**	11	68	70		529	**71**	10	70	72		278	**72**	11	71	73		**3**	**	**1**	ns

SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S4. Blood pressure measurements and heart rate mean levels by educational level and period. Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Systolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	DS	95% CI			n	mean	DS	95% CI			n	mean	DS	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1249	**135**	17	*134*	*136*	***	1183	**130**	15	*129*	*131*	***	725	**131**	14	*130*	*132*	***	**-4**	***	**1**	ns
Lower education	1730	**136**	18	*135*	*137*		1018	**133**	17	*132*	*134*		303	**134**	16	*132*	*135*		**-3**	**	**0.2**	ns

Diastolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	DS	95% CI			n	mean	DS	95% CI			n	mean	DS	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1249	**87**	11	*86*	*87*	ns	1183	**83**	10	*83*	*84*	ns	725	**77**	10	*77*	*78*	ns	**-9**	***	**-6**	***
Lower education	1730	**86**	11	*86*	*87*		1018	**84**	10	*83*	*85*		303	**78**	10	*77*	*79*		**-8**	***	**-6**	***

Systolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	DS	95% CI			n	mean	DS	95% CI			n	mean	DS	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1046	**133**	16	*132*	*134*	***	913	**129**	15	*128*	*130*	***	537	**130**	13	*129*	*131*	***	**-3**	***	**1**	ns
Lower education	1305	**134**	17	*133*	*135*		680	**131**	16	*130*	*133*		205	**133**	15	*131*	*135*		**-1**	ns	**1**	ns

Diastolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	DS	95% CI			n	mean	DS	95% CI			n	mean	DS	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1046	**86**	10	*85*	*86*	ns	913	**83**	10	*82*	*83*	ns	537	**77**	10	*76*	*78*	ns	**-9**	***	**-6**	***
Lower education	1305	**85**	10	*85*	*86*		680	**83**	10	*83*	*84*		205	**77**	9	*76*	*78*		**-8**	***	**-6**	***

Heart rate (beats per minute)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	DS	95% CI			n	mean	DS	95% CI			n	mean	DS	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1244	**66**	11	*65*	*67*	ns	1183	**68**	9	*68*	*69*	ns	725	**71**	11	*70*	*72*	**	**5**	***	**2**	***
Lower education	1730	**66**	11	*65*	*67*		1018	**68**	10	*68*	*69*		303	**74**	12	*73*	*76*		**8**	***	**6**	***

Means and standard deviations age-standardized by ISTAT Italian population 2000, 2010 and 2019 respectively. SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. Higher education - high school or college; lower education - primary or middle school. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S5. Blood pressure measurements and heart rate mean levels by educational level and period. Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Systolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1052	**130**	16	129	131	***	1167	**124**	15	123	124	***	725	**120**	15	119	122	***	-9	***	-3	***
Lower education	1887	**133**	18	132	134		1017	**129**	18	128	130		339	**126**	17	124	127		-7	***	-4	**

Diastolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1052	**81**	10	81	82	***	1167	**78**	9	77	78	***	725	**72**	11	72	73	**	-9	***	-5	***
Lower education	1887	**83**	10	82	83		1017	**79**	10	79	80		339	**74**	10	73	75		-8	***	-5	***

Systolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	928	**128**	16	127	129	***	992	**121**	14	120	122	***	593	**119**	15	118	120	***	-9	***	-2	**
Lower education	1331	**129**	16	129	130		651	**127**	16	126	128		203	**124**	16	121	126		-6	***	-3	*

Diastolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	928	**81**	10	80	81	***	992	**77**	9	76	78	***	593	**71**	10	71	72	*	-9	***	-6	***
Lower education	1331	**81**	10	81	82		651	**78**	9	78	79		203	**73**	10	72	75		-8	***	-5	***

Heart rate (beats per minute)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1047	**69**	11	69	70	ns	1167	**71**	9	70	72	ns	725	**73**	10	72	73	ns	3	***	2	**
Lower education	1884	**70**	11	69	70		1017	**71**	10	71	72		339	**73**	11	72	74		3	***	2	**

Means and standard deviations age-standardized by ISTAT Italian population 2000, 2010 and 2019 respectively. SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. Higher education - high school or college; lower education - primary or middle school. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Lombardy, Piedmont, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S6. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by age class and period. Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Blood pressure drug treatment

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				***				
35-44	717	5	3 6		530	5	3 7		248	4	2 7		-0.4	ns	-0.5	ns
45-54	752	15	12 17		588	18	15 21		248	15	10 19		-0.4	ns	-4	ns
55-64	784	26	23 29		564	34	30 38		277	39	33 44		13	***	4	ns
65-74	732	38	34 41		536	53	49 57		258	52	45 58		14	**	-1	ns

Raised blood pressure

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				***				
35-44	717	33	30 37		530	26	22 29		248	19	14 23		-15	***	-7	*
45-54	752	46	43 50		588	40	36 44		248	26	20 31		-21	***	-14	***
55-64	784	59	56 63		564	46	41 50		277	35	29 40		-25	***	-11	**
65-74	732	70	67 73		536	55	51 60		258	43	37 49		-27	***	-12	**

Hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				**				
35-44	717	35	31 38		530	28	24 32		248	21	16 26		-14	***	-7	*
45-54	752	51	47 54		588	46	42 50		248	32	26 38		-19	***	-14	**
55-64	784	64	61 68		564	62	58 66		277	58	53 64		-6	ns	-3	ns
65-74	732	76	72 79		536	76	72 80		258	74	69 79		-2	ns	-2	ns

Undiagnosed hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				**				***				***				
35-44	249	67	62 73		149	54	46 62		52	62	48 75		-6	ns	8	ns
45-54	380	52	47 57		269	40	34 46		79	35	25 46		-16	**	-4	ns
55-64	505	48	44 52		349	32	27 37		162	23	17 30		-25	***	-8	ns
65-74	553	39	35 43		407	25	20 29		191	21	16 27		-18	***	-3	ns

Diagnosed but untreated hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				ns				
35-44	249	18	14 23		149	29	22 36		52	17	7 28		-1	ns	-12	ns
45-54	380	19	15 23		269	20	16 25		79	19	10 28		0.0	ns	-1	ns
55-64	505	12	9 14		349	13	9 16		162	10	6 15		-1	ns	-2	ns
65-74	553	10	8 13		407	6	3 8		191	9	5 13		-1	ns	3	ns

Uncontrolled hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				ns				
35-44	249	10	7 14		149	9	4 13		52	10	2 18		-1	ns	1	ns
45-54	380	21	17 25		269	27	22 32		79	27	17 36		5	ns	-1	ns
55-64	505	32	28 37		349	29	24 34		162	25	19 32		-7	ns	-4	ns
65-74	553	43	39 47		407	43	38 48		191	28	22 35		-15	**	-14	**

Controlled hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				ns				***				***				
35-44	249	4	1 6		149	9	4 13		52	12	3 20		8	*	3	ns
45-54	380	8	5 11		269	13	9 17		79	19	10 28		11	**	6	ns
55-64	505	8	5 10		349	26	22 31		162	41	33 48		33	***	14	**
65-74	553	7	5 9		407	27	23 31		191	41	34 48		34	***	14	**

CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S7. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by age class and period. Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Blood pressure drug treatment

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	715	2	1	3		514	3	1	4		237	1	0	3	-1	ns	-2	ns
45-54	769	15	12	17		577	12	9	14		271	12	8	16	-2	ns	1	ns
55-64	778	31	27	34		584	31	28	35		280	28	22	33	-3	ns	-4	ns
65-74	693	46	42	50		529	54	50	58		278	56	50	62	10	**	2	ns

Raised blood pressure

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	715	15	12	17		514	6	4	9		237	5	2	8	-9	**	-1	ns
45-54	769	33	30	37		577	18	15	21		271	13	9	16	-21	***	-5	*
55-64	778	50	47	54		584	34	30	38		280	20	15	25	-30	***	-14	***
65-74	693	68	65	72		529	54	50	58		278	31	25	36	-38	***	-23	***

Hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	715	15	13	18		514	8	6	11		237	6	3	9	-9	**	-2	ns
45-54	769	38	35	41		577	25	21	28		271	21	17	26	-17	***	-4	ns
55-64	778	58	55	61		584	49	45	53		280	40	35	46	-18	***	-8	*
65-74	693	77	74	80		529	73	69	76		278	64	59	70	-12	***	-8	*

Undiagnosed hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	110	62	53	71		43	40	25	54		15	47	21	72	-15	ns	7	ns
45-54	292	45	40	51		144	39	31	47		58	29	18	41	-16	*	-10	ns
55-64	451	33	29	38		285	24	19	28		113	21	14	29	-12	*	-2	ns
65-74	532	32	28	36		384	20	16	23		179	11	6	15	-22	***	-9	**

Diagnosed but untreated hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					**								
35-44	110	23	15	31		43	26	13	39		15	33	9	57	11	ns	8	ns
45-54	292	16	12	21		144	15	9	20		58	14	5	23	-3	ns	-1	ns
55-64	451	14	10	17		285	12	8	16		113	11	5	16	-3	ns	-2	ns
65-74	532	8	6	10		384	6	4	9		179	2	0	4	-6	***	-4	***

Uncontrolled hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	110	10	4	16		43	12	2	21		15	0	0	0	-10	-	-12	-
45-54	292	26	21	31		144	19	12	25		58	16	6	25	-11	ns	-3	ns
55-64	451	39	35	44		285	33	28	39		113	18	11	25	-22	***	-16	**
65-74	532	49	45	53		384	48	43	53		179	35	28	42	-14	***	-14	***

Controlled hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns								
35-44	110	5	1	10		43	23	11	36		15	20	0	40	15	*	-3	ns
45-54	292	12	8	16		144	28	20	35		58	41	29	54	29	***	14	ns
55-64	451	14	10	17		285	31	26	36		113	50	41	60	37	***	20	**
65-74	532	11	8	14		384	26	21	30		179	53	45	60	41	***	27	*

CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S8. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by educational class and period. Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Blood pressure drug treatment

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	1249	18	16	20		1183	24	22	27		725	26	23	29		8	***	2	ns
Lower education	1730	19	18	21		1018	25	22	28		303	24	19	29		5	ns	-1	ns

Raised blood pressure

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	1249	48	45	51		1183	35	33	38		725	28	25	31		-20	***	-7	**
Lower education	1730	51	49	54		1018	43	40	46		303	34	29	39		-17	***	-9	**

Hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					*					ns					ns				
Higher education	1249	51	49	54		1183	48	45	51		725	43	40	47		-8	**	-4	ns
Lower education	1730	55	53	58		1018	51	48	54		303	46	40	52		-9	**	-5	ns

Undiagnosed hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns	n				ns				
Higher education	621	53	49	57		555	38	34	42		314	36	30	41		-18	***	-2	ns
Lower education	1063	54	51	57		610	40	36	44		168	38	30	45		-16	**	-2	ns

Diagnosed but untreated hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	621	16	13	19		555	20	17	23		314	13	10	17		-3	ns	-6	*
Lower education	1063	15	13	17		610	16	13	19		168	16	10	21		1	***	-0.4	ns

Uncontrolled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	621	24	21	28		555	21	18	25		314	21	17	26		-3	ns	0.1	ns
Lower education	1063	25	22	27		610	29	25	32		168	26	20	33		2	***	-2	ns

Controlled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					*				
Higher education	621	6	4	8		555	21	18	25		314	30	25	35		24	***	8	**
Lower education	1063	7	5	8		610	15	12	18		168	20	14	26		13	**	5	ns

Prevalence are age-standardized by ISTAT Italian population 2000, 2010 and 2019 respectively. CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Higher education - high school or college; lower education - primary or middle school.Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S9. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by educational class and period. Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Blood pressure drug treatment

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***					**				
Higher education	1052	16	14	19		1167	19	16	21		725	19	17	22		3	ns	1	ns
Lower education	1887	23	22	25		1017	26	23	28		339	27	23	32		4	ns	2	ns

Raised blood pressure

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					***					**				
Higher education	1052	35	32	38		1167	22	19	24		725	14	12	17		-21	***	-7	***
Lower education	1887	42	40	44		1017	29	26	32		339	21	17	25		-21	***	-8	**

Hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					***					**				
Higher education	1052	40	37	43		1167	31	28	34		725	28	25	31		-12	***	-3	ns
Lower education	1887	47	45	49		1017	40	37	43		339	39	34	44		-8	**	-1	ns

Undiagnosed hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	337	47	42	53		311	36	31	42		192	27	21	34		-20	***	-9	*
Lower education	1037	43	40	46		534	25	21	28		172	29	23	36		-14	**	5	ns

Diagnosed but untreated hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	337	19	14	23		311	15	11	19		192	16	11	22		-2	ns	1	ns
Lower education	1037	15	13	18		534	17	13	20		172	13	8	18		-3	***	-4	*

Uncontrolled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					ns					ns				
Higher education	337	23	19	28		311	22	18	27		192	15	10	20		-8	*	-7	*
Lower education	1037	31	29	34		534	28	25	32		172	17	12	23		-14	***	-11	ns

Controlled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	337	11	7	14		311	26	21	31		192	41	34	48		31	***	15	**
Lower education	1037	10	8	12		534	31	27	34		172	40	33	48		30	***	10	ns

Prevalence are age-standardized by ISTAT Italian population 2000, 2010 and 2019 respectively. CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Higher education - high school or college; lower education - primary or middle school. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S10. Age-standardized blood pressure mean values, and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements by sex and Italian Region. Italian resident men and women aged 35–74 years, the CUORE Project Survey 2018-2019.

2018-2019

MEN

Italian Region	n	Systolic blood pressure (mmHg)				Diastolic blood pressure (mmHg)				Raised blood pressure			Hypertension			Controlled hypertension		
		mean	SD	95%CI		mean	SD	95%CI		%	95% CI		%	95% CI		%	95% CI	
Abruzzo	102	**134**	14	*132*	*137*	**78**	10	*76*	*80*	**36**	27	*45*	**47**	37	*56*	**18**	10	*25*
Calabria	101	**132**	13	*130*	*135*	**76**	9	*75*	*78*	**31**	22	*40*	**49**	39	*59*	**31**	22	*40*
Liguria	104	**127**	12	*125*	*130*	**76**	10	*74*	*78*	**20**	12	*27*	**40**	30	*49*	**31**	22	*40*
Lazio	99	**130**	13	*127*	*133*	**79**	10	*77*	*81*	**29**	20	*38*	**47**	37	*57*	**31**	22	*40*
Lombardy	98	**134**	15	*131*	*137*	**78**	9	*76*	*80*	**37**	27	*46*	**48**	38	*58*	**19**	11	*26*
Piedmont	104	**129**	13	*126*	*131*	**75**	9	*73*	*77*	**18**	11	*26*	**35**	26	*45*	**43**	34	*53*
Emilia Romagna	104	**134**	15	*131*	*137*	**79**	10	*77*	*81*	**30**	21	*39*	**42**	33	*51*	**20**	12	*27*
Basilicata	106	**134**	15	*132*	*137*	**80**	10	*78*	*82*	**35**	26	*44*	**48**	39	*58*	**27**	19	*36*
Tuscany	108	**129**	13	*127*	*132*	**77**	9	*75*	*79*	**28**	20	*37*	**40**	31	*50*	**25**	17	*33*
Sicily	105	**132**	13	*129*	*134*	**78**	10	*76*	*80*	**33**	24	*42*	**44**	35	*54*	**27**	18	*35*

WOMEN

Italian Region	n	Systolic blood pressure (mmHg)				Diastolic blood pressure (mmHg)				Raised blood pressure			Hypertension			Controlled hypertension		
		mean	SD	95%CI		mean	SD	95%CI		%	95% CI		%	95% CI		%	95% CI	
Abruzzo	104	**122**	17	*118*	*125*	**73**	10	*71*	*75*	**14**	8	*21*	**31**	22	*40*	**45**	35	*54*
Calabria	109	**121**	14	*119*	*124*	**70**	10	*68*	*72*	**16**	9	*23*	**40**	31	*50*	**48**	38	*57*
Liguria	107	**117**	15	*114*	*120*	**72**	11	*70*	*74*	**15**	8	*22*	**30**	21	*38*	**32**	23	*40*
Lazio	114	**124**	14	*122*	*127*	**76**	9	*74*	*78*	**16**	9	*22*	**35**	26	*43*	**68**	60	*77*
Lombardy	100	**127**	18	*124*	*131*	**75**	11	*73*	*77*	**24**	16	*33*	**37**	27	*46*	**35**	25	*44*
Piedmont	113	**117**	13	*115*	*119*	**70**	9	*68*	*71*	**8**	3	*13*	**16**	10	*23*	**43**	34	*53*
Emilia Romagna	106	**127**	16	*124*	*130*	**76**	11	*74*	*78*	**24**	16	*32*	**40**	30	*49*	**32**	23	*41*
Basilicata	114	**121**	16	*118*	*124*	**72**	10	*70*	*74*	**16**	9	*23*	**31**	23	*39*	**22**	15	*30*
Tuscany	97	**120**	15	*117*	*123*	**72**	9	*70*	*74*	**15**	8	*23*	**22**	14	*31*	**22**	14	*30*
Sicily	102	**124**	14	*121*	*127*	**74**	9	*72*	*76*	**17**	10	*24*	**37**	27	*46*	**63**	54	*73*

SD: standard deviations. Means, standard deviations and prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2019. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: treated and SBP < 140 mmHg and DBP < 90 mmHg. Regional data for 1998–2002 and 2008–2012 CUORE Project surveys were available at http://www.cuore.iss.it/eng/survey/cuoredata.

Table S11. Blood pressure and heart rate measurements and prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control, (age-adjusted using the European standard population) by sex and period. Italian resident men and women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

	1998-2002 n=2985				2008-2012 n=2218				2018-2019 n=1031				2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	mean	SD	95% CI		mean	SD	95% CI		mean	SD	95% CI		Diff	t-test p-value	Diff	t-test p-value
Systolic blood pressure - SBP (mmHg)	136	18	136	137	132	16	132	133	132	14	131	132	-5	***	-1	ns
Diastolic blood pressure - DBP (mmHg)	86	11	86	87	84	10	83	84	77	10	77	78	-9	***	-6	***
SBP not under drug treatment (mmHg)	134	17	133	135	131	16	130	131	131	14	130	132	-3	***	0.3	ns
DBP not under drug treatment (mmHg)	85	10	85	86	83	10	83	84	77	10	76	77	-9	***	-6	***
Heart rate (beats per minute)	66	11	66	66	69	10	68	69	72	12	71	72	6	***	3	***
	%	95% CI			%	95% CI			%	95% CI			Diff	chi-squared p-value	Diff	chi-squared p-value
Blood pressure drug treatment	20	18	21		26	24	27		25	23	28		6	**	-0.4	ns
Raised blood bressure	51	49	53		41	39	43		30	27	32		-21	***	-11	***
Hypertension	55	53	57		51	49	53		44	41	47		-11	***	-7	**
Hypertension																
Undiagnosed	53	50	55		39	36	41		37	32	41		-16	***	-2	ns
Diagnosed but untreated	15	14	17		18	16	20		14	11	17		-1	ns	-3	ns
Uncontrolled	26	23	28		26	23	28		22	18	26		-4	ns	-4	ns
Controlled	7	5	8		18	16	20		27	23	31		20	***	9	***

WOMEN

	1998-2002 n=2951				2008-2012 n=2185				2018-2019 n=1066				2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	mean	SD	95% CI		mean	SD	95% CI		mean	SD	95% CI		Diff	t-test p-value	Diff	t-test p-value
Systolic blood pressure - SBP (mmHg)	132	18	131	132	127	17	126	127	122	16	121	123	-10	***	-5	***
Diastolic blood pressure - DBP (mmHg)	82	10	82	83	79	9	78	79	73	11	72	73	-9	***	-6	***
SBP not under drug treatment (mmHg)	129	16	128	129	124	15	123	125	120	15	119	121	-9	***	-4	***
DBP not under drug treatment (mmHg)	81	10	80	81	78	9	77	78	72	10	71	72	-9	***	-6	***
Heart rate (beats per minute)	70	11	69	70	71	9	71	71	73	11	72	73	3	***	2	***
	%	95% CI			%	95% CI			%	95% CI			Diff	chi-squared p-value	Diff	chi-squared p-value
Blood pressure drug treatment	22	20	23		23	21	25		22	19	24		0.3	ns	-1	ns
Raised blood bressure	40	38	41		26	24	28		16	14	18		-23	***	-10	***
Hypertension	45	43	46		36	34	38		31	28	34		-14	***	-5	**
Hypertension																
Undiagnosed	44	42	47		31	28	34		28	24	33		-16	***	-3	ns
Diagnosed but untreated	16	14	18		15	13	18		16	12	20		0.3	ns	1	ns
Uncontrolled	30	27	32		26	24	29		16	12	19		-14	***	-11	***
Controlled	10	9	12		27	24	30		40	35	45		30	***	13	***

Means, standard deviation and prevalence are age-standardized by European standard population 2013.SD: standard deviation. CI: confidence interval. Diff: mean or percentage difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means or prevalence. t-test to compare mean values between periods. Chi-squared test to compare prevalences between periods. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S12. Blood pressure measurements and heart rate mean levels by educational level and period (age-adjusted using the European standard population). Italian resident men aged 35–74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

MEN

Systolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1249	**135**	17	*135*	*136*	***	1183	**131**	15	*130*	*131*	***	725	**131**	14	*130*	*132*	***	**-5**	***	**0.1**	ns
Lower education	1730	**137**	18	*136*	*138*		1018	**134**	17	*133*	*135*		303	**134**	16	*132*	*135*		**-3**	**	**-0.3**	ns

Diastolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1249	**87**	11	*86*	*87*	*ns*	1183	**83**	10	*83*	*84*	*ns*	725	**77**	10	*77*	*78*	*ns*	**-9**	***	**-6**	***
Lower education	1730	**86**	11	*86*	*87*		1018	**84**	10	*83*	*84*		303	**78**	10	*77*	*79*		**-8**	***	**-6**	***

Systolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1046	**134**	16	*133*	*135*	***	913	**129**	15	*128*	*130*	***	537	**130**	13	*129*	*131*	***	**-4**	***	**1**	ns
Lower education	1305	**134**	17	*133*	*135*		680	**132**	16	*131*	*133*		205	**133**	15	*131*	*135*		**-1**	ns	**1**	ns

Diastolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1046	**86**	10	*85*	*86*	*ns*	913	**83**	10	*82*	*83*	*ns*	537	**77**	10	*76*	*78*	*ns*	**-9**	***	**-6**	***
Lower education	1305	**85**	10	*85*	*86*		680	**83**	10	*83*	*84*		205	**77**	9	*76*	*78*		**-8**	***	**-6**	***

Heart rate (beats per minute)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1244	**66**	11	*65*	*67*	*ns*	1183	**66**	11	*65*	*67*	*ns*	725	**71**	11	*70*	*71*	**	**5**	***	**5**	***
Lower education	1730	**66**	11	*65*	*67*		1018	**66**	12	*66*	*67*		303	**74**	12	*73*	*76*		**8**	***	**8**	***

Means and standard deviations age-standardized by European standard population 2013. SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. Higher education - high school or college; lower education - primary or middle school. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S13. Blood pressure measurements and heart rate mean levels by educational level and period (age-adjusted using the European standard population). Italian resident women aged 35–74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

WOMEN

Systolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1052	**130**	16	*129*	*131*	***	1167	**124**	15	*123*	*125*	***	725	**120**	15	*119*	*121*	***	**-10**	***	**-4**	***
Lower education	1887	**133**	18	*132*	*134*		1017	**130**	18	*129*	*131*		339	**125**	17	*123*	*127*		**-8**	***	**-4**	***

Diastolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1052	**81**	10	*81*	*82*	***	1167	**78**	9	*77*	*78*	***	725	**72**	11	*72*	*73*	**	**-9**	***	**-6**	***
Lower education	1887	**83**	10	*82*	*83*		1017	**79**	10	*79*	*80*		339	**74**	10	*73*	*75*		**-9**	***	**-5**	***

Systolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	928	**128**	16	*127*	*129*	***	992	**122**	14	*121*	*122*	***	593	**119**	15	*117*	*120*	***	**-9**	***	**-3**	***
Lower education	1331	**129**	16	*129*	*130*		651	**127**	16	*126*	*128*		203	**123**	16	*121*	*125*		**-6**	***	**-4**	**

Diastolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	928	**81**	10	*80*	*81*	***	992	**77**	9	*77*	*78*	***	593	**71**	10	*70*	*72*	*	**-9**	***	**-6**	***
Lower education	1331	**81**	10	*81*	*82*		651	**78**	9	*78*	*79*		203	**73**	10	*72*	*75*		**-8**	***	**-5**	***

Heart rate (beats per minute)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1047	**69**	11	*69*	*70*	*ns*	1167	**71**	9	*70*	*71*	*ns*	725	**73**	10	*72*	*73*	*ns*	**3**	***	**2**	**
Lower education	1884	**70**	11	*69*	*70*		1017	**71**	9	*71*	*72*		339	**73**	11	*72*	*75*		**4**	***	**2**	**

Means and standard deviations age-standardized by European standard population 2013. SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. Higher education - high school or college; lower education - primary or middle school. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S14. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by educational class and period (age-adjusted using the European standard population). Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Blood pressure drug treatment

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	1249	19	16	21		1183	26	23	28		725	26	23	29		7	**	0.2	ns
Lower education	1730	20	18	22		1018	26	24	29		303	24	19	29		4	ns	-2	ns

Raised blood pressure

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	1249	49	46	52		1183	36	33	39		725	28	25	31		-21	***	-8	**
Lower education	1730	52	50	55		1018	44	41	47		303	34	29	39		-18	***	-10	**

Hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					*					ns					ns				
Higher education	1249	53	50	55		1183	49	46	52		725	43	40	47		-9	***	-6	*
Lower education	1730	56	54	59		1018	53	50	56		303	46	40	52		-10	**	-7	*

Undiagnosed hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	621	53	49	57		555	36	32	40		314	36	31	41		-17	***	-0.2	ns
Lower education	1063	53	50	56		610	39	35	43		168	38	31	46		-15	**	-1	ns

Diagnosed but untreated hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	621	16	13	19		555	19	16	22		314	13	10	17		-2	ns	-6	*
Lower education	1063	15	12	17		610	16	13	18		168	15	10	21		1	***	-0.1	ns

Uncontrolled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	621	25	22	29		555	22	19	26		314	21	17	26		-4	ns	-1	ns
Lower education	1063	26	23	28		610	30	26	33		168	26	19	33		0.5	***	-4	ns

Controlled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					*				
Higher education	621	6	4	8		555	22	19	26		314	30	24	35		23	***	7	*
Lower education	1063	7	5	8		610	15	12	18		168	20	14	26		13	**	5	ns

Prevalence are age-standardized by age-standardized by European standard population 2013. CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Higher education - high school or college; lower education - primary or middle school. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S15. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by educational class and period (age-adjusted using the European standard population). Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Blood pressure drug treatment

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***					**				
Higher education	1052	16	14	19		1167	19	17	21		725	19	16	22		2	ns	-0.4	ns
Lower education	1887	24	22	25		1017	26	24	29		339	27	22	31		3	ns	0.4	ns

Raised blood pressure

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					***					**				
Higher education	1052	35	32	38		1167	22	20	24		725	14	11	16		-21	***	-8	***
Lower education	1887	42	40	44		1017	30	27	32		339	21	16	25		-21	***	-9	**

Hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					***					**				
Higher education	1052	40	37	43		1167	32	29	34		725	27	24	30		-13	***	-5	*
Lower education	1887	47	45	49		1017	41	38	44		339	38	33	43		-9	**	-3	ns

Undiagnosed hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	337	47	42	52		311	36	30	41		192	28	21	34		-19	***	-8	ns
Lower education	1037	43	40	46		534	25	21	28		172	31	24	38		-12	**	6	ns

Diagnosed but untreated hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	337	19	14	23		311	15	11	19		192	17	12	23		-1	ns	2	ns
Lower education	1037	15	13	18		534	16	13	19		172	13	8	18		-2	***	-3	*

Uncontrolled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					*					ns				
Higher education	337	24	19	28		311	23	18	27		192	14	9	19		-9	*	-8	*
Lower education	1037	32	29	34		534	29	25	33		172	17	11	22		-15	***	-12	ns

Controlled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	337	11	7	14		311	27	22	31		192	40	33	47		30	***	14	**
Lower education	1037	10	8	12		534	30	26	34		172	40	32	47		29	***	9	ns

Prevalence are age-standardized by age-standardized by European standard population 2013. CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Higher education - high school or college; lower education - primary or middle school. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1 and 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 and 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5 and 6
Bias	9	Describe any efforts to address potential sources of bias	14
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 and 6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	na
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6 and in all tables
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6 and table s1
		(b) Indicate number of participants with missing data for each variable of interest	6 and in all tables

Outcome data	15*	Report numbers of outcome events or summary measures	6 and in all tables
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-12 and in all tables
		(*b*) Report category boundaries when continuous variables were categorized	6-12 and in related tables
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-12 and in all tables
Discussion			
Key results	18	Summarise key results with reference to study objectives	6-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Trends of blood pressure, raised blood pressure, hypertension and its control among Italian adults: CUORE Project cross-sectional health examination surveys 1998/2008/2018

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Trends of blood pressure, raised blood pressure, hypertension and its control among Italian adults: CUORE Project cross-sectional health examination surveys 1998/2008/2018

Trends of blood pressure in Italian adults

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Abstract

Objectives: To assess in the Italian general adult population trends of blood pressure (BP) and prevalence of raised blood pressure (RBP), hypertension and its control in order to evaluate population health and care, and the achievement of a RBP 25% relative reduction as recommended by the WHO at population level.

Design: Results comparison of health examination surveys, cross-sectional observational studies based on health examination of randomly selected age and sex stratified samples including resident aged 35-74 years. Data of 2018/2019 survey were compared with the previous ones collected in 1998/2002 and 2008/2012.

Setting: Health examination surveys conducted in Italy within the CUORE Project following standardized methodologies.

Participants: 2985 men and 2955 women examined in 1998/2002, 2218 men and 2204 women examined in 2008/2012, 1031 men and 1066 women examined in 2018/2019.

Primary and secondary outcome measures: Age-standardized mean of BP, prevalence of RBP (systolic BP and/or diastolic BP >= 140/90 mmHg), hypertension (presenting or being treated for RBP) and its awareness and control, according to sex, age class and educational level.

Results: In 2018/2019, a significant reduction was observed in systolic BP and diastolic BP in men (1998/2002: 136/86; 2008/2012: 132/84; 2018/2019: 132/78 mmHg) and women (132/82, 126/78, 122/73 mmHg), and in the prevalence of RBP (50%, 40% and 30% in men, 39%, 25%, and 16% in women) and of hypertension (54%, 49% and 44% in men, 45%, 35% and 32% in women). Trends were consistent by age and education attainment. In 2018/2019, hypertensive men and women with controlled BP were only 27% and 41%, but a significant favorable trend was observed.

Conclusions: Data from 2018/2019 underlined that RBP is still commonly observed in the Italian population aged 35-74 years, however, the WHO RBP target at that time may be considered met.

Word count: 292

Keywords: epidemiology, blood pressure, raised blood pressure, hypertension, health examination survey.

Strengths and limitations of this study

- Use of blood pressure measurements to estimate mean of blood pressure and the prevalence of raised blood pressure and hypertension.
- Recruitment of randomly selected age and sex specific samples of residents in 10 Italian Regions with coverage of the Northern, Central and Southern Italian territory.
- Adoption of standardized procedures and methods to collect data in the three health examination surveys.
- Assessment of blood pressure indicators by sex, age-classes and educational levels.
- Inadequacy of blood pressure measurement in a single day for the diagnosis of raised blood pressure and hypertension.

INTRODUCTION

Raised blood pressure (BP) is a condition constituting a leading cause of premature death and disability worldwide, since it significantly increases the risk of heart attack, stroke, kidney failure, dementia and blindness [1]. The main contributors to raised BP are unhealthy eating behaviours – among which sodium excess – physical inactivity, excess of weight, smoking habit, harmful use of alcohol and exposure to persistent stress [2].

The value of blood pressure, in particular of systolic blood pressure (SBP), is included in the risk charts for estimating the probability of incurring or dying from a cardiovascular event, both for the strong etiological significance and for its simplicity and low cost [3-5].

To combat global mortality from non-communicable diseases (NCDs), at the Sixtysixth World Health Assembly in 2013 Member States developed a Global Plan of Action, for 2013-2020 setting global targets that include achieving a 25% relative reduction in the prevalence of raised BP or contain the prevalence of raised BP, according to national circumstances by 2025, proposed to leading a 33% of relative reduction by 2030, using 2010 as a baseline [6,7]. The World Health Organization (WHO) is supporting countries to meet this global target and to reduce hypertension as part of WHO's Thirteenth General Programme of Work (2019–2023), which focuses on measurable impacts on people's health at country level.

In the Italian adult population, within regional studies using several methodologies and definitions, high prevalence of raised BP was found since the 70's and the 80's when it resulted just over 50% for those aged 35-69 years [8-12].

Integrated NCDs programmes implemented through a primary health care approach are an affordable and sustainable way for countries to tackle hypertension. In Italy, the prevention of NCDs is supported by the "Gaining Health: making healthy choices easy" Programme and the National Preventive Plans (NPPs), which were implemented in a context in which NCDs were estimated to account for 91% of all deaths in the period 2000-2016 [13], with a decreasing trend of premature death since 2000 to 2016 for both men and women aged between 30 and 70 years.

WHO recommended improving country-level surveillance and monitoring as a top priority in the fight against NCDs, also providing data disaggregated by age, gender, and socioeconomic groups [14, 15]. Monitoring should provide internationally comparable assessments of the trends in NCDs and related risk factors over time, help to benchmark the situation in individual countries versus others in the same region or development category, provide a foundation for advocacy, policy development and coordinated action [14]. Age-standardized prevalence of raised BP among adults and mean systolic BP are among the 25 indicators suggested by the WHO in order to monitor global and national progress in the prevention and control of NCDs. [15]

This study aimed to assess temporal trends for mean values of BP and heart rate measurements, and for prevalence of raised BP, hypertension, awareness and control of hypertension in the Italian population aged 35–74 years, according to sex, age class, educational level, and Region using data measured within the CUORE Project national health examination surveys (HESs) 1998–2002, 2008–2012, and 2018–2019.

METHODS

Study design

Three HESs were conducted in Italy within the CUORE Project. The first survey was conducted from May 1998 to December 2002 in all Italian Regions, enrolling a random sample of 100 men and 100 women aged 35–74 years for every 1.5 million inhabitants (participation rate 50%). The second

survey was conducted from March 2008 to July 2012, investigating a random sample of 110 men and 110 women aged 35–79 years for every 1.5 million residents in all Italian Regions (participation rate 53%). The third survey was conducted from April 2018 to December 2019, in 10 Regions (out of 20) chosen in the North, Central, and South Italy, using a random sample of 100 men and 100 women aged 35–74 years in each examined Region (participation rate 40%). Within the three HESs, probability samples included persons randomly selected from resident registries through stratification by sex and age group (35–44, 45–54, 55–64, 65–74, 75-79).

The three HESs were conducted by the Italian National Institute of Health (Istituto Superiore di Sanità-ISS); the first and second surveys in collaboration with the national scientific association of hospital cardiologists (ANMCO–Associazione Nazionale Medici Cardiologi Ospedalieri) and its foundation (Fondazione per il Tuo cuore - Heart Care Foundation). Surveys details were published elsewhere [16-19]. The three HESs were approved by the Ethical Committee of the ISS; all participants received an informative note and signed an informed consent. The three HESs are recognized within the Italian National Statistical Program. The second and third surveys were also recognized within the European HES collaboration [20, 21].

Study procedures and methods

The CUORE Project HESs used international standardized procedures and methods for the data collection and measurements [16-19].

BP measurements were performed applying the appropriate cuff to the right arm, while the participant was in a sitting position after 5 minutes at rest. During the 1998-2002 and 2008-2012 HES, SBP and DBP were identified at the beginning of the first and fifth phase of the Korotkoff sounds using a mercury sphygmomanometer; during the 2018-2019 HES an oscillometric device (Omron HEM-907) was used. Two consecutive readings were recorded in the first survey and three consecutive readings were recorded in the second and third survey, one minute apart. Heart rate was measured at the wrist between the first and the second measurements; it was measured at the right wrist by placing the middle fingers of the left hand on it to locate the radial artery - when a pulse was found, the number of beats felt within a one-minute period was counted using a stop watch as a time references. The presence of a previous diagnosis of hypertension was collected by a standardized questionnaire, as well as information on pharmacological treatment; the first was investigated by asking if any doctor or other healthcare operator had previously indicated that the blood pressure was high, the second by asking if in the last two weeks they had taken medications prescribed by a doctor to lower blood pressure and by checking the boxes of the drugs being used.

Patient and Public Involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Statistical analysis

The statistical comparison of the 1998–2002, 2008–2012, and 2018–2019 CUORE Project HESs data included 35- to 74-year-old residents in 10 Regions, distributed in north, central, and south Italy, involved in all the surveys: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

The average of the first and second BP measurement was used for the statistical analysis. As suggested by the WHO, raised blood pressure was defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg [6, 15]. Hypertensives were defined as those with SBP≥140 mmHg and/or DBP≥90 mmHg or under specific pharmacological treatment and were divided into groups of "undiagnosed", "diagnosed but untreated", "uncontrolled" (treated and SBP≥ 140 mmHg and/or DBP≥ 90 mmHg) and "controlled" (treated and SBP<140 mmHg and DBP<90 mmHg). The European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) also consider these cut off values of RBP and hypertension [22].

Educational level was selected as a proxy of socio-economic level; social class was dichotomized as those with primary/middle school attainment (≤8 years, lower education) and high school/university degree (>8 years, higher education).

Mean, standard deviation (SD), and 95% confidence interval of SBP, DBP (in all participants and in those not under treatment for hypertension) and heart rate, as well as prevalence and 95% confidence interval of raised BP, hypertension and its awareness and control were assessed by sex, age group (35–44, 45–54, 55–64, and 65–74 years), and periods and, for those with available information, by educational level.

Following the suggestion reported in the WHO Global NCDs Action Plan 2013–2020 [6, 10], indicators, where appropriate, were age standardized using the direct method, referring to the age- and sex-specific distributions of the Italian adult population in 2000, 2010, and 2019 (Italian National Institute of Statistics-ISTAT), for the 1998–2002, 2008–2012, and 2018–2019 HESs respectively [23]. Data were also age standardized using the European Standard Population (EuStPop) 2013 for international comparisons [24].

Indicators assessed in the most recent period, 2018–2019, were compared with those of previous periods, 1998–2002 and 2008–2012. The associations between indicators and age class and educational level were also assesed within periods. Regarding continuous indicators, a t-test was used to compare indicators means between periods, and analysis of variance was used to compare them within periods by age class and educational level. Regarding categorical indicators, the chi-square test was used to compare prevalence indicators between periods and, within periods, by age class and educational level. Comparisons of indicators between periods were also conducted, adjusting by age and educational level, using linear (for continuous indicators) and logistic (for categorical indicators) regression models, considering indicators as dependent variables, and period (2018–2019/1998–2002 or 2018–2019/2008–2012), age (35–54/55–74 years) and educational level (high/low) as independent variables; the statistical significance of the period was reported in tables. Two-sided p-values <0.05 were considered statistically significant. Statistical analyses were performed using SAS software, release 9.4.

RESULTS

After the exclusions of persons with missing data for SBP or DBP or use of specific drug treatments (8 persons in 1998, 18 in 2008 and 9 in 2018), 2985 men and 2955 women (mean age ± SD: men 55 ± 11, women 54 ± 11), 2218 men and 2204 women (mean age ± SD: men 55 ± 11, women 55 ± 11),

and 1031 men and 1066 women (mean age ± SD: men 55 ± 11, women 55 ± 11) were included in the analysis of the 1998–2002, 2008–2012, and 2018–2019 HESs, respectively (S1 Table).

Blood pressure and heart rate measurements

The evaluation of the temporal trend of the mean BP shows in the period 2018-2019 as compared to twenty years before a significant reduction in SBP and DBP in both men (132/78 mmHg in 2018-2019 with a 3% of reduction for SBP, 10% for DBP) and women (122/73 mmHg, with a reduction of 7% and 11% respectively), while in the period 2018-2019 compared to ten years earlier, a reduction in mean SBP is observed only in women (3%), being stable in men, and in mean DBP both in men and women (7%) (Table 1). Similar trends are also observed for those not under antihypertensive drugs, and by age groups and education level (Tables 1, S2, S3, S4 and S5, Figures 1 and 2).
Within the 1998, 2008, and 2018 periods, mean SBP and DBP was higher in men than in women, regardless of antihypertensive drug treatment use, class of age and educational level, although not always statistically significant, especially in the 1998-2002 period considering that the difference increased progressively over time, passing from 3% in 1998-2002 to 4% in 2008-2012 until it reached 8% in 2018-2019 (Tables 1, S2, S3, S4, and S5, Figures 1 and 2). Within those periods, in both men and women, mean SBP and DBP, regardless of antihypertensive drug treatment use, progressively increased by age group and was tendentially higher in those with a lower level of education, except DBP in men (Tables S2, S3, S4, and S5). The mean SBP difference between educational levels increased progressively in the 1998, 2008, and 2018 periods in both men and women (men: 2%, 3%, and 4%; women: 7%, 8%, and 12%) (Table S4 and S5, Figures 1 and 2).
The mean heart rate was progressively increasing in the three surveys periods, both in men and women, in all age groups and education levels, remaining between 66 and 74 beats per minute. Within the 1998, 2008, and 2018 periods, no significant differences are observed in the mean heart rate by age group, with the exception of women in 1998-2002 for whom it decreases starting from 55 years; there are no differences between levels of education with the exception of men in 2018-2019 for whom there is an average level of heart rate higher in the lowest level of education.

Table1. Age-standardized blood pressure and heart rate measurements and prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control by sex and period. Men and women residing in Italy aged 35-74 years, The CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

	MEN															
	1998-2002				2008-2012				2018-2019				2018-2019 vs 1998-2002			2018-2019 vs 2008-2012		
	n=2985				n=2218				n=1031									
	mean	SD	95% CI		mean	SD	95% CI		mean	SD	95% CI		Diff	t-test sign^	Regression sign^^	Diff	t-test sign^	Regression sign^^
Systolic blood pressure - SBP (mmHg)	**136**	18	*135*	*136*	**132**	16	*131*	*132*	**132**	14	*131*	*132*	**-4**	***	***	**-0,3**	ns	ns
Diastolic blood pressure - DBP (mmHg)	**86**	11	*86*	*87*	**84**	10	*83*	*84*	**78**	10	*77*	*78*	**-9**	***	***	**-6**	***	***
SBP not under drug treatment (mmHg)	**134**	17	*133*	*134*	**130**	15	*129*	*131*	**131**	14	*130*	*132*	**-3**	***	**	**1**	ns	ns
DBP not under drug treatment (mmHg)	**85**	10	*85*	*86*	**83**	10	*83*	*84*	**77**	10	*76*	*78*	**-9**	***	***	**-6**	***	***
Heart rate (beats per minute)	**66**	11	*66*	*66*	**68**	10	*68*	*69*	**72**	12	*71*	*72*	**6**	***	***	**3**	***	***
	%	95% CI			%	95% CI			%	95% CI			Diff	chi-squared sign^	Logistic sign^^	Diff	chi-squared sign^	Logistic sign^^
Blood pressure drug treatment	**19**	*17*	*20*		**24**	*22*	*26*		**25**	*23*	*28*		**7**	***	***	**1**	ns	ns
Raised blood pressure	**50**	*48*	*52*		**40**	*38*	*42*		**30**	*27*	*32*		**-20**	***	***	**-10**	***	***
Hypertension	**54**	*52*	*55*		**49**	*47*	*52*		**44**	*41*	*47*		**-9**	***	***	**-5**	**	**
Hypertension																		
Undiagnosed	**53**	*51*	*56*		**40**	*37*	*42*		**36**	*32*	*41*		**-17**	***	***	**-3**	ns	ns
Diagnosed but untreated	**15**	*14*	*17*		**19**	*16*	*21*		**14**	*11*	*18*		**-1**	ns	ns	**-4**	*	ns
Uncontrolled	**25**	*23*	*27*		**25**	*22*	*27*		**22**	*19*	*26*		**-2**	ns	**	**-2**	ns	*
Controlled	**6**	*5*	*8*		**17**	*15*	*19*		**27**	*23*	*31*		**20**	***	***	**10**	***	***

	WOMEN															
	1998-2002 n=2955				2008-2012 n=2204				2018-2019 n=1066				2018-2019 vs 1998-2002			2018-2019 vs 2008-2012		
	mean	SD	95% CI		mean	SD	95% CI		mean	SD	95% CI		Diff	t-test sign^	Regression sign^^	Diff	t-test sign^	Regression sign^^
Systolic blood pressure - SBP (mmHg)	**132**	18	*131*	*132*	**126**	16	*125*	*127*	**122**	16	*121*	*123*	**-10**	***	***	**-4**	***	***
Diastolic blood pressure - DBP (mmHg)	**82**	10	*82*	*82*	**78**	9	*78*	*79*	**73**	11	*72*	*74*	**-9**	***	***	**-6**	***	***
SBP not under drug treatment (mmHg)	**129**	16	*128*	*129*	**124**	15	*123*	*124*	**120**	15	*119*	*121*	**-9**	***	***	**-4**	***	***
DBP not under drug treatment (mmHg)	**81**	10	*80*	*81*	**78**	9	*77*	*78*	**72**	10	*71*	*73*	**-9**	***	***	**-6**	***	***
Heart rate (beats per minute)	**70**	11	*69*	*70*	**71**	9	*71*	*71*	**73**	10	*72*	*73*	**3**	***	***	**2**	***	***
	%	95% CI			%	95% CI			%	95% CI			Diff	chi-squared sign^	Logistic sign^^	Diff	chi-squared sign^	Logistic sign^^
Blood pressure drug treatment	**22**	*20*	*23*		**22**	*20*	*24*		**23**	*20*	*25*		**1**	ns	**	**1**	ns	ns
Raised blood pressure	**39**	*38*	*41*		**25**	*24*	*27*		**16**	*14*	*19*		**-23**	***	***	**-9**	***	***
Hypertension	**45**	*43*	*46*		**35**	*33*	*37*		**32**	*29*	*34*		**-13**	***	***	**-4**	*	ns
Hypertension																		
Undiagnosed	**44**	*42*	*47*		**32**	*28*	*35*		**28**	*23*	*32*		**-17**	***	***	**-4**	ns	**
Diagnosed but untreated	**16**	*14*	*18*		**16**	*13*	*18*		**15**	*12*	*19*		**-0,4**	ns	**	**-0,4**	ns	ns
Uncontrolled	**30**	*27*	*32*		**26**	*23*	*29*		**16**	*13*	*20*		**-13**	***	***	**-10**	**	**
Controlled	**10**	*9*	*12*		**27**	*24*	*30*		**41**	*36*	*46*		**31**	***	***	**14**	***	***

SD: standard deviation; CI: confidence interval; Diff: mean or percentage difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means or prevalence. Means, standard deviations, and prevalence were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. ^ t-test to compare mean values between periods; chi-square test to compare prevalence between periods. ^^ Linear regression and logistic models were assessed considering indicators as dependent variable and period (2018–2019/1998–2002 or 2018–2019/2008–2012), age (35–54/55–74 years), and educational level (high/low) as independent variables; the statistical significance of the period was reported. *** p < 0.0001; ** p < 0.01; *p < 0.05; ns not significant p-value. Raised blood pressure: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Hypertension drug treatment, raised blood pressure and hypertension

The prevalence of antihypertensive drug treatment use in men showed a significant increase by 7% in 2018-2019 compared to twenty years earlier, it remained stable for men compared to ten years earlier and for women in the three survey periods (Table 1), however a significant increase was observed in 2018-2019 compared to twenty years earlier in men aged 55 years and over and women aged 65 years and over (Tables S6 and S7). The general increase in the use of antihypertensive drug treatment in men was especially observed among those with higher education level; in women, a generally stable prevalence was observed regardless of education level (Tables S8 and S9). Antihypertensive drug treatment use, was higher in men than in women, in 1998-2002, and reached, in 2018-2019, more similar values between men (25%) and women (23%).

The prevalence of raised BP was 30% in men and 16% in women in 2018-2019, significantly decreased compared to twenty and ten years earlier: in men it decreased by 20% and 10% respectively and in women 23% and 9% respectively (Table 1). The decreasing trend of raised BP was progressively higher by age classes, reaching, in 2018-2019 compared to 1998-2002, the 27% in men and 38% in women aged 65-74 years, while it was similar between educational levels both in men and women (Tables S6, S7, S8, S9, Figures 1 and 2).

The prevalence of hypertension was 44% in men and 32% in women in the 2018-2019, significantly decreased compared to twenty and ten years earlier: in men it decreased by 9% and 5% respectively and in women 13% and 4% respectively (Table 1); in men the decrease was observed among those aged 35 to 54 years both compared to twenty and ten years earlier, in women in all age groups compared to twenty years earlier, while from 55 to 74 years of age compared to the previous ten years; similar decreasing trend was observed between educational levels with a more favourable trend among more educated women (Tables S6, S7, S8 and S9, Figures 1 and 2).

As expected, within periods, both in men and women, prevalence of raised BP and hypertension significantly increased by age group and was tendentially higher in those with a lower level of education (Tables S6, S7, S8, S9, Figures 1 and 2). Prevalence of raised BP and hypertension decreased or remained stable in all Italian Regions both in men and women (Figures 3 and 4, and Table S10).

Awareness and control of hypertension

In 2018-2019, prevalence of undiagnosed hypertension resulted in 36% and 28% of hypertensive men and women, with a decreasing trend of 17% in comparison with twenty years earlier both in men and women and 3-4 % in comparison with ten years earlier (Table 1); these trends were found in particular in those aged 45 years and over and were similar by educational level, with some advantage in women with higher education (Tables S6, S7, S8 and S9). Within periods, both in men and women, prevalence of undiagnosed hypertension was higher among younger men and women but similar between educational levels (Tables S6, S7, S8 and S9).

Prevalence of not controlled hypertension was found to be halved in women, from 30% of 1998-2002 to 16% in 2018-2019 (Table 1); favorable, but much more contained, trend was found in men with a reduction of 2% (Table 1). Within periods, both in men and women, prevalence of uncontrolled hypertension was found increasing by age classes and tendentially higher in those with lower educational level (Tables S6, S7, S8 and S9).

Although in 2018-2019 only 27% of hypertensive men and 41% of hypertensive women had their blood pressure under control, a positive growth trend of hypertension under control was observed both in men and women, with an increase in 2018-2019, compared to 20 years earlier, of 20% in men and 31% in women (10% and 14 % respectively compared to ten years earlier) (Table 1). An

important increase was observed in men from the age of 55 years and in women in all age groups; similar trend for more or less educated men, while a more favorable trend is observed among more educated women (Tables S6, S7, S8 and S9, Figures 1 and 2). In 2008-2012 and 2018-2019, in men, prevalence of controlled hypertension increases by age classes (in women only in the last survey), and in the latter two surveys it is higher in men with higher education level (Tables S6, S7, S8 and S9).

Results, age standardized according to the European standard population 2013, are available in Tables S11, S12, S13, S14 and S15.

DISCUSSION

Data of measured BP in random samples of the general Italian population aged 35–74 years during three HESs conducted in 1998–2002, 2008–2012, and 2018–2019, showed a significant reduction, in 2018-2019 compared to twenty years earlier, of SBP and DBP mean levels and prevalence of raised BP and hypertension. The reductions were consistent with respect to sex, age classes and education level and were detected to different extents in almost all Italian Regions. This favorable decline in mean blood pressure and in the prevalence of raised BP and hypertension was observed in 2018-2019 even when compared with ten years earlier, except for mean SBP in men which was stable. Although around 7 out of 10 men and 6 out of 10 women with raised BP still in 2018-2019 did not have their blood pressure under control (because it is not diagnosed, diagnosed but not treated or treated but not under control), an important increase in raised BP control was observed in 2018-2019 compared to twenty years earlier, for men mostly due to a decrease in the prevalence of undiagnosed high blood pressure and for women also due to a reduction in the prevalence of uncontrolled RBP.

These results, which to our knowledge are based on the most recent national measured data on Italian general adult population, responds to the WHO's request to provide information on effectiveness of national policies and strategies, showing, in relation to the objective indicated in the Global Action Plan 2013-2020 (25% relative reduction in the prevalence of raised BP or containment of the prevalence of raised BP by 2025, proposed leading to a 33% of relative reduction by 2030), a significant decline from 1998-2020 to 2018-2019 in the prevalence of raised BP, from 50% to 30% in men and from 39% to 16% in women, equal to a relative reduction of 41% and 58% respectively, and also a significant decline from 2008-2012 to 2018-2019, from 40% to 30% in men and from 25% to 16% in women, equal to a relative reduction of 25% and 36% respectively [6].

Mean values of SBP and DBP, as well as prevalence of raised blood pressure trends are consistent with those of other studies conducted in the Italian adult population. NCD Risk Factor Collaboration, that pooled data of population-based studies with measured blood pressure in adults aged 18 years and older from 200 countries, showed that within the 36 Italian surveys (at community, subnational, and national levels, including the CUORE Project surveys 1998–2002 and 2008–2012), mean values of SBP and DBP, as well as prevalence of RBP decreased during 1995–2015 period [25, 26].

In some other European countries, such as United Kingdom, Switzerland, Spain, Sweden, Norway, Netherlands, Luxemburg, Ireland, Germany, France, Finland, Belgium and Austria, a decline of blood pressure levels was also observed with various intensities both in men and women, while in other countries, mainly from Eastern Europe, such as Slovenia, Slovakia, Serbia, Romania, Poland, Lithuania, Hungary, Greece, Czech Republic and Portugal, a trend of decline was observed in women and a stable or slightly increasing trend in men; in other countries, such as Moldova, Croatia, Bosnia

and Herzegovina and Albania, a stable or an increasing trend is still ongoing both in men and women [25, 26].

High-income countries have begun to reduce hypertension in their populations through strong public health policies such as the reduction of salt content in processed food and widely available early diagnosis and treatment that tackle hypertension and other risk factors together [2, 27]. Also in Italy, an explanation of the reasons why a decrease in mean blood pressure and in the prevalence of raised blood pressure is observed in the general adult population might be on the one hand the enhancement of its early detection, treatment and control and on the other hand successful national programmes of primary prevention which have led to an increase in the normal weight prevalence and to the reduction of the daily consumption of salt in the general adult population, despite the average levels of daily potassium consumption being not yet adequate [16-18]. In the last past two decades, the "Gaining Health" Programme and NPPs in Italy were oriented to reduce risk factors associated to the increase of blood pressure, such as physical inactivity, excess of weight and salt consumption, as well as the smoking habit, through intersectional strategies at both population (e.g., facilitating the choice of correct lifestyles) and individual levels (e.g., motivational counselling and specific therapeutic groups), promoting, and supporting national surveillance systems and monitoring studies, and through voluntary agreements for salt reduction in food products, school and workplace programs, and public awareness campaigns [28]. As an example, aimed directly at the diagnosis and control of raised BP, in the NPP 2005-2008 the promotion of a multifactorial cardiovascular diseases (CVD) risk assessment, based also on BP measurements, and its monitoring over time in clinical practice has been explicitly included. As well as, NPP 2014-2019 also focused on the early identification and integrated assessment of persons with NCDs risk factors, to be directed towards an adequate systemic management, able to enhance personal resources for the conscious adoption of correct life, or when necessary, towards suitable multidisciplinary therapeutic and assistance paths.

Additional findings of the study, including higher level of blood pressure and raised BP/hypertension in men than in women and more severe values in the southern Italy Regions and tendentially in people with lower education levels, are consistent with results from other Italian and European Studies [25,26,29], and are in line with the association of excess of weight and salt consumption with gender, education level and Italian macro-area [16, 17,19, 30, 31].

As far as, the favourable trend of increase in hypertension awareness, treatment, and control is concerned, it could be due to the greater diffusion and compliance with the guidelines for hypertension in clinical practice that include simplified recommendations. In Italy, over the period of our analysis, the antihypertensive treatment was based on the guidelines drawn up by the ESC/ESH [22, 32-34] which indicated as threshold for immediate treatment BP ≥180/110 or BP of 140-179/90-109 (depending on CVD risk stratification) after lifestyle modifications, with a treatment target that has changed over time (2003: BP<140/90 mmHg; 2007: BP<140/90 mmHg and BP<130/80 mmHg in high CVD risk; 2013: BP<140/90 mmHg; 2018: DBP<80 mmHg for all and SBP 120-129 mmHg for persons aged<65 years or SBP 130-139 mmHg for persons aged≥65 years). The progressively lower thresholds for diagnosing hypertension and the beginning of treatment also may have contributed to this favourable trend based on the threshold of 140/90 mm Hg. In addition, over time, treatment efficacy and control for some patients suffering from smaller side-effects of the earliest generations of drugs improved thanks to the availability of newer drugs [35].

Early detection and treatment of raised BP and other risk factors, as well as public health policies that reduce exposure to behavioural risk factors, have contributed to the gradual decline in mortality due to heart disease and stroke in Italy and other high-income countries over the last three decades [36, 37].

Strengths and limitations

Major strengths of this study are the following: the use of standardized procedures and methods to assess blood pressure measurements, allowing objective and reliable estimates of SBP, DBP and raised blood pressure; the checking of drug boxes to assess the use of specific pharmacological treatments; a good national coverage with the enrolment of study participants from half of the Italian regions distributed in northern, central, and southern Italy; the random selection and the sex and age classes stratification of samples from the general population.

Conversely, we acknowledge some study limitations, which should be taken in consideration when interpreting results. First, because of the choice of urban districts for the random selection of the study participants within the surveys, the results may not be representative of the habits of the population living in rural areas. The participation rates in the surveys were lower than desirable, yet consistent, with lower contact rates occurring in more highly urbanized areas and with a decreasing trend of participation observed in HESs in other European countries [38]. The cross-sectional design of the study does not allow to assess causality of the associations between SBP, DBP and raised blood pressure and educational level. There were differences in the educational level distribution between the three 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 [39]. The use of mercury sphygmomanometer in the 1998-2002 and 2008-2012 surveys and of an oscillometric device in the 2018-2019 survey (due to the EU regulation 847/2012 that banned the sale of mercury sphygmomanometers from 10 April 2014 onwards [40]) may affect comparison among surveys [41]; however, the oscillometric device used in HES 2018-2019 was certified according to international validation protocol to ensure that the device measures accurately in comparison with the mercury sphygmomanometer; in addition it should prevent the observer's error due to the use of a mercury sphygmomanometer, and the common standardized protocol based on aspects such as room temperature, disturbing noises, lighting, adequacy of the table and chair for the measurement, interaction between the survey participant and the measurer, availability of different cuffs may minimize variation due to measurement technique [21, 42, 43]. Anyway, with all device types, mercury and aneroid sphygmomanometers, and oscillometric devices, calibration error may bias the results [44]. Hypertension diagnosis should be based on several BP readings taken on several occasions (at least two), as recommended by international guidelines [22]; however, epidemiological studies are based on BP measurement in a single visit, possibly with two or more measurements repeated during the same visit [21, 45].

Conclusions

BP assessment in three independent surveys on the Italian population aged 35-74 years, carried out in 10 Regions approximately 10 years apart from each other, showed a significant reduction of BP mean values and prevalence of raised BP and hypertension in 2018-2019 compared to twenty years earlier, with a favourable trend also observed compared to ten years earlier. This reduction was independent of gender, age and educational level and met the 25% target for reduction/containment of the RBP prevalence indicated in the WHO Global Action Plan 2013-2020 by 2025 with baseline 2010. Albeit in 2018-2019 underdiagnoses and non-control of elevated blood pressure was still largely prevalent in Italy, a favourable trend in the control of raised BP has been observed.

Although systematic and periodic monitoring are necessary to observe the trend and control of blood pressure in the coming years, also in relation to the direct and indirect effects of the COVID-19 pandemic, these results have major public health implications in so much as they encourage the

initiatives undertaken by the Italian Ministry of Health in order to contain risk factors associated to the onset of raised BP at individual and population level through the "Gaining Health: making healthy choices easy" Programme and the NPPs. In continuity with the NPP 2014-2019, the NPP 2020-2025 renewed the commitment to the health promotion and the prevention of NCDs by providing preventive and protective interventions according to a life-course approach and aiming at the early identification and management of persons with risk factors.

Prevention and control of raised BP involve multi-stakeholder collaboration, such as governments, academia, the food and beverage industry and civil society. In view of the enormous public health benefits of BP control, some concerted action has been implemented and data demonstrate that the prevention of raised BP is today an attainable goal.

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Competing Interests: Italian Ministry of Health defined the needs and use of data for evidence based policy making and collaborate in the interpretation of results for health promotion and prevention activities and planning health services. Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO) and the Fondazione per il Tuo cuore onlus (Heart Care Foundation–HCF) had a role a role in the choice of collaborating centers, in the management of funding for the support of local centers and in the interpretation of results.

Author Contributions: Conceptualization, CD and LP; methodology, CD, CLN and LP; software, FV; formal analysis, CD; investigation, CD, CLN, ADL, EP and BB; resources, CD, DG, PB, LP and MMG ; data curation, CD, CLN and LP; writing—original draft preparation, CD; writing—review and editing, CD, ADL, CLN, EP, BB, FV, SV, FG, GO, MMG, DG, PB, and LP; visualization, CD; supervision, CD, LP and GO; project administration, CD; funding acquisition, CD, LP and MMG. All authors have read and agreed to the published version of the manuscript."

Informed Consent Statement: All invited persons received an informative note and signed an informed consent to participate.

Data Sharing Statement: The data are not publicly available due to ethical and legal restrictions on data sharing.

Ethics Approval Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethical Committee of the Italian National Institute of Health (Istituto Superiore di Sanità - ISS) by 11 March 2008 (Prot. PRE 150/08), 11 November 2009 (Prot. PRE/569/09) and 14 March 2018 (Prot. PRE 1176/18).

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FIGURES

Figure 1. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident men aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

Bars refer to 95% confidence intervals. Statistics by educational level were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Higher education—high school or college; lower education—primary or middle school. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: under drug treatment for hypertension with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Figure 2. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

Bars refer to 95% confidence intervals. Statistics by educational level were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Higher education—high school or college; lower education—primary or middle school. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: under drug treatment for hypertension with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Figure 3. Prevalence of raised blood pressure based on measurements, by sex, Regions, and period. Italian resident men and women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.

Figure 4. Prevalence of hypertension based on measurements, by sex, Regions, and period. Italian resident men and women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment.

FIG 1

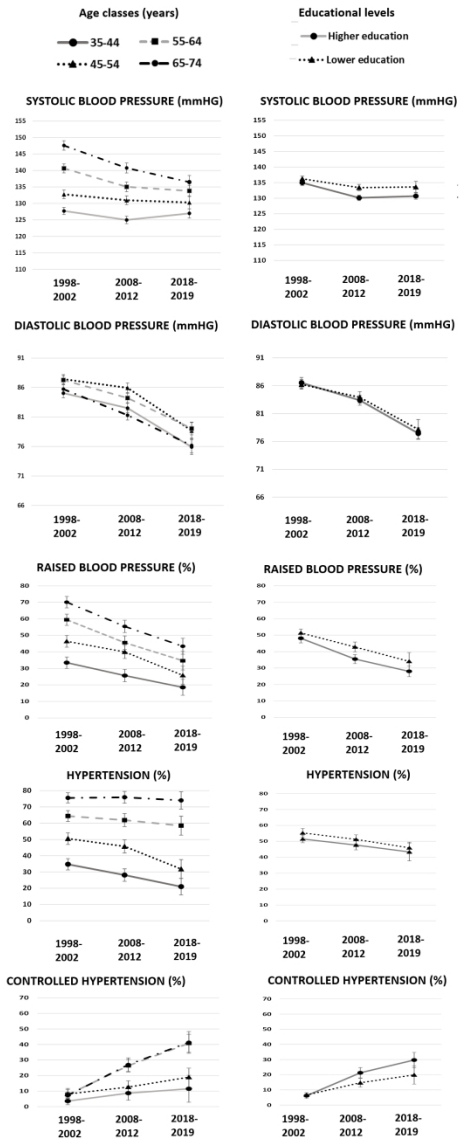

Figure 1. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident men aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.
Bars refer to 95% confidence intervals. Statistics by educational level were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Higher education—high school or college; lower education—primary or middle school. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: under drug treatment for hypertension with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

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FIG 2

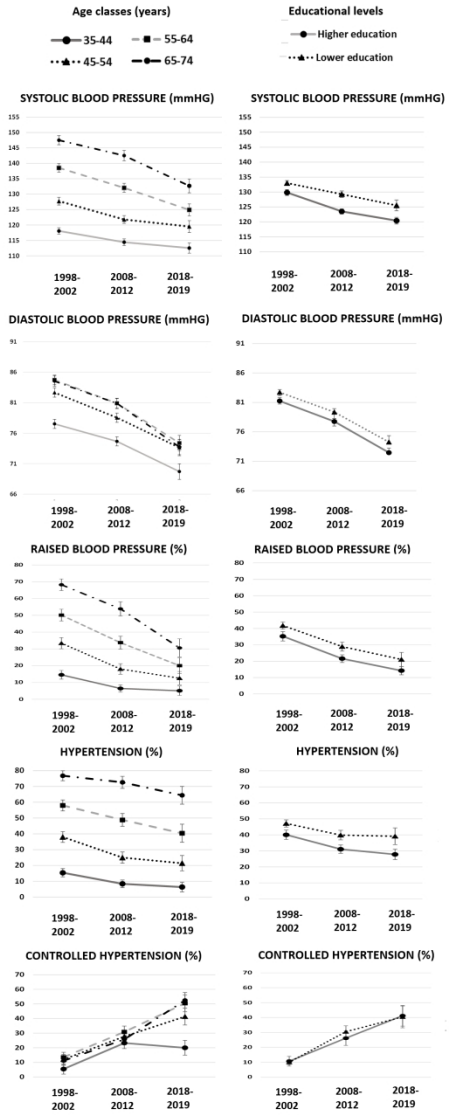
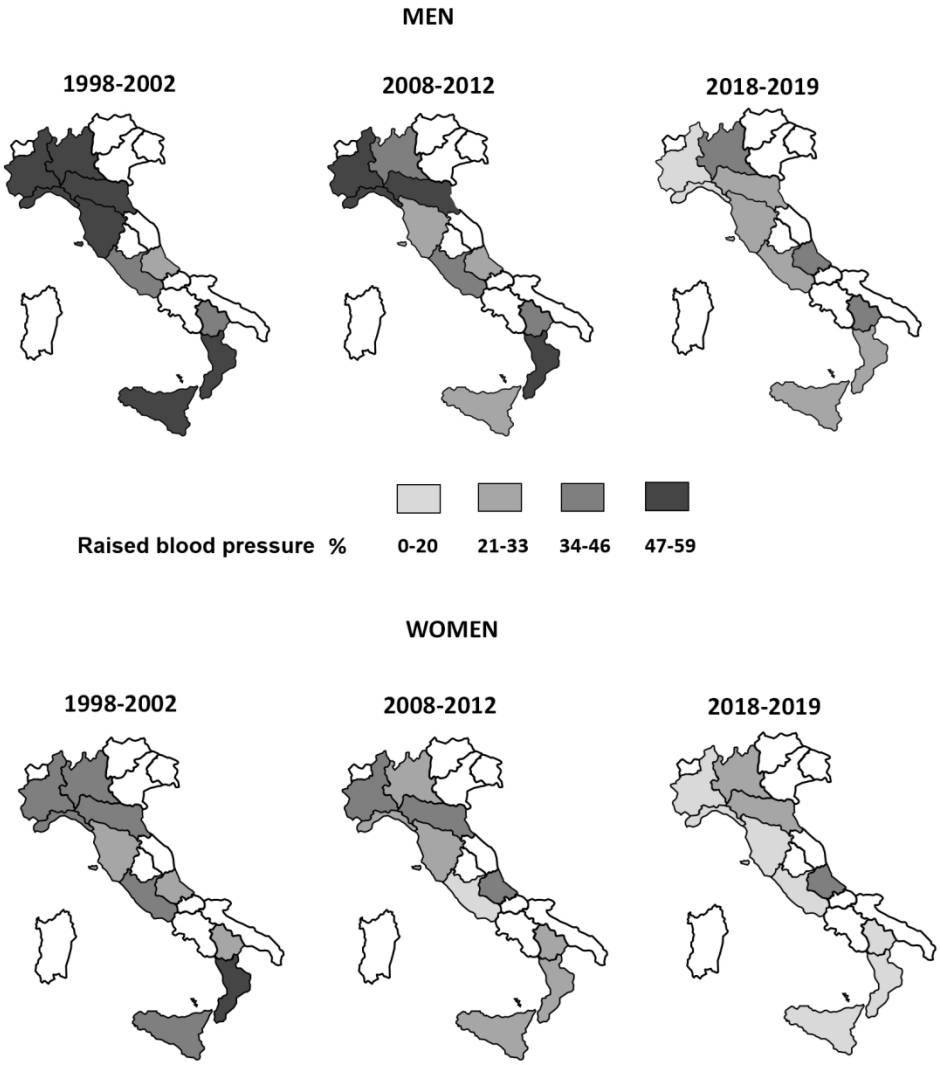


Figure 2. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.
Bars refer to 95% confidence intervals. Statistics by educational level were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Higher education—high school or college; lower education—primary or middle school. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: under drug treatment for hypertension with systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

366x594mm (150 x 150 DPI)

Fig 3



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Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.

287x345mm (150 x 150 DPI)

Fig 4

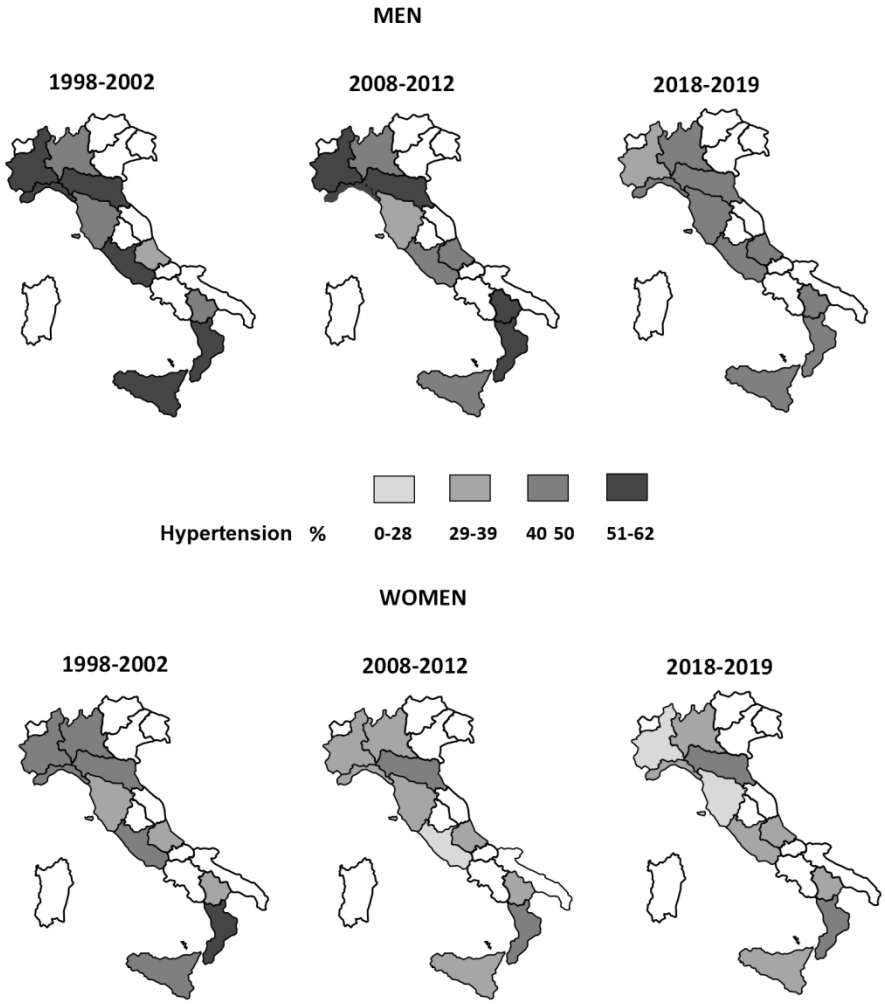

Figure 4. Prevalence of hypertension based on measurements, by sex, Regions, and period. Italian resident men and women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019. Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2000, 2010, and 2019, respectively. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment.

287x367mm (150 x 150 DPI)

Table S1. Demographic characteristics of men and women with available blood pressure measurements and information on the use of specific drug treatment within the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

	MEN					
	1998-2002		2008-2012		2018-2019	
Age class (years)						
	n	**%**	**n**	**%**	**n**	**%**
35-44	717	24	530	24	248	24
45-54	752	25	588	27	248	24
55-64	784	26	564	25	277	27
65-74	732	25	536	24	258	25
Educational level						
	n	**%**	**n**	**%**	**n**	**%**
Higher education	1249	42	1183	54	725	71
Lower education	1730	58	1018	46	303	29
	WOMEN					
	1998-2002		2008-2012		2018-2019	
Age class (years)						
	n	**%**	**n**	**%**	**n**	**%**
35-44	715	24	514	23	237	22
45-54	769	26	577	26	271	25
55-64	778	26	584	27	280	26
65-74	693	23	529	24	278	26
Educational level						
	n	%	n	%	n	%
Higher education	1052	36	1167	53	725	68
Lower education	1887	64	1017	47	339	32

Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily. Higher education - high school or college; lower education - primary or middle school.

Table S2. Blood pressure and heart rate measurements mean levels by age class and period. Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Systolic blood pressure (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						***				
35-44	717	**128**	15	127	129		530	**125**	13	124	126		248	**127**	11	126	128		**-1**	ns	**2**	*
45-54	752	**133**	18	131	134		588	**131**	16	130	132		248	**130**	16	128	132		**-2**	*	**-1**	ns
55-64	784	**141**	20	139	142		564	**135**	17	134	136		277	**134**	14	132	135		**-7**	***	**-1**	ns
65-74	732	**148**	20	146	149		536	**141**	18	139	142		258	**136**	17	134	138		**-11**	***	**-4**	**

Diastolic blood pressure (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						**				
35-44	717	**85**	11	84	86		530	**83**	10	82	83		248	**76**	10	75	77		**-9**	***	**-7**	***
45-54	752	**87**	11	87	88		588	**86**	10	85	87		248	**79**	11	77	80		**-9**	***	**-7**	***
55-64	784	**87**	11	87	88		564	**84**	10	83	85		277	**79**	9	78	80		**-8**	***	**-5**	***
65-74	732	**86**	10	85	86		536	**81**	10	80	82		258	**76**	10	75	77		**-10**	***	**-5**	***

Systolic blood pressure not under drug treatment (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						***				
35-44	682	**127**	14	126	128		504	**125**	13	123	126		237	**127**	11	125	128		**-0.2**	ns	**2**	*
45-54	640	**131**	17	130	132		481	**129**	16	127	130		212	**128**	14	126	130		**-3**	*	**-1**	ns
55-64	581	**137**	19	136	139		370	**133**	17	131	135		170	**133**	14	131	135		**-4**	**	**-0.2**	ns
65-74	454	**143**	20	142	145		252	**138**	18	136	140		125	**138**	18	134	141		**-6**	**	**-1**	ns

Diastolic blood pressure not under drug treatment (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						**						***						ns				
35-44	682	**85**	10	84	85		504	**82**	10	81	83		237	**75**	10	74	77		**-9**	***	**-7**	***
45-54	640	**86**	11	86	87		481	**85**	10	84	86		212	**77**	10	76	78		**-9**	***	**-8**	***
55-64	581	**86**	10	85	87		370	**84**	10	83	85		170	**78**	9	77	79		**-8**	***	**-6**	***
65-74	454	**84**	10	83	85		252	**81**	10	80	82		125	**77**	11	75	79		**-8**	***	**-4**	**

Heart rate (beats per minute)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						ns						ns						ns				
35-44	715	**66**	10	65	67		530	**68**	9	67	69		248	**72**	12	70	73		**6**	***	**4**	***
45-54	750	**66**	11	65	67		588	**69**	10	68	70		248	**72**	11	71	74		**6**	***	**3**	***
55-64	783	**66**	11	65	67		564	**68**	10	68	69		277	**72**	12	70	73		**6**	***	**3**	***
65-74	732	**66**	11	65	67		536	**69**	10	68	69		258	**70**	12	69	72		**4**	***	**2**	ns

SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S3. Blood pressure and heart rate measurements mean levels by age class and period. Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Systolic blood pressure (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						***				
35-44	715	**118**	14	117	119		514	**114**	13	113	116		237	**113**	13	111	114		**-6**	***	**-2**	ns
45-54	769	**128**	18	126	129		577	**122**	15	121	123		271	**120**	16	118	121		**-8**	***	**-2**	*
55-64	778	**139**	20	137	140		584	**132**	18	131	134		280	**125**	16	123	127		**-14**	***	**-7**	***
65-74	693	**147**	20	146	149		529	**143**	20	141	144		278	**133**	19	130	135		**-15**	***	**-10**	***

Diastolic blood pressure (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						***				
35-44	715	**78**	10	77	78		514	**75**	9	74	75		237	**70**	10	68	71		**-8**	***	**-5**	***
45-54	769	**83**	11	82	83		577	**79**	9	78	79		271	**74**	11	72	75		**-9**	***	**-5**	***
55-64	778	**85**	10	84	85		584	**81**	10	80	82		280	**74**	11	73	76		**-10**	***	**-7**	***
65-74	693	**85**	10	84	85		529	**81**	10	80	82		278	**74**	11	72	75		**-11**	***	**-7**	***

Systolic blood pressure not under drug treatment (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						***				
35-44	698	**118**	14	116	119		499	**114**	12	113	115		234	**112**	13	111	114		**-5**	***	**-1**	ns
45-54	657	**125**	17	124	126		510	**120**	15	119	122		238	**118**	15	116	120		**-7**	***	**-2**	*
55-64	539	**134**	18	132	135		401	**128**	17	126	130		203	**123**	17	121	126		**-10**	***	**-4**	**
65-74	374	**142**	18	140	144		244	**138**	20	135	140		122	**127**	16	124	130		**-15**	***	**-10**	***

Diastolic blood pressure not under drug treatment (mmHg)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						***						***						**				
35-44	698	**77**	10	76	78		499	**74**	8	74	75		234	**70**	10	68	71		**-8**	***	**-5**	***
45-54	657	**81**	10	81	82		510	**78**	9	77	79		238	**73**	11	71	74		**-9**	***	**-5**	***
55-64	539	**83**	10	82	83		401	**79**	9	79	80		203	**73**	11	72	75		**-9**	***	**-6**	***
65-74	374	**83**	9	82	83		244	**80**	9	79	81		122	**71**	9	70	73		**-11**	***	**-9**	***

Heart rate (beats per minute)

Age class (years)	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 vs 1998-2002 Diff	t-test sign	2018-2019 vs 2008-2012 Diff	t-test sign
						**						*ns*						*ns*				
35-44	711	**71**	11	70	72		514	**72**	9	71	72		237	**74**	11	73	75		**3**	**	**2**	**
45-54	769	**70**	10	69	71		577	**71**	9	70	71		271	**73**	10	72	74		**3**	***	**3**	**
55-64	776	**69**	10	68	70		584	**71**	9	70	72		280	**72**	10	71	73		**3**	***	**1**	ns
65-74	690	**69**	11	68	70		529	**71**	10	70	72		278	**72**	11	71	73		**3**	**	**1**	ns

SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S4. Blood pressure measurements and heart rate mean levels by educational level and period. Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Systolic blood pressure (mmHg)

Educational level	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 Diff	t-test sign	2018-2019 Diff	t-test sign
						***						***						***				
Higher education	1249	**135**	17	*134*	*136*		1183	**130**	15	*129*	*131*		725	**131**	14	*130*	*132*		**-4**	***	**1**	ns
Lower education	1730	**136**	18	*135*	*137*		1018	**133**	17	*132*	*134*		303	**134**	16	*132*	*135*		**-3**	**	**0.2**	ns

Diastolic blood pressure (mmHg)

Educational level	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 Diff	t-test sign	2018-2019 Diff	t-test sign
						ns						ns						ns				
Higher education	1249	**87**	11	*86*	*87*		1183	**83**	10	*83*	*84*		725	**77**	10	*77*	*78*		**-9**	***	**-6**	***
Lower education	1730	**86**	11	*86*	*87*		1018	**84**	10	*83*	*85*		303	**78**	10	*77*	*79*		**-8**	***	**-6**	***

Systolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 Diff	t-test sign	2018-2019 Diff	t-test sign
						***						***						***				
Higher education	1046	**133**	16	*132*	*134*		913	**129**	15	*128*	*130*		537	**130**	13	*129*	*131*		**-3**	***	**1**	ns
Lower education	1305	**134**	17	*133*	*135*		680	**131**	16	*130*	*133*		205	**133**	15	*131*	*135*		**-1**	ns	**1**	ns

Diastolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 Diff	t-test sign	2018-2019 Diff	t-test sign
						ns						ns						ns				
Higher education	1046	**86**	10	*85*	*86*		913	**83**	10	*82*	*83*		537	**77**	10	*76*	*78*		**-9**	***	**-6**	***
Lower education	1305	**85**	10	*85*	*86*		680	**83**	10	*83*	*84*		205	**77**	9	*76*	*78*		**-8**	***	**-6**	***

Heart rate (beats per minute)

Educational level	1998-2002 n	mean	DS	95% CI		ANOVA within period sign	2008-2012 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 n	mean	DS	95% CI		ANOVA within period sign	2018-2019 Diff	t-test sign	2018-2019 Diff	t-test sign
						ns						ns						**				
Higher education	1244	**66**	11	*65*	*67*		1183	**68**	9	*68*	*69*		725	**71**	11	*70*	*72*		**5**	***	**2**	***
Lower education	1730	**66**	11	*65*	*67*		1018	**68**	10	*68*	*69*		303	**74**	12	*73*	*76*		**8**	***	**6**	***

Means and standard deviations age-standardized by ISTAT Italian population 2000, 2010 and 2019 respectively. SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. Higher education - high school or college; lower education - primary or middle school. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S5. Blood pressure measurements and heart rate mean levels by educational level and period. Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Systolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1052	**130**	16	129	131	***	1167	**124**	15	123	124	***	725	**120**	15	119	122	***	-9	***	-3	***
Lower education	1887	**133**	18	132	134		1017	**129**	18	128	130		339	**126**	17	124	127		-7	***	-4	**

Diastolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1052	**81**	10	81	82	***	1167	**78**	9	77	78	***	725	**72**	11	72	73	**	-9	***	-5	***
Lower education	1887	**83**	10	82	83		1017	**79**	10	79	80		339	**74**	10	73	75		-8	***	-5	***

Systolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	928	**128**	16	127	129	***	992	**121**	14	120	122	***	593	**119**	15	118	120	***	-9	***	-2	**
Lower education	1331	**129**	16	129	130		651	**127**	16	126	128		203	**124**	16	121	126		-6	***	-3	*

Diastolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	928	**81**	10	80	81	***	992	**77**	9	76	78	***	593	**71**	10	71	72	*	-9	***	-6	***
Lower education	1331	**81**	10	81	82		651	**78**	9	78	79		203	**73**	10	72	75		-8	***	-5	***

Heart rate (beats per minute)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019		2018-2019	
	n	mean	std	95% CI			n	mean	std	95% CI			n	mean	std	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1047	**69**	11	69	70	ns	1167	**71**	9	70	72	ns	725	**73**	10	72	73	ns	3	***	2	**
Lower education	1884	**70**	11	69	70		1017	**71**	10	71	72		339	**73**	11	72	74		3	***	2	**

Means and standard deviations age-standardized by ISTAT Italian population 2000, 2010 and 2019 respectively. SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. Higher education - high school or college; lower education - primary or middle school. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Lombardy, Piedmont, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S6. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by age class and period. Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Blood pressure drug treatment

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				***				
35-44	717	5	3 6		530	5	3 7		248	4	2 7		-0.4	ns	-0.5	ns
45-54	752	15	12 17		588	18	15 21		248	15	10 19		-0.4	ns	-4	ns
55-64	784	26	23 29		564	34	30 38		277	39	33 44		13	***	4	ns
65-74	732	38	34 41		536	53	49 57		258	52	45 58		14	**	-1	ns

Raised blood pressure

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				***				
35-44	717	33	30 37		530	26	22 29		248	19	14 23		-15	***	-7	*
45-54	752	46	43 50		588	40	36 44		248	26	20 31		-21	***	-14	***
55-64	784	59	56 63		564	46	41 50		277	35	29 40		-25	***	-11	**
65-74	732	70	67 73		536	55	51 60		258	43	37 49		-27	***	-12	**

Hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				**				
35-44	717	35	31 38		530	28	24 32		248	21	16 26		-14	***	-7	*
45-54	752	51	47 54		588	46	42 50		248	32	26 38		-19	***	-14	**
55-64	784	64	61 68		564	62	58 66		277	58	53 64		-6	ns	-3	ns
65-74	732	76	72 79		536	76	72 80		258	74	69 79		-2	ns	-2	ns

Undiagnosed hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				**				***				***				
35-44	249	67	62 73		149	54	46 62		52	62	48 75		-6	ns	8	ns
45-54	380	52	47 57		269	40	34 46		79	35	25 46		-16	**	-4	ns
55-64	505	48	44 52		349	32	27 37		162	23	17 30		-25	***	-8	ns
65-74	553	39	35 43		407	25	20 29		191	21	16 27		-18	***	-3	ns

Diagnosed but untreated hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				ns				
35-44	249	18	14 23		149	29	22 36		52	17	7 28		-1	ns	-12	ns
45-54	380	19	15 23		269	20	16 25		79	19	10 28		0.0	ns	-1	ns
55-64	505	12	9 14		349	13	9 16		162	10	6 15		-1	ns	-2	ns
65-74	553	10	8 13		407	6	3 8		191	9	5 13		-1	ns	3	ns

Uncontrolled hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				***				***				ns				
35-44	249	10	7 14		149	9	4 13		52	10	2 18		-1	ns	1	ns
45-54	380	21	17 25		269	27	22 32		79	27	17 36		5	ns	-1	ns
55-64	505	32	28 37		349	29	24 34		162	25	19 32		-7	ns	-4	ns
65-74	553	43	39 47		407	43	38 48		191	28	22 35		-15	**	-14	**

Controlled hypertension

Age class (years)	1998-2002 n	%	95% CI	Chi-squared test within period sign	2008-2012 n	%	95% CI	Chi-squared test within period sign	2018-2019 n	%	95% CI	Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
				ns				***				***				
35-44	249	4	1 6		149	9	4 13		52	12	3 20		8	*	3	ns
45-54	380	8	5 11		269	13	9 17		79	19	10 28		11	**	6	ns
55-64	505	8	5 10		349	26	22 31		162	41	33 48		33	***	14	**
65-74	553	7	5 9		407	27	23 31		191	41	34 48		34	***	14	**

CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S7. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by age class and period. Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Blood pressure drug treatment

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	715	2	1	3		514	3	1	4		237	1	0	3	-1	ns	-2	ns
45-54	769	15	12	17		577	12	9	14		271	12	8	16	-2	ns	1	ns
55-64	778	31	27	34		584	31	28	35		280	28	22	33	-3	ns	-4	ns
65-74	693	46	42	50		529	54	50	58		278	56	50	62	10	**	2	ns

Raised blood pressure

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	715	15	12	17		514	6	4	9		237	5	2	8	-9	**	-1	ns
45-54	769	33	30	37		577	18	15	21		271	13	9	16	-21	***	-5	*
55-64	778	50	47	54		584	34	30	38		280	20	15	25	-30	***	-14	***
65-74	693	68	65	72		529	54	50	58		278	31	25	36	-38	***	-23	***

Hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	715	15	13	18		514	8	6	11		237	6	3	9	-9	**	-2	ns
45-54	769	38	35	41		577	25	21	28		271	21	17	26	-17	***	-4	ns
55-64	778	58	55	61		584	49	45	53		280	40	35	46	-18	***	-8	*
65-74	693	77	74	80		529	73	69	76		278	64	59	70	-12	***	-8	*

Undiagnosed hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	110	62	53	71		43	40	25	54		15	47	21	72	-15	ns	7	ns
45-54	292	45	40	51		144	39	31	47		58	29	18	41	-16	*	-10	ns
55-64	451	33	29	38		285	24	19	28		113	21	14	29	-12	*	-2	ns
65-74	532	32	28	36		384	20	16	23		179	11	6	15	-22	***	-9	**

Diagnosed but untreated hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					**								
35-44	110	23	15	31		43	26	13	39		15	33	9	57	11	ns	8	ns
45-54	292	16	12	21		144	15	9	20		58	14	5	23	-3	ns	-1	ns
55-64	451	14	10	17		285	12	8	16		113	11	5	16	-3	ns	-2	ns
65-74	532	8	6	10		384	6	4	9		179	2	0	4	-6	***	-4	***

Uncontrolled hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***								
35-44	110	10	4	16		43	12	2	21		15	0	0	0	-10	-	-12	-
45-54	292	26	21	31		144	19	12	25		58	16	6	25	-11	ns	-3	ns
55-64	451	39	35	44		285	33	28	39		113	18	11	25	-22	***	-16	**
65-74	532	49	45	53		384	48	43	53		179	35	28	42	-14	***	-14	***

Controlled hypertension

Age class (years)	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns								
35-44	110	5	1	10		43	23	11	36		15	20	0	40	15	*	-3	ns
45-54	292	12	8	16		144	28	20	35		58	41	29	54	29	***	14	ns
55-64	451	14	10	17		285	31	26	36		113	50	41	60	37	***	20	**
65-74	532	11	8	14		384	26	21	30		179	53	45	60	41	***	27	*

CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S8. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by educational class and period. Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Blood pressure drug treatment

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	1249	18	16	20		1183	24	22	27		725	26	23	29		8	***	2	ns
Lower education	1730	19	18	21		1018	25	22	28		303	24	19	29		5	ns	-1	ns

Raised blood pressure

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	1249	48	45	51		1183	35	33	38		725	28	25	31		-20	***	-7	**
Lower education	1730	51	49	54		1018	43	40	46		303	34	29	39		-17	***	-9	**

Hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					*					ns					ns				
Higher education	1249	51	49	54		1183	48	45	51		725	43	40	47		-8	**	-4	ns
Lower education	1730	55	53	58		1018	51	48	54		303	46	40	52		-9	**	-5	ns

Undiagnosed hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns	n				ns				
Higher education	621	53	49	57		555	38	34	42		314	36	30	41		-18	***	-2	ns
Lower education	1063	54	51	57		610	40	36	44		168	38	30	45		-16	**	-2	ns

Diagnosed but untreated hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	621	16	13	19		555	20	17	23		314	13	10	17		-3	ns	-6	*
Lower education	1063	15	13	17		610	16	13	19		168	16	10	21		1	***	-0.4	ns

Uncontrolled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	621	24	21	28		555	21	18	25		314	21	17	26		-3	ns	0.1	ns
Lower education	1063	25	22	27		610	29	25	32		168	26	20	33		2	***	-2	ns

Controlled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					*				
Higher education	621	6	4	8		555	21	18	25		314	30	25	35		24	***	8	**
Lower education	1063	7	5	8		610	15	12	18		168	20	14	26		13	**	5	ns

Prevalence are age-standardized by ISTAT Italian population 2000, 2010 and 2019 respectively. CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Higher education - high school or college; lower education - primary or middle school.Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S9. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by educational class and period. Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Blood pressure drug treatment

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***					**				
Higher education	1052	16	14	19		1167	19	16	21		725	19	17	22		3	ns	1	ns
Lower education	1887	23	22	25		1017	26	23	28		339	27	23	32		4	ns	2	ns

Raised blood pressure

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					***					**				
Higher education	1052	35	32	38		1167	22	19	24		725	14	12	17		-21	***	-7	***
Lower education	1887	42	40	44		1017	29	26	32		339	21	17	25		-21	***	-8	**

Hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					***					**				
Higher education	1052	40	37	43		1167	31	28	34		725	28	25	31		-12	***	-3	ns
Lower education	1887	47	45	49		1017	40	37	43		339	39	34	44		-8	**	-1	ns

Undiagnosed hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	337	47	42	53		311	36	31	42		192	27	21	34		-20	***	-9	*
Lower education	1037	43	40	46		534	25	21	28		172	29	23	36		-14	**	5	ns

Diagnosed but untreated hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	337	19	14	23		311	15	11	19		192	16	11	22		-2	ns	1	ns
Lower education	1037	15	13	18		534	17	13	20		172	13	8	18		-3	***	-4	*

Uncontrolled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					ns					ns				
Higher education	337	23	19	28		311	22	18	27		192	15	10	20		-8	*	-7	*
Lower education	1037	31	29	34		534	28	25	32		172	17	12	23		-14	***	-11	ns

Controlled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	337	11	7	14		311	26	21	31		192	41	34	48		31	***	15	**
Lower education	1037	10	8	12		534	31	27	34		172	40	33	48		30	***	10	ns

Prevalence are age-standardized by ISTAT Italian population 2000, 2010 and 2019 respectively. CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Higher education - high school or college; lower education - primary or middle school. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S10. Age-standardized blood pressure mean values, and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements by sex and Italian Region. Italian resident men and women aged 35–74 years, the CUORE Project Survey 2018-2019.

2018-2019

MEN

Italian Region	n	Systolic blood pressure (mmHg)				Diastolic blood pressure (mmHg)				Raised blood pressure			Hypertension			Controlled hypertension		
		mean	SD	95%CI		mean	SD	95%CI		%	95% CI		%	95% CI		%	95% CI	
Abruzzo	102	**134**	14	*132*	*137*	**78**	10	*76*	*80*	**36**	27	*45*	**47**	37	*56*	**18**	10	*25*
Calabria	101	**132**	13	*130*	*135*	**76**	9	*75*	*78*	**31**	22	*40*	**49**	39	*59*	**31**	22	*40*
Liguria	104	**127**	12	*125*	*130*	**76**	10	*74*	*78*	**20**	12	*27*	**40**	30	*49*	**31**	22	*40*
Lazio	99	**130**	13	*127*	*133*	**79**	10	*77*	*81*	**29**	20	*38*	**47**	37	*57*	**31**	22	*40*
Lombardy	98	**134**	15	*131*	*137*	**78**	9	*76*	*80*	**37**	27	*46*	**48**	38	*58*	**19**	11	*26*
Piedmont	104	**129**	13	*126*	*131*	**75**	9	*73*	*77*	**18**	11	*26*	**35**	26	*45*	**43**	34	*53*
Emilia Romagna	104	**134**	15	*131*	*137*	**79**	10	*77*	*81*	**30**	21	*39*	**42**	33	*51*	**20**	12	*27*
Basilicata	106	**134**	15	*132*	*137*	**80**	10	*78*	*82*	**35**	26	*44*	**48**	39	*58*	**27**	19	*36*
Tuscany	108	**129**	13	*127*	*132*	**77**	9	*75*	*79*	**28**	20	*37*	**40**	31	*50*	**25**	17	*33*
Sicily	105	**132**	13	*129*	*134*	**78**	10	*76*	*80*	**33**	24	*42*	**44**	35	*54*	**27**	18	*35*

WOMEN

Italian Region	n	Systolic blood pressure (mmHg)				Diastolic blood pressure (mmHg)				Raised blood pressure			Hypertension			Controlled hypertension		
		mean	SD	95%CI		mean	SD	95%CI		%	95% CI		%	95% CI		%	95% CI	
Abruzzo	104	**122**	17	*118*	*125*	**73**	10	*71*	*75*	**14**	8	*21*	**31**	22	*40*	**45**	35	*54*
Calabria	109	**121**	14	*119*	*124*	**70**	10	*68*	*72*	**16**	9	*23*	**40**	31	*50*	**48**	38	*57*
Liguria	107	**117**	15	*114*	*120*	**72**	11	*70*	*74*	**15**	8	*22*	**30**	21	*38*	**32**	23	*40*
Lazio	114	**124**	14	*122*	*127*	**76**	9	*74*	*78*	**16**	9	*22*	**35**	26	*43*	**68**	60	*77*
Lombardy	100	**127**	18	*124*	*131*	**75**	11	*73*	*77*	**24**	16	*33*	**37**	27	*46*	**35**	25	*44*
Piedmont	113	**117**	13	*115*	*119*	**70**	9	*68*	*71*	**8**	3	*13*	**16**	10	*23*	**43**	34	*53*
Emilia Romagna	106	**127**	16	*124*	*130*	**76**	11	*74*	*78*	**24**	16	*32*	**40**	30	*49*	**32**	23	*41*
Basilicata	114	**121**	16	*118*	*124*	**72**	10	*70*	*74*	**16**	9	*23*	**31**	23	*39*	**22**	15	*30*
Tuscany	97	**120**	15	*117*	*123*	**72**	9	*70*	*74*	**15**	8	*23*	**22**	14	*31*	**22**	14	*30*
Sicily	102	**124**	14	*121*	*127*	**74**	9	*72*	*76*	**17**	10	*24*	**37**	27	*46*	**63**	54	*73*

SD: standard deviations. Means, standard deviations and prevalences were age-standardized by Italian National Institute of Statistics-ISTAT Italian population 2019. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Controlled hypertension: treated and SBP < 140 mmHg and DBP < 90 mmHg. Regional data for 1998–2002 and 2008–2012 CUORE Project surveys were available at http://www.cuore.iss.it/eng/survey/cuoredata.

Table S11. Blood pressure and heart rate measurements and prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control, (age-adjusted using the European standard population) by sex and period. Italian resident men and women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

	1998-2002 n=2985				2008-2012 n=2218				2018-2019 n=1031				2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	mean	SD	95% CI		mean	SD	95% CI		mean	SD	95% CI		Diff	t-test p-value	Diff	t-test p-value
Systolic blood pressure - SBP (mmHg)	136	18	136	137	132	16	132	133	132	14	131	132	-5	***	-1	ns
Diastolic blood pressure - DBP (mmHg)	86	11	86	87	84	10	83	84	77	10	77	78	-9	***	-6	***
SBP not under drug treatment (mmHg)	134	17	133	135	131	16	130	131	131	14	130	132	-3	***	0.3	ns
DBP not under drug treatment (mmHg)	85	10	85	86	83	10	83	84	77	10	76	77	-9	***	-6	***
Heart rate (beats per minute)	66	11	66	66	69	10	68	69	72	12	71	72	6	***	3	***
	%	95% CI			%	95% CI			%	95% CI			Diff	chi-squared p-value	Diff	chi-squared p-value
Blood pressure drug treatment	20	18	21		26	24	27		25	23	28		6	**	-0.4	ns
Raised blood bressure	51	49	53		41	39	43		30	27	32		-21	***	-11	***
Hypertension	55	53	57		51	49	53		44	41	47		-11	***	-7	**
Hypertension																
Undiagnosed	53	50	55		39	36	41		37	32	41		-16	***	-2	ns
Diagnosed but untreated	15	14	17		18	16	20		14	11	17		-1	ns	-3	ns
Uncontrolled	26	23	28		26	23	28		22	18	26		-4	ns	-4	ns
Controlled	7	5	8		18	16	20		27	23	31		20	***	9	***

WOMEN

	1998-2002 n=2951				2008-2012 n=2185				2018-2019 n=1066				2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	mean	SD	95% CI		mean	SD	95% CI		mean	SD	95% CI		Diff	t-test p-value	Diff	t-test p-value
Systolic blood pressure - SBP (mmHg)	132	18	131	132	127	17	126	127	122	16	121	123	-10	***	-5	***
Diastolic blood pressure - DBP (mmHg)	82	10	82	83	79	9	78	79	73	11	72	73	-9	***	-6	***
SBP not under drug treatment (mmHg)	129	16	128	129	124	15	123	125	120	15	119	121	-9	***	-4	***
DBP not under drug treatment (mmHg)	81	10	80	81	78	9	77	78	72	10	71	72	-9	***	-6	***
Heart rate (beats per minute)	70	11	69	70	71	9	71	71	73	11	72	73	3	***	2	***
	%	95% CI			%	95% CI			%	95% CI			Diff	chi-squared p-value	Diff	chi-squared p-value
Blood pressure drug treatment	22	20	23		23	21	25		22	19	24		0.3	ns	-1	ns
Raised blood bressure	40	38	41		26	24	28		16	14	18		-23	***	-10	***
Hypertension	45	43	46		36	34	38		31	28	34		-14	***	-5	**
Hypertension																
Undiagnosed	44	42	47		31	28	34		28	24	33		-16	***	-3	ns
Diagnosed but untreated	16	14	18		15	13	18		16	12	20		0.3	ns	1	ns
Uncontrolled	30	27	32		26	24	29		16	12	19		-14	***	-11	***
Controlled	10	9	12		27	24	30		40	35	45		30	***	13	***

Means, standard deviation and prevalence are age-standardized by European standard population 2013.SD: standard deviation. CI: confidence interval. Diff: mean or percentage difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means or prevalence. t-test to compare mean values between periods. Chi-squared test to compare prevalences between periods. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S12. Blood pressure measurements and heart rate mean levels by educational level and period (age-adjusted using the European standard population). Italian resident men aged 35–74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

MEN

Systolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1249	**135**	17	*135*	*136*	***	1183	**131**	15	*130*	*131*	***	725	**131**	14	*130*	*132*	***	**-5**	***	**0.1**	ns
Lower education	1730	**137**	18	*136*	*138*		1018	**134**	17	*133*	*135*		303	**134**	16	*132*	*135*		**-3**	**	**-0.3**	ns

Diastolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1249	**87**	11	*86*	*87*	*ns*	1183	**83**	10	*83*	*84*	*ns*	725	**77**	10	*77*	*78*	*ns*	**-9**	***	**-6**	***
Lower education	1730	**86**	11	*86*	*87*		1018	**84**	10	*83*	*84*		303	**78**	10	*77*	*79*		**-8**	***	**-6**	***

Systolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1046	**134**	16	*133*	*135*	***	913	**129**	15	*128*	*130*	***	537	**130**	13	*129*	*131*	***	**-4**	***	**1**	ns
Lower education	1305	**134**	17	*133*	*135*		680	**132**	16	*131*	*133*		205	**133**	15	*131*	*135*		**-1**	ns	**1**	ns

Diastolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1046	**86**	10	*85*	*86*	*ns*	913	**83**	10	*82*	*83*	*ns*	537	**77**	10	*76*	*78*	*ns*	**-9**	***	**-6**	***
Lower education	1305	**85**	10	*85*	*86*		680	**83**	10	*83*	*84*		205	**77**	9	*76*	*78*		**-8**	***	**-6**	***

Heart rate (beats per minute)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1244	**66**	11	*65*	*67*	*ns*	1183	**66**	11	*65*	*67*	*ns*	725	**71**	11	*70*	*71*	**	**5**	***	**5**	***
Lower education	1730	**66**	11	*65*	*67*		1018	**66**	12	*66*	*67*		303	**74**	12	*73*	*76*		**8**	***	**8**	***

Means and standard deviations age-standardized by European standard population 2013. SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. Higher education - high school or college; lower education - primary or middle school. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S13. Blood pressure measurements and heart rate mean levels by educational level and period (age-adjusted using the European standard population). Italian resident women aged 35–74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

WOMEN

Systolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1052	**130**	16	*129*	*131*	***	1167	**124**	15	*123*	*125*	***	725	**120**	15	*119*	*121*	***	**-10**	***	**-4**	***
Lower education	1887	**133**	18	*132*	*134*		1017	**130**	18	*129*	*131*		339	**125**	17	*123*	*127*		**-8**	***	**-4**	***

Diastolic blood pressure (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1052	**81**	10	*81*	*82*	***	1167	**78**	9	*77*	*78*	***	725	**72**	11	*72*	*73*	**	**-9**	***	**-6**	***
Lower education	1887	**83**	10	*82*	*83*		1017	**79**	10	*79*	*80*		339	**74**	10	*73*	*75*		**-9**	***	**-5**	***

Systolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	928	**128**	16	*127*	*129*	***	992	**122**	14	*121*	*122*	***	593	**119**	15	*117*	*120*	***	**-9**	***	**-3**	***
Lower education	1331	**129**	16	*129*	*130*		651	**127**	16	*126*	*128*		203	**123**	16	*121*	*125*		**-6**	***	**-4**	**

Diastolic blood pressure not under drug treatment (mmHg)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	928	**81**	10	*80*	*81*	***	992	**77**	9	*77*	*78*	***	593	**71**	10	*70*	*72*	*	**-9**	***	**-6**	***
Lower education	1331	**81**	10	*81*	*82*		651	**78**	9	*78*	*79*		203	**73**	10	*72*	*75*		**-8**	***	**-5**	***

Heart rate (beats per minute)

Educational level	1998-2002					ANOVA within period sign	2008-2012					ANOVA within period sign	2018-2019					ANOVA within period sign	2018-2019 vs 1998-2002		2018-2019 vs 2008-2012	
	n	mean	SD	95% CI			n	mean	SD	95% CI			n	mean	SD	95% CI			Diff	t-test sign	Diff	t-test sign
Higher education	1047	**69**	11	*69*	*70*	*ns*	1167	**71**	9	*70*	*71*	*ns*	725	**73**	10	*72*	*73*	*ns*	**3**	***	**2**	**
Lower education	1884	**70**	11	*69*	*70*		1017	**71**	9	*71*	*72*		339	**73**	11	*72*	*75*		**4**	***	**2**	**

Means and standard deviations age-standardized by European standard population 2013. SD: standard deviation; CI: confidence interval. Diff: mean difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of means. Higher education - high school or college; lower education - primary or middle school. ANOVA: Analysis of Variance to compare variables among age classes within periods. t-test to compare variables between periods. *** p-value<0.0001; ** p-value<0.01; *p-value<0.05; ns not significant p-value. Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S14. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by educational class and period (age-adjusted using the European standard population). Italian resident men aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

MEN

Blood pressure drug treatment

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	1249	19	16	21		1183	26	23	28		725	26	23	29		7	**	0.2	ns
Lower education	1730	20	18	22		1018	26	24	29		303	24	19	29		4	ns	-2	ns

Raised blood pressure

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	1249	49	46	52		1183	36	33	39		725	28	25	31		-21	***	-8	**
Lower education	1730	52	50	55		1018	44	41	47		303	34	29	39		-18	***	-10	**

Hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					*					ns					ns				
Higher education	1249	53	50	55		1183	49	46	52		725	43	40	47		-9	***	-6	*
Lower education	1730	56	54	59		1018	53	50	56		303	46	40	52		-10	**	-7	*

Undiagnosed hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	621	53	49	57		555	36	32	40		314	36	31	41		-17	***	-0.2	ns
Lower education	1063	53	50	56		610	39	35	43		168	38	31	46		-15	**	-1	ns

Diagnosed but untreated hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	621	16	13	19		555	19	16	22		314	13	10	17		-2	ns	-6	*
Lower education	1063	15	12	17		610	16	13	18		168	15	10	21		1	***	-0.1	ns

Uncontrolled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	621	25	22	29		555	22	19	26		314	21	17	26		-4	ns	-1	ns
Lower education	1063	26	23	28		610	30	26	33		168	26	19	33		0.5	***	-4	ns

Controlled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					*				
Higher education	621	6	4	8		555	22	19	26		314	30	24	35		23	***	7	*
Lower education	1063	7	5	8		610	15	12	18		168	20	14	26		13	**	5	ns

Prevalence are age-standardized by age-standardized by European standard population 2013. CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Higher education - high school or college; lower education - primary or middle school. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

Table S15. Prevalence of blood pressure treatment, raised blood pressure, hypertension and state of hypertension control based on measurements, by educational class and period (age-adjusted using the European standard population). Italian resident women aged 35–74 years, the CUORE Project Surveys 1998-2002, 2008-2012 and 2018-2019.

WOMEN

Blood pressure drug treatment

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					***					***					**				
Higher education	1052	16	14	19		1167	19	17	21		725	19	16	22		2	ns	-0.4	ns
Lower education	1887	24	22	25		1017	26	24	29		339	27	22	31		3	ns	0.4	ns

Raised blood pressure

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					***					**				
Higher education	1052	35	32	38		1167	22	20	24		725	14	11	16		-21	***	-8	***
Lower education	1887	42	40	44		1017	30	27	32		339	21	16	25		-21	***	-9	**

Hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					***					**				
Higher education	1052	40	37	43		1167	32	29	34		725	27	24	30		-13	***	-5	*
Lower education	1887	47	45	49		1017	41	38	44		339	38	33	43		-9	**	-3	ns

Undiagnosed hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					**					ns				
Higher education	337	47	42	52		311	36	30	41		192	28	21	34		-19	***	-8	ns
Lower education	1037	43	40	46		534	25	21	28		172	31	24	38		-12	**	6	ns

Diagnosed but untreated hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	337	19	14	23		311	15	11	19		192	17	12	23		-1	ns	2	ns
Lower education	1037	15	13	18		534	16	13	19		172	13	8	18		-2	***	-3	*

Uncontrolled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					**					*					ns				
Higher education	337	24	19	28		311	23	18	27		192	14	9	19		-9	*	-8	*
Lower education	1037	32	29	34		534	29	25	33		172	17	11	22		-15	***	-12	ns

Controlled hypertension

Educational level	1998-2002 n	%	95% CI		Chi-squared test within period sign	2008-2012 n	%	95% CI		Chi-squared test within period sign	2018-2019 n	%	95% CI		Chi-squared test within period sign	2018-2019 vs 1998-2002 Diff	chi-squared sign	2018-2019 vs 2008-2012 Diff	chi-squared sign
					ns					ns					ns				
Higher education	337	11	7	14		311	27	22	31		192	40	33	47		30	***	14	**
Lower education	1037	10	8	12		534	30	26	34		172	40	32	47		29	***	9	ns

Prevalence are age-standardized by age-standardized by European standard population 2013. CI: confidence interval. Diff: prevalence difference between 2018–2019 and 1998–2002 or 2018–2019 and 2008–2012; the values are approximated taking into account the first decimal of prevalence. Higher education - high school or college; lower education - primary or middle school. Chi-squared test to compare prevalences between periods and among age classes within the period. Raised blood pressure: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 and/or under specific pharmacological treatment. Hypertension is divided into 'undiagnosed, 'diagnosed but untreated', 'uncontrolled' (treated and SBP≥ 140 mmHg or DBP≥ 90 mmHg) and 'controlled' (treated and SBP < 140 mmHg and DBP < 90 mmHg). Pool of the following Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1 and 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5 and 6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5 and 6
Bias	9	Describe any efforts to address potential sources of bias	14
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 and 6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	na
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6 and in all tables
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	na
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6 and table s1
		(b) Indicate number of participants with missing data for each variable of interest	6 and in all tables

Outcome data	15*	Report numbers of outcome events or summary measures	6 and in all tables
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-12 and in all tables
		(*b*) Report category boundaries when continuous variables were categorized	6-12 and in related tables
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-12 and in all tables
Discussion			
Key results	18	Summarise key results with reference to study objectives	6-13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	12-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.