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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

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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 \pm SD: men 55 \pm 11, women 54 \pm 11), 2218 men and 2204 women (mean age \pm SD: men 55 \pm 11, women 55 \pm 11),

and 1031 men and 1066 women (mean age \pm SD: men 55 \pm 11, women 55 \pm 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															
			-2002				-2012		- 7		2019			2018-20 vs 1998-2			2018-20 vs 2008-2	
		n=2	985			n=2	218			n=1	031			10 2000			10 2000	
	mean	SD	95% C	7	mean	SD	959	% 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 1	36	132	16	131	132	132	14	131	132	-4	***	***	-0,3	ns	ns
Diastolic blood pressure - DBP (mmHg)	86	11	86 8	37	84	10	83	84	78	10	77	78	-9	***	***	-6	***	***
SBP not under drug treatment (mmHg)	134				130	15	129	131	131	14	130	132	-3	***	**	1	ns	ns
DBP not under drug treatment (mmHg)	85				83	10	83	84	77	10	76	78	-9	***	***	-6	***	***
Heart rate (beats per minute)	66				68	10	68	69	72	12	71	72	6	***	***	3	***	***
	%	95	% CI		% <u>95% CI</u>			% <u>95% CI</u>			÷	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 Uncontrolled	15	14	17		19	16	21		14	11	18		-1	ns	ns **	-4	*	ns *
Controlled	25 6	23	27 o		25 17	22	27 10		22	19	26 31		-2 20	ns ***	***	-2 10	ns ***	***
Controlled	О	5	8		1/	15	19		27	23	31		20		******	10		4.4.4

		WOMEN																					
		1998	-2002		;	2008	-2012		2	2018-	2019			2018-20	019		2018-20)19					
		n=2	955			n=2	204			n=1	066			vs 1998-	2002		vs 2008-2	2012					
	mean	SD	959	% CI	mean	SD	959	% CI	mean	SD	959	% (I	Diff	t-test sign^	Regression sign^^	Diff	t-test sign^	Regression sign^^					
	mean				mean				mean		337	<u> </u>	5	2.8.1	2.6	J	3.8.1	2.8					
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	<i>78</i>	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	***	***					
														chi-			chi-						
	%	95	% CI		%	95	% CI		%	95	% CI		Diff	squared sign^	Logistic sign^^	Diff	squared sign^	Logistic sign^^					
				-			-					•		J	J			J					
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	<i>37</i>		32	29	34		-13	***	***	-4	*	ns					
Hypertension			4-			•	0.5				2.2			***	*******								
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 < 0.001; *** p < 0.01; ** p < 0.05; ns not significant p-value. Raised blood pressure ≥90 mmHg or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥10 mmHg or diastolic blood pressure ≥90 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 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 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.

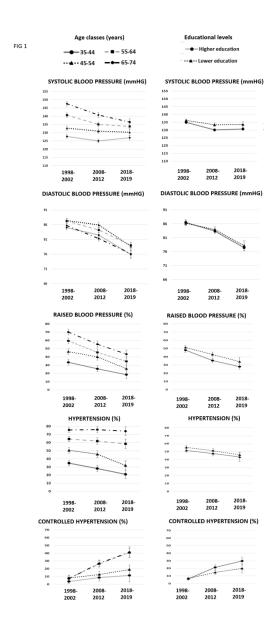


Figure 1. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident men aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

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)

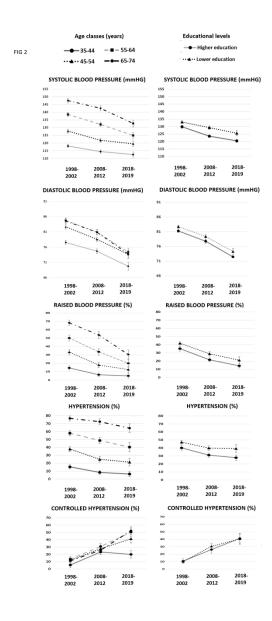


Figure 2. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident women aged 35-74 years, the CUORE Project Surveys 1998-2002, 2008-2012, and 2018-2019.

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)

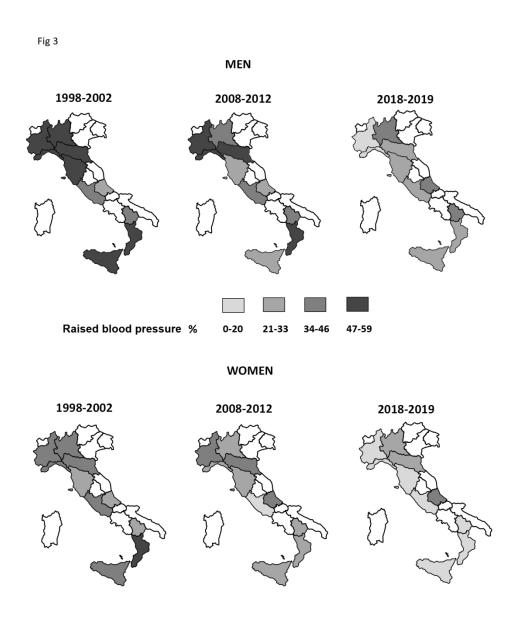


Figure 3. Prevalence of raised blood pressure based on measurements, by sex, Regions, and period.

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)

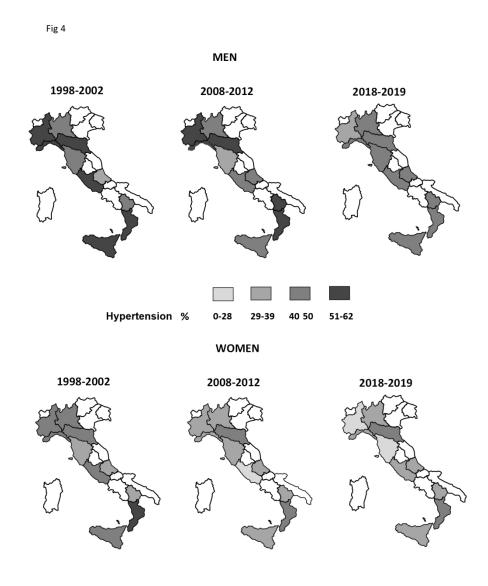


Figure 4. Prevalence of hypertension based on measurements, by sex, Regions, and period. Italian resident men and women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019. Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, 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.

			ME	N		
	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
			14/01	454		
			WON			
	1998-	2002	WON 2008-		2018-	2019
	1998-	2002			2018-	2019
Age class (years)	1998-	2002			2018-	2019
Age class (years)	1998- n	2002			2018- n	2019
Age class (years) 35-44			2008-	2012		
	n	%	2008- n	2012	n	%
35-44	n 715	% 24	2008- n 514	2012 % 23	n 237	% 22
35-44 45-54	n 715 769	% 24 26	2008- n 514 577	2012 % 23 26	n 237 271	% 22 25
35-44 45-54 55-64	n 715 769 778	% 24 26 26	2008- n 514 577 584	% 23 26 27	n 237 271 280	% 22 25 26
35-44 45-54 55-64 65-74	n 715 769 778	% 24 26 26	2008- n 514 577 584	% 23 26 27	n 237 271 280	% 22 25 26
35-44 45-54 55-64 65-74	n 715 769 778 693	% 24 26 26 23	2008- n 514 577 584 529	% 23 26 27 24	n 237 271 280 278	% 22 25 26 26

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.

												ME	N									
										Syste	olic blo	ood pre	essur	e (mm	Hg)							
		19	998-2	2002		ANOVA within		20	08-2	012		ANOVA within		20	18-2	019		ANOVA within	2018- vs 1998	·2019 8-2002	2018 vs 200	
Age class (years)	n	mean	DS	95%	6 CI	period sign ***	n	mean	DS	95%	s a	period sign	n	mean	DS	95%	6 CI	period sign ***	Diff	t-test sign	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 65-74	784 732	141 148	20 20	139 146	142 149		564 536	135 141	17 18	134 139	136 142		277 258	134 136	14 17	132 134	135 138		-7 -11	***	-1 -4	ns **
03-74	732	140	20	140	143		330	141	10			lood pr				104	130		-11			
		19	998-2	2002		ANOVA		20	08-2		.onc bi	ANOVA	essu	•	18-2	019		ANOVA	2018-		2018	
Age class					_	within period	_					within period						within period	vs 199	8-2002 t-test	vs 200	8-2012 t-test
(years)	n	mean	DS	95%	6 CI	sign ***	n	mean	DS	95%	s cı	sign ***	n	mean	DS	95%	6 CI	sign -	Diff	sign	Diff	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 65-74	784 732	87 86	11 10	87 85	88 86		564 536	84 81	10 10	83 80	85 82		277 258	79 76	9 10	78 75	80 77		-8 -10	***	-5 -5	***
03-74	102	00	10	00	00		000		10		02		200	70	10	7.5	.,,		-10		-5	
								Systoli	c blo	od pre	ssure	not un	der d	lrug tro	eatm	ent (n	nmHg)		2010	2242	2010	2010
		19	98-2	2002		ANOVA						ANOVA		20	18-2	019		ANOVA	2018- vs 1998		2018 vs 200	
Age class						within period						within period						within period		t-test		t-test
(years)	n	mean	DS	95%	6 CI	sign ***	n	mean	DS	95%	a	sign ***	n	mean	DS	95%	6 CI	sign - ***	Diff	sign	Diff	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 65-74	581 454	137 143	19 20	136 142	139 145		370 252	133 138	17 18	131 136	135 140		170 125	133 138	14 18	131 134	135 141		-4 -6	**	-0.2 -1	ns ns
							C	Diastoli	ic blo	od pre	essure	not un	der (drug tr	eatn	nent (ı	nmHg	:)				
		10	998-2	2002		ANOVA			08-2	•		ANOVA			18-2	•		ANOVA	2018-	2019	2018	-2019
A			750-2	2002		within		20	00-2	012		within period		20	10-2	013		within	vs 199		vs 200	
Age class (years)	n	mean	DS	95%	6 CI	period sign **	n	mean	DS	95%	s cı	sign ***	n	mean	DS	95%	6 CI	period sign - ns	Diff	t-test sign	Diff	t-test sign
35-44	682	85	10	84	85		504	82	10	81	83		237	75	10	74	77	5	-9	***	-7	***
45-54	640	86	11	86	87		481	85	10	84	86		212	77	10	76	78		-9	***	-8	***
55-64 65-74	581 454	86 84	10 10	85 83	87 85		370 252	84 81	10 10	83 80	85 82		170 125	78 77	9 11	77 75	79 79		-8 -8	***	-6 -4	***
03 74		• •																	-0			
										Hea	art rat	e (beat	s pei	r minut	te)				2010	2242	2010	2010
		19	998-2	2002		ANOVA within		20	08-2	012		ANOVA within		20	18-2	019		ANOVA within	2018- vs 1998	8-2002		-2019 8-2012
Age class (years)	n	mean	DS	95%	6 CI	period sign	n	mean	DS	95%	s cı	period sign	n	mean	DS	95%	6 CI	period sign	Diff	t-test sign	Diff	t-test sign
35-44	715	66	10	65	67	ns	530	68	9	67	69	ns	248	72	12	70	73	ns	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<0.001; ** 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.

65-74

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.

												NOME	V									
										Systoli	c bloo	d press	ure ((mmHg)								
		19	98-20	002		ANOVA within		20	08-2	012		ANOVA within		2018	3-201	١9		ANOVA within	2018 vs 199	-2019 8-2002		-2019 8-2012
Age class (years)	n	mean	DS	95%	6 CI	period sign	n	mean	DS	95%	í CI	period sign	n	mean	DS	_9	5% CI	period sign	Diff	t-test sign	Diff	t-test sign
35-44	715	118	14	117	119		514	114	13	113	116		237	113	13	11	1 114		-6	***	-2	ns
45-54	769	128	18	126	129		577	122	15	121	123		271	120	16		8 121		-8	***	-2	*
55-64 65-74	778 693	139 147	20 20	137 146	140 149		584 529	132 143	18 20	131 141	134 144		280 278	125 133	16 19		3 127 0 135		-14 -15	***	-7 -10	***
												ad nrac										
		10	00.34	002				20	ı 08-2		ic biod		sure	(mmHg	-				2018	-2019	2018	-2019
		19:	98-2	002		ANOVA within		20	08-2	012		ANOVA within		2018	3-201	19		ANOVA within	vs 199	8-2002	vs 200	8-2012
Age class (years)	n	mean	DS	95%	6 CI	period sign	n	mean	DS	95%	6 CI	period sign	n	mean	DS	_ 9	5% CI	period sign	Diff	t-test sign	Diff	t-test sign
35-44	715	78	10	77	78	***	514	75	9	74	75	***	237	70	10	6	3 71	***	-8	***	-5	***
45-54	769	83	11	82	83		577	79	9	78	79		271	74	11	7			-9	***	-5	***
55-64	778	85	10	84	85		584	81	10	80	82		280	74	11	7			-10	***	-7	***
65-74	693	85	10	84	85		529	81	10	80	82		278	74	11	7:	2 75		-11	***	-7	***
							Sys	stolic k	olood	l press	ure no	ot unde	r dru	g treat	ment	t (n	nmHg)					
		19	98-2	002		ANOVA within		20	08-2	012		ANOVA within		2018	3-2019			ANOVA within	2018 vs 199	-2019 8-2002		-2019 8-2012
Age class (years)	n	mean	DS	95%	6 CI	period sign -	n	mean	DS	95%	6 CI	period sign	n	mean	DS	_9	5% CI	period sign	Diff	t-test sign	Diff	t-test sign
35-44	698	118	14	116	119		499	114	12	113	115		234	112	13	11	1 114		-5	***	-1	ns
45-54	657	125	17	124	126		510	120	15	119	122		238	118	15		6 120		-7	***	-2	*
55-64 65-74	539 374	134 142	18 18	132 140	135 144		401 244	128 138	17 20	126 135	130 140		203 122	123 127	17 16		1 126 4 130		-10 -15	***	-4 -10	**
03-74	0, 1	172	10	110															-13		-10	
							Dia				sure n		er dru	ug treat		-	nmHg)		2018	-2019	2018	-2019
		19	98-2	002		ANOVA within		20	08-2	012		ANOVA within		2018	3-201	L9		ANOVA within	vs 199			8-2012
Age class (years)	n	mean	DS	95%	6 CI	period sign	n	mean	DS	95%	í CI	period sign	n	mean	DS	_9	5% CI	period sign	Diff	t-test sign	Diff	t-test sign
35-44	698	77	10	76	78	***	499	74	8	74	75	***	234	70	10	6	3 71	**	-8	***	-5	***
45-54	657	81	10	81	82		510	78	9	77	79		238	73	11	7			-9	***	-5	***
55-64	539	83	10	82	83		401	79	9	79 70	80		203	73	11	7:			-9	***	-6	***
65-74	374	83	9	82	83		244	80	9	79	81		122	71	9	/	73		-11	***	-9	***
										Heart	rate	(beats	oer m	ninute)								
		19	98-2	002		ANOVA within	2000-2012			ANOVA within		2018	3-201	19		ANOVA within		-2019 8-2002		-2019 8-2012		
ge class (years)	n	mean	DS	95%	 6 CI	period sign	n	mean	DS	95%	 6 CI	period sign	n	mean	DS	9	5% CI	period sign	Diff	t-test sign	Diff	t-test sign
						**						ns						ns		ub -8-		
		71	11	70	72		514	72	9	71	72		237	74	11	7	3 75		3	**	2	**
35-44 45-54	711 769	70	10	69	71		577	71	9	70	71		271	73	10	7:	2 74		3	***	3	**

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<0.001; *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.

71 10

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.

N	Λ	F	Λ
1	"	_	1

		MEN																				
								Sy	/sto	lic b	lood	pressur	re (m	ımHg)								
		1998	-200)2		OVA thin		2008	3-20)12		ANOVA within		201	8-20)19		ANOVA within)18-)19		018- 019
Educational level	n	mean	DS_	95%	pe CI si	riod ign **	n	mean	DS	959	% CI	period sign	n	mean	DS _	95%	6 CI	period sign ***	Diff	t-test sign	Diff	t-test sign
Higher education Lower education	1249 1730	135 136	17 1 18 1	134 135	136 137		1183 1018			129 132	131 134		725 303	131 134		130 132			-4 -3	***	1 0.2	ns ns
								Di	ast	olic b	lood	pressu	re (n	nmHg)							
		1998	-200)2		OVA thin		2008	3-20)12		ANOVA within		201	8-20)19		ANOVA within)18-)19		018- 019
Educational level	n	mean	DS_	95%	pe	riod ign	n	mean	DS	959	% CI	period sign	n	mean	DS	95%	6 CI	period sign	Diff	t-test sign	Diff	t-test sign
Higher education Lower education	1249 1730	87 86			87 87	ns	1183 1018		10 10	83 83	84 85	ns	725 303	77 78	10 10	77 77	78 79	ns	-9 -8	***	-6 -6	***
Lower education	1730	00		00	07	C: ea											-		-0		-0	
						Sys	tolic b	ilooa p	ores	sure	not	under d	arug	treatr	nen	t (mi	m n g,		20	18-	20	018-
		1998-2002				OVA thin	2000-2012				ANOVA 2018-2019 within						ANOVA		019		019	
Educational level	n	mean	DS_	95%	pe CI si	riod ign	n	mean	DS	955	% CI	period sign	n	mean	DS	95%	6 CI	within period sign	Diff	t-test sign	Diff	t-test sign
Higher education	1046	133	16 :	132		**	913	129	15	128	130	***	537	130	13	129	131	***	-3	***	1	ns
Lower education	1305	134	17 1	133	135		680	131	16	130	133		205	133	15	131	135		-1	ns	1	ns
						Dias	tolic l	blood	pre	ssure	e not	under	drug	treat	mer	nt (m	mHg	:)				
		1998	3-200)2	AN	OVA		2008	8-20)12		ANOVA		201	8-20)19		ANOVA)18-)19		018- 019
Educational level				<u>-</u>	— wi	thin					T	within period						within period		t-test		t-test
Edded: Ond Tevel	n	mean	DS_	95%	CI si	ign ns	n	mean	DS	959	% CI	sign ns	n	mean	DS _	95%	6 CI	sign ns	Diff	sign	Diff	sign
Higher education	1046	86			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	***
								H	lea	rt ra	te (be	eats pe	r mir	ute)								
	1998-2002					OVA thin	20		2008-2012		ANOVA within		201	8-20)19		ANOVA within)18-)19		018- 019	
Educational level	n	mean	DS_	95%	CI si	e riod i gn ns	n	mean	DS	955	% CI	period sign ns	n	mean	DS	95%	6 CI	period sign **	Diff	t-test sign	Diff	t-test sign
Higher education	1244	66	11	65		13	1183	68	9	68	69	113	725	71	11	70	72		5	***	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: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, and Sicily.

74 12 73 76

1018 68 10 68 69

66 11 *65 67*

Lower education

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

	WOMEN																					
								Sys	toli	c blo	od pı	essure	(mm	Hg)								
		4000		00		ANOVA		2000	20	4.5		ANOVA		204	0.20	10		ANOVA		18-		18-
		1998	3-20	02		within -		2008	-20.	12		within		201	8-20	119		within		019		019
Educational level	n	mean	std	95%	6 CI	period sign ***	n	mean	std	95%	% CI	period sign	n	mean	std _	95%	% CI	period sign - ***	Diff	t-test sign	Diff	t-test sign
Higher education Lower education	1052 1887	130 133	16 18	129 132	131 134		1167 1017	124 129		123 128	124 130		725 339	120 126		119 124	122 127		-9 -7	***	-3 -4	***
								Dia	stol	ic blo	ood p	ressure	(mn	nHg)								
		1998	3-20	02		ANOVA		2008	3-20:	12		ANOVA within		201	8-20	19		ANOVA within)18-)19)18-)19
Educational level	n	mean	std	95%	6 CI	period sign	n	mean	std	95%	% CI	period sign	n	mean	std	95%	% CI	period sign	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	***
						Svst	olic bl	ıq boo	ess	ure r	not ui	nder dr	ug tr	eatme	ent (mml	Hg)					
						ANOVA						ANOVA	2010 2010							18-		18-
		1998	3-20	02		within		2008	08-2012		within		201	8-20)19		within	20	019		019	
Educational level	n	mean	std	95%	6 CI	period sign ***	n	mean	std _	95%	% CI	period sign ***	n	mean	std _	95%	% CI	period sign ***	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	*
						Diast	olic b	lood p	ress	ure	not u	nder dr	ug tr	eatm	ent ((mm	Hg)					
		1998	R-20	02		ANOVA		2008	-20	12		ANOVA		201	8-20	119		ANOVA)18-)19)18-)19
		1330		<u> </u>		within _ period						within , period			-			within period		t-test		t-test
Educational level	n	mean	std	95%	6 CI	sign ***	n	mean	std _.	959	6 CI	sign ***	n	mean	std _	959	% CI	sign - *	Diff	sign	Diff	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 (k							(bea	eats per minute)													
	1998-2002			ANOVA within		2008	3-20:	12		ANOVA		201	8-20)19		ANOVA within)18-)19)18-)19		
Educational level						period						within , period						period	Diff	t-test		t-test
-3000000101010001	n	mean	std	95%	6 CI	sign ns	n	mean	std	95%	% CI	sign ns	n	mean	std	95%	% CI	sign ns		sign		sign
Higher education	1047	69	11	69	70	113	1167	71	9	70	72		725	73	10	72	73	.13	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.

								IV	1EN								
							Bloc	od pressure	drug	treat	ment						
		1998-2	2002	Chi-squared test within	2	2008-2	2012	Chi-squared test within	2	018-2	2019		Chi-squared test within		18-2019 998-2002		8-2019 08-2012
Age class				period sign				period sign					period sign	Diff	chi- squared	Diff	chi- square
(years)	n	%	95% CI	- ***	n	%	95% CI	- ***	n	%	95%	CI	***		sign		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		14		13	***	4	ns
65-74	732	38	34 41		536	53	49 57	Raised blo	258	52		58		14	**	-1	ns
								Maiseu Dio	ou pi	essui	-			20	18-2019	2015	8-2019
	· ·	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	2018-2	2019		Chi-squared		998-2002		08-2012
Age class				test within period				test within period					test within period	Diff	chi-	Diff	chi-
(years)	n	%	95% CI	sign	n	%	95% CI	sign	n	%	95%	CI	sign	υш	squared sign	DIII	square sign
	910			***				***			10000		***				
35-44	717	33	30 37		530	26	22 29		248	19		23		-15	***	-7	*
45-54	752	46	43 50		588	40	36 44		248	26		31		-21	***	-14	***
55-64 65-74	784 732	59 70	56 63 67 73		564 536	46 55	41 50 51 60		277 258	35 43		10 19		-25 -27	***	-11 -12	**
03-74	732	70	07 73		330	33	51 60				37	+3		-21		-12	
								Hyper	tensio	on					40.0040	201	
	1	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019		Chi-squared		18-2019 998-2002		8-2019 08-2012
Age class				test within period				test within period					test within period		chi-		chi-
(years)	n	%	95% CI	sign	n	%	95% CI	sign	n	%	95%	CI	sign	Diff	squared sign	Diff	square sign
				***				***				J.	**				
35-44	717	35	31 38		530	28	24 32		248	21		26		-14	***	-7	*
45-54	752	51	47 54		588	46	42 50		248	32		38		-19	***	-14	**
55-64	784	64	61 68		564	62	58 66		277	58		54		-6	ns	-3	ns
65-74	732	76	72 79		536	76	72 80		258	74		79		-2	ns	-2	ns
							Ur	ndiagnosed	nype	rtens	ion			20	10 2010	2016	2010
	1	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019		Chi-squared		18-2019 998-2002		8-2019 08-2012
Age class				test within period				test within period					test within period		chi-		chi-
(years)	n	%	95% CI	sign	n	%	95% CI	sign	n	%	95%	CI	sign	Diff	squared sign	Diff	square
				**				***					***				
35-44	249	67	62 73		149	54	46 62		52	62		75		-6	ns	8	ns
45-54	380	52	47 57		269	40	34 46		79	35		16		-16	**	-4	ns
55-64 65-74	505 553	48 39	44 52 35 43		349 407	32 25	27 37 20 29		162	23		30 27		-25 -18	***	-8 -3	ns
03-74	333	35	33 43		407				191					-10		-3	ns
							Diagnos	ed but unt	reated	d hyp	erten	iois	n		40.0040	204	8-2019
	1	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019		Chi-squared		18-2019 998-2002		08-2019
Age class				test within period				test within period					test within period	Diff	chi-	Diff	chi-
(years)	n	%	95% CI	sign	n	%	95% CI	sign	n	%	95%	CI	sign	Diff	squared sign	Diff	square
				***				***					ns				
35-44	249	18	14 23		149	29	22 36		52	17		28		-1	ns	-12	ns
45-54	380	19	15 23		269	20	16 25		79	19		28		0.0	ns	-1	ns
55-64 65-74	505 553	12 10	9 14 8 13		349 407	13 6	9 16 3 8		162 191	10 9		15 13		-1 -1	ns ns	-2 3	ns ns
03-74	222	10	U 13		407	J						ر		-1	115	,	115
							Ur	ncontrolled	hype	rtens	ion						
	1	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019		Chi-squared		18-2019 998-2002		8-2019 08-2012
Al				test within				test within					test within	V5 1	chi-	VS 201	chi-
Age class (years)				period sign		0.0		period sign		0.6			period sign	Diff	squared	Diff	square
	n	%	95% CI	***	n	%	95% CI	***	n	%	95%	Cl	ns		sign		sign
					149	9	4 13		52	10	2	18		-1	ns	1	ns
35-44	249	10	7 14			27	22 32		79	27	17	36		5	ns	-1	ns
35-44 45-54	249 380	10 21	7 14 17 25		269	21											
					269 349	29	24 34		162	25	19	32		-7	ns	-4	ns
45-54	380	21	17 25						162 191	25 28	19 22			-7 -15	ns **	-4 -14	ns **
45-54 55-64	380 505	21 32	17 25 28 37		349	29	24 34 38 48	Controlled	191	28	22						
45-54 55-64	380 505 553	21 32 43	17 25 28 37 39 47		349 407	29 43	24 34 38 48		191 hyper	28 tensio	<i>22</i> on			-15		-14	
45-54 55-64	380 505 553	21 32	17 25 28 37 39 47	Chi-squared test within	349 407	29	24 34 38 48	Chi-squared	191 hyper	28	<i>22</i> on		Chi-squared test within	-15 20	** 18-2019 998-2002	-14 2018	** 8-2019 08-2012
45-54 55-64 65-74 Age class	380 505 553	21 32 43	17 25 28 37 39 47	test within period	349 407	29 43	24 34 38 48	Chi-squared test within period	191 hyper	28 tensio	<i>22</i> on		test within period	-15 20	** 18-2019 998-2002 chi-	-14 2018	** 8-2019 08-2012 chi-
45-54 55-64 65-74	380 505 553	21 32 43	17 25 28 37 39 47	test within	349 407	29 43	24 34 38 48	Chi-squared test within period sign	191 hyper	28 tensio	<i>22</i> on	35	test within period sign	-15 20 vs 1	** 18-2019 998-2002	-14 2018 vs 200	** 8-2019 08-2012 chi-
45-54 55-64 65-74 Age class (years)	380 505 553	21 32 43 1998-2	17 25 28 37 39 47 2002	test within period	349 407	29 43 2008- 2	24 34 38 48 C2012	Chi-squared test within period	191 hyperi 2	28 tensio	22 on 2019	35 CI	test within period	-15 20 vs 1	** 18-2019 998-2002 chi- squared sign	-14 2018 vs 200 Diff	** 8-2019 08-2012 chi- square sign
45-54 55-64 65-74 Age class (years)	380 505 553 1 n	21 32 43 1998-2	17 25 28 37 39 47 2002 95% CI 1 6	test within period sign	349 407 n 149	29 43 2008-7 %	24 34 38 48 C2012 95% C1 4 13	Chi-squared test within period sign	191 hypert	28 ttensio	22 on 2019 95%	35 CI 20	test within period sign	-15 20 vs 1 Diff	** 18-2019 998-2002 chi- squared	-14 2018 vs 200 Diff	** 8-2019 08-2012 chi- square- sign
45-54 55-64 65-74 Age class (years)	380 505 553	21 32 43 1998-2	17 25 28 37 39 47 2002	test within period sign	349 407	29 43 2008- 2	24 34 38 48 C2012	Chi-squared test within period sign	191 hyperi 2	28 tensio	22 on 2019 95% 3 10	35 CI	test within period sign	-15 20 vs 1	** 18-2019 998-2002 chi- squared sign	-14 2018 vs 200 Diff	** 8-2019 08-2012 chi- squared

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.

3-20									WOMEN								
						- 1	Blood	pres	sure drug	trea	tme	nt					
1	199	3-200	2	Chi-squared		200	8-201	2	Chi-squared		201	8-201	L9		998-2002		18-2019 008-2012
n	%	95%	6 CI	period sign	n	%	95%	6 CI	period sign	n	%	959	% CI	Diff	squared	Diff	chi- squared sign
715	2	1	3	***	514	3	1	4	***	237	1	0	3	-1		-2	ns
769	15	12	17		577	12	9	14		271	12	8	16	-2	ns	1	ns
		27 42	34 50				28 50	35 58				<i>22 50</i>	33 62	-3 10	ns **	-4 2	ns ns
							R	laised	l blood pre	essur	re						
1	1998	3-200	2	Chi-squared		200	8-201	.2	Chi-squared		201	8-201	L9				18-2019 008-2012
	0/	050	(CI	test within period sign		0/	050	<i>(6</i>)	test within period sign		0/	050	V 61	Diff	chi- squared	Diff	chi-
				***	-	_			***								
															***		ns *
778		47	54			34	30	38		280		15	25	-30	***	-14	***
693	68	65	72		529	54	50	58		278	31	25	36	-38	***	-23	***
								H	ypertensio	n							
1	1998	3-200	2	Chi-squared		200	8-201	2	Chi-squared		201	8-201	19				18-2019 008-2012
				test within period					test within period						chi-		chi- squared
n	%	959	6 CI	sign -	n	%	95%	6 CI	sign	n	%	959	6 CI		sign	D	sign
715	15	13	18	***	514	8	6	11	***	237	6	3	9	-9	* *	-2	ns
769		35	41				21	28		271	21	17	26	-17	***	-4	ns
778	58	55	61		584	49	45	53		280	40	35	46	-18	***	-8	*
693	77	74	80		529	73	69	76		278	64	59	70	-12	***	-8	*
							Unc	liagno	osed hype	rtens	sion	ř					
1	1998	3-200	2	Chi-squared		200	8-201	2	Chi-squared		201	8-201	L 9				18-2019 008-2012
		7:		test within period					test within period						chi-		chi-
n	%	95%	6 CI	sign ***	n	%	95%	6 CI	sign ***	n	%	959	% CI	Diff	squared sign	Diff	squared sign
		53	71		43	40	25	54		15	47	21	72	-15	ns	7	ns
																	ns ns
		28	36				16	23				6	15	-22	***	-9	**
						Diag	nose	d but	untreated	hyp	ert	ensio	n				
1	199	3-200	2	Chi-squared		200	8-201	2	Chi-squared		201	8-201	L9		998-2002		18-2019 008-2012
n	%	95%	6 C I	period sign	n	%	95%	6 C I	period sign	n	%	959	% CI	Diff	chi- squared sign	Diff	chi- squared sign
110	23	15	31	***	43	26	13	39	**	15	33	9	57	11	ns	8	ns
		12	21				9	20		58	14	5	23	-3	ns	-1	ns
		10	17				8	16				5	16	-3	ns	-2	ns ***
532	8	6	10		384	6							4	-6	***	-4	***
							Unc	ontro	olled hype	rtens	sion	1		20	10 2010	201	18-2019
	1998	3-200	12	Chi-squared		200	8-201	2	Chi-squared		201	8-201	19		998-2002		008-2012
n	%	95%	6 CI	period sign	n	%	95%	6 CI	period sign	n	%	959	% CI	Diff	squared sign	Diff	chi- squared sign
110	10	4	16	***	43	12	2	21	***	15	0	0	0	-10	-	-12	-
292	26	21	31		144	19	12	25		58	16	6	25	-11	ns	-3	ns
		35	44				28	39				11	25	-22	***	-16	**
532	49	45	53		384	48						28	42	-14	***	-14	***
							Co	ntrol	led hypert	ensi	on						
1	1998	3-200	2	Chi-squared test within		200	8-201	2	Chi-squared test within		201	8-201	19		998-2002		18-2019 008-2012
				period sign		%	95%	(C'	period sign		0/		V 61	Diff	chi- squared	Diff	chi- squared
_	0/	050	(()	Jig.i													
n	%	959		ns	n	-			ns	n	%	959	- 121		sign		sign
110	5	1	10	_	43	23	11	36	ns	15	20	0	40	15	sign *	-3 14	ns
	5 12			_		23 28			ns		20 41		- 121	15 29 37	*	-3 14 20	
	n 715 769 778 693	n % 715 2 769 15 778 31 693 46 1998 n % 715 15 769 33 778 50 693 68 1998 n % 110 62 292 45 451 33 532 32 1998 n % 110 23 292 16 451 14 532 8 1998 n % 110 10 292 26 451 39 532 49	n % 95% 715 2 1 769 15 12 778 31 27 693 46 42 1998-200 n % 95% 715 15 12 769 33 30 778 50 47 693 68 65 1998-200 n % 95% 715 15 13 769 38 35 778 58 55 693 77 74 1998-200 n % 95% 110 62 53 292 45 40 451 33 29 532 32 28 1998-200 n % 95% 110 23 15 292 16 12 451 14 10 532 8 6	715 2 1 3 769 15 12 17 778 31 27 34 693 46 42 50 1998-2002 n % 95% CI 715 15 12 17 769 33 30 37 778 50 47 54 693 68 65 72 1998-2002 n % 95% CI 715 15 13 18 769 38 35 41 778 58 55 61 693 77 74 80 1998-2002 n % 95% CI 110 62 53 71 292 45 40 51 451 33 29 38 532 32 28 36 1998-2002 n % 95% CI 110 23 15 31 291 6 12 21 451 14 10 17 532 8 6 10 1998-2002 n % 95% CI	n % 95% CI	n % 95% CI rest within period sign n	1998-2002	1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 110 62 53 71 43 40 25 144 39 31 445 133 29 38 285 24 19 384 20 16 Chi-squared test within period sign n % 95% CI 110 62 53 71 43 40 25 144 39 31 285 24 19 384 20 16 Chi-squared test within period sign n % 95% CI 110 23 15 31 44 4 39 31 285 24 19 384 20 16 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 1998-2002 Chi-squared test within period sign n % 95% CI 144 15 9 25% CI	1998-2002	1998-2002	1998-2002	1998-2002	1998-2002	1998-2002	1998-2002 Chi-spaned rest within period sign N	1998-2002 Chi-squared test within period sign N 95% CI Chi-squared test within period sign N 9	1998-2002 Chi-squared less within period sign N 95% CI Chi-squared less within

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.

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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.

	_								MI	EN							
									pressure	drug	treat	tment		20	18-2019	201	18-2019
	19	998-7	2002	Chi-squared test within period	2	008-	201	2	Chi-squared test within period		2018	-2019	Chi-squared test within period		998-2002 chi-		008-2019 chi-
Educational level	n	%	95% CI	sign — ns	n	%	95	% CI	sign ns	n	%	95% CI	sign - ns	Diff	squared sign	Diff	squared sign
Higher education Lower education	1249 1730	18 19	16 20 18 2)	1183 1018	24 25	22 22		113	725 303	26 24	23 29 19 29	713	8 5	*** ns	2 -1	ns ns
								F	Raised bloc	od pre	ssur	e					
	1	998-	2002	Chi-squared test within	2	008-	201	2	Chi-squared test within	2	2018	-2019	Chi-squared test within		18-2019 998-2002 chi-		18-2019 008-2012 chi-
Educational level	n	%	95% CI	period sign	n	%	95	% CI	period sign	n	%	95% CI	period sign	Diff	squared sign	Diff	squared sign
Higher education Lower education	1249 1730	48 51	45 5 49 5		1183 1018	35 43	33 40	38 46	**	725 303	28 34	25 31 29 39	ns	-20 -17	***	-7 -9	**
									Hypert	ensio	n						
	1	998-	2002	Chi-squared	2	008-	201	2	Chi-squared		2018	-2019	Chi-squared		18-2019 998-2002		18-2019 008-2012
Educational level	n	%	95% CI	test within period sign	n	%	95	% CI	test within period sign	n	%	95% CI	test within period sign	Diff	chi- squared sign		chi- squared sign
Higher education	1249 1730	51 55	49 54 53 58		1183 1018	48 51	45 48	51 54	ns	725 303	43 46	40 47 40 52	ns	-8 -9	**	-4 -5	ns ns
Lower education	1750	33	55 56	,	1010	J1	70		P1					-9		-3	113
	1	000	2002	AMOR TO STORY OF A	,	000	201		diagnosed					20	18-2019	201	18-2019
	1:	990-	2002	Chi-squared test within period		008-	-201	2	Chi-squared test within period	-	2010-	-2019	Chi-squared test within period	vs 1	998-2002 chi-	vs 20	008-2012 chi-
Educational level	n	%	95% CI	sign — ns	n	%	95	% CI	sign ns	n	%	95% CI	sign - ns	Diff	squared sign	Diff	squared sign
Higher education Lower education	621 1063	53 54	49 57 51 57		555 610	38 40	34 36	42 44		314 168	36 38	30 41 30 45		-18 -16	***	-2 -2	ns ns
							Diag	gnose	d but untr	eated	l hyp	ertensio	n				
	1	998-	2002	Chi-squared test within	2	008-	201	2	Chi-squared test within	2	2018	-2019	Chi-squared test within		18-2019 998-2002		18-2019 008-2012
Educational level	n	%	95% CI	period sign	n	%	95	% C I	period sign	n	%	95% CI	period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	621 1063	16 15	13 15 13 17		555 610	20 16	17 13	23 19	ns	314 168	13 16	10 17 10 21	ns	-3 1	ns ***	-6 -0.4	* ns
								Und	controlled	hypei	rtens	ion					
	1	998-	2002	Chi-squared test within	2	008-	201	2	Chi-squared test within	1	2018-	-2019	Chi-squared test within		18-2019 998-2002		18-2019 108-2012
Educational level	n	%	95% CI	period sign	n	%	95	% CI	period sign	n	%	95% CI	period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	621 1063	24 25	21 28 22 21		555 610	21 29	18 25		**	314 168	21 26	17 26 20 33	ns	-3 2	ns ***	0.1	ns ns
								Co	ontrolled h	ypert	ensi	on					
	1	998-2	2002	Chi-squared test within	2	008-	201	2	Chi-squared test within	7	2018	-2019	Chi-squared test within		18-2019 998-2002 chi-	0.00	18-2019 008-2012 chi-
Educational level	n	%	95% CI	period sign — ns	n	%	95	% CI	period sign **	n	%	95% CI	period sign - *	Diff	squared sign	Diff	squared sign
Higher education Lower education	621 1063	6 7	4 8 5 8		555 610	21 15	18 12			314 168	30 20	25 35 14 26		24 13	***	8 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.

								Blo	od p	ressure dr	ug tre	eatm	ent						
	19	998-2	2002			2	008-	2012			2	018-	2019)			18-2019 998-2002		8-2019 08-2012
tional level					Chi-squared test within period sign					Chi-squared test within period sign					Chi-squared test within period sign		chi- squared sign	Diff	chi- squared
	n	%	95%	CI	***	n	%	95%	6 CI	***	n	%	95%	6 CI	**				
lucation ucation	1052 1887	16 23	14 22	19 25		1167 1017	19 26	16 23	21 28		725 339	19 27	17 23	22 32		3	ns ns	1 2	ns ns
									Rai	sed blood	press	ure							
	1	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	2018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
onal level					test within period sign					test within period sign					test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
	n	%	95%	CI	**	n	%	95%	6 CI	***	n	%	95%	6 CI	**		sign		sign
ation ation	1052 1887	35 42	32 40	38 44		1167 1017	22 29	19 26	24 32		725 339	14 21	12 17	17 25		-21 -21	***	-7 -8	***
										Hyperter	nsion								
	1	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	2018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
al level					test within period sign					test within period sign					test within period sign		chi- squared sign		chi- squared sign
	n	%	95%	CI	**	n	%	95%	6 CI	***	n	%	95%	6 CI	**		3igii		Jigii
ducation ducation	1052 1887	40 47	37 45	43 49		1167 1017	31 40	28 37	34 43		725 339	28 39	25 34	31 44		-12 -8	***	-3 -1	ns ns
								u	Jndia	gnosed hy	perte	nsio	n						
	19	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
ional level	n	%	95%	C	test within period sign	n	%	95%	(C)	test within period sign	n	%	95%	(CI	test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
					ns					**					ns				
education education	337 1037	47 43	42 40	53 46		311 534	36 25	31 21	42 28		192 172	27 29	21 23	34 36		-20 -14	***	-9 5	ns
							Di	agno	sed	but untrea	ted h	yper	tens	ion					
	19	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
onal level	п	%	95%	í CI	test within period sign	п	%	95%	á CI	test within period sign	п	%	95%	á CI	test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
			1000		ns					ns					ns				
ucation ucation	337 1037	19 15	14 13	23 18		311 534	15 17	11	19 20		192 172	16 13	8	22 18		-2 -3	ns ***	1 -4	ns *
								U	Jnco	ntrolled hy	perte	nsio	n						
	19	998-2	2002		Chi-squared test within	2	008-	2012		Chi-squared test within	2	2018-	2019)	Chi-squared test within		18-2019 998-2002		8-2019 108-2012
onal level					period sign					period sign					period sign	Diff	chi- squared	Diff	chi- squared
	n	%	95%		**	n	%	95%		ns	n	%	95%		ns		sign		sign
lucation lucation	337 1037	23 31	19 29	28 34		311 534	22 28	18 25	27 32		192 172	15 17	10 12	20 23		-8 -14	***	-7 -11	ns *
									Cont	trolled hyp	erten	sion							
	19	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
					test within period sign					test within period sign					test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
tional level		01											_						
onal level	n	%	95%	CI	ns	n	%	95%	6 CI	ns	n	%	95%	6 CI	ns		oig.i		-

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

									М	EN								
		Syst		ood pres nHg)	sure	Dias		ood pres nHg)	sure		ised blo pressure		Ну	pertens	ion	_	ontrolle pertens	_
Italian Region	n	mean	SD	95	%CI	mean	SD	959	%CI	%	95%	S CI	%	95%	s CI	%	95%	S 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	<i>75</i>	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	<i>75</i>	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	<i>3</i> 5

WOMEN

		Syst		od pres nHg)	sure	Dias		ood pres nHg)	sure		ised blo pressure		Ну	pertens	ion		ontrolle pertensi	
Italian Region	n	mean	SD	959	%CI	mean	SD	959	%CI	%	95%	6 CI	%	95%	S CI	%	95%	S CI
Abruzzo	104	122	17	118	125	73	10	71	<i>7</i> 5	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	<i>57</i>
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		2	2008	-2012	2	2	018	2019)	201	8-2019	201	8-2019
		n=2	985			n=2	218			n=1	031		vs 19	98-2002	vs 20	08-2012
	mean	SD	959	% CI	mean	SD	959	% CI	mean	SD	959	6 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	***
														chi-		chi-
	%	959	% CI		%	959	% CI		%	959	% CI		Diff	squared p-value	Diff	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	***

								W	OIVIEN							
		1998- n=2:	2002 951		2	008	-2012 185	!	2	018 n=1	- 201 9			8-2019 98-2002		8-2019 08-2012
	mean	SD	959	% CI	mean	SD	959	6 CI	mean	SD	959	% 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	***
													Diff	chi- squared	Diff	chi- squared
	%	959	6 CI		%	95	% CI		%	95	% CI			p-value		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	22	122					7200		200					25.27		
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	***

WOMEN

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										
									Systo	lic bloo	d press	ure (mmHg	g)							
		199	98-20	002	ANOVA		20	08-2	012		ANOVA		20	18-2	2019		ANOVA		-2019 8-2002		-2019 8-2012
Educational level	n	mean	SD _	95% CI	within period sign ***	n	mean	SD _	95	% CI	within period sign	n	mean	SD_	95%	s CI	within period sign	Diff	t-test sign	Diff	t-test sign
Higher education Lower education	1249 1730	135 137	17 18	135 136 136 138		1183 1018	131 134	15 17	130 133	131 135		725 303	131 134	14 16	130 132	132 135		-5 -3	***	0.1 -0.3	ns ns
								ı	Diasto	olic bloc	d press	ure ((mmH	g)							
		199	98-20	002	ANOVA		20	08-2	012		ANOVA		20	18-2	2019		ANOVA		-2019 8-2002		-2019 8-2012
Educational level	n	mean	SD_	95% CI	within period sign	n	mean	SD_	95	% CI	within period sign	n	mean	SD_	95%	s CI	within period sign	Diff	t-test sign	Diff	t-test sign
Higher education Lower education	1249 1730	87 86	11 11	86 87 86 87	ns	1183 1018	83 84	10 10	83 83	84 84	ns	725 303	77 78	10 10	77 77	78 79	ns	-9 -8	***	-6 -6	***
						Sys	tolic b	lood	l pres	sure no	t unde	r dru ;	g treat	tmei	nt (mr	nHg)					
		199	98-20	002	ANOVA		20	08-2	012		ANOVA		20	18-2	2019		ANOVA		-2019 8-2002		-2019 8-2012
Educational level	n	mean	SD_	95% CI	within period sign	n	mean	SD_	95	% CI	within beriod sign	n	mean	SD_	95%	í CI	within period	Diff	t-test sign	Diff	t-test sign
Higher education	1046 1305	134 134	16 17	133 135 133 135	***	913 680	129 132	15 16	128 131	130 133	***	537 205	130 133	13 15	129 131	131 135	***	-4 -1	*** ns	1 1	ns ns
Lower education	1000	104	.,	700 700						ssure n	nt unde							-1	113	•	113
		100	98-20	002		J.0		08-2	•						2019				-2019 8-2002		-2019 8-2012
Educational level	_	mean		95% CI	ANOVA within period sign		mean			% CI	ANOVA within period sign	_	mean		95%	(CI	_ ANOVA within period sign	Diff	t-test sign	Diff	t-test sign
Higher education	n 1046	86	10	85 86	ns	n 913	83	10	82	83	ns	n 537	77	10	76	78	ns ns	-9	***	-6	***
Lower education	1305	85	10	85 86		680	83	10	83	84		205	77	9	76	78		-8	***	-6	***
									Hea	rt rate (beats p	er m	inute))							
		199	98-20	002	_ ANOVA		20	08-2	012		ANOVA		20	18-2	2019		ANOVA		-2019 8-2002		-2019 8-2012
Educational level	n	mean	SD	95% CI	within period sign	n	mean	SD _	95	% CI	within period sign	n	mean	SD	95%	s CI	within period sign	Diff	t-test sign	Diff	t-test sign
Higher education Lower education	1244 1730	66 66	11 11	65 67 65 67	ns	1183 1018	66 66	11 12	65 66	67 67	ns	725 303	71 74	11 12	70 73	71 76	**	5 8	***	5 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<0.001; *p-value<0.001; ** p-value<0.001; ** p-val 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.

•											V	VOMEN	ı									
									S	ystoli	c bloo	d press	ure (mmHg	:)							
						ANOVA						ANOVA						ANOVA	2018			-2019
		199	8-200	02		within		200	8-20	12		within		201	8-20	19		within	vs 199	8-2002	vs 200	8-2012
Educational level						period sign						period sign						period sign	Diff	t-test sign	Diff	t-test sign
	n	mean	SD	959	% CI	***	n	mean	SD	95%	6 CI	- ***	n	mean	SD	959	% CI	***		0		
Higher education	1052	130	16	129	131		1167	124	15	123	125		725	120	15		121		-10	***	-4	***
Lower education	1887	133	18	132	134		1017	130	18	129	131		339	125	17	123	127		-8	***	-4	***
									D	iastol	ic bloc	d press	ure ((mmHį	g)							
		199	8-200	02		ANOVA		200	8-20	12		ANOVA		201	8-20	19		ANOVA	2018- vs 199			-2019 8-2012
				-		within period						within period						within period		t-test		t-test
Educational level	n	mean	SD	959	% CI	sign	n	mean	SD	95%	6 CI	sign	n	mean	SD	959	% CI	sign	Diff	sign	Diff	sign
11:-1	1052	81	10	81	82	***	1167	78	9	77	78	***	725	72	11	72	73	**	•	***	_	***
Higher education Lower education	1887	83	10	82	83		1017	79	10	77 79	80		339	74	10	73	75		-9 -9	***	-6 -5	***
							Sys	tolic b	ood	press	ure no	t unde	r dru	g treat	men	t (mı	mHg)		2018-	2010	2010	-2019
		199	8-200	02		ANOVA		200	8-20	12		ANOVA		201	8-20	19		ANOVA	vs 199			8-2012
Educational level						within period						within period						within period	Diff	t-test	Diff	t-test
Educational level	n	mean	SD	959	% CI	sign	n	mean	SD	95%	6 CI	sign -	n	mean	SD	959	% CI	sign	Dill	sign	Dill	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	**
							Diag	talic h	lood	nross	uro n	ot unde	r dru	ıg tres	tmai	at (m	mHa	1				
							Dias	otolic b	1000	press	uie iii	ot unde	ı uıu	ig ti ca	tillei				2018	2019	2018	-2019
		199	8-200	02		ANOVA within		200	8-20	12		ANOVA within		201	8-20	19		ANOVA within	vs 199	8-2002	vs 200	8-2012
Educational level						period						period						period	Diff	t-test	Diff	t-test
	n	mean	SD	959	% CI	sign ***	n	mean	SD	959	6 CI	sign ***	n	mean	SD	959	% CI	sign		sign		sign
Higher education	928	81	10	80	81	4.4.4	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 p	or m	inuta)								
										i icai t	rate (beats p	ei iii	illute					2018	2019	2018	-2019
		199	8-200	02		ANOVA within		200	8-20	12		ANOVA within		201	8-20	19		ANOVA within	vs 199	8-2002	vs 200	8-2012
Educational level						period						period						period	Diff	t-test	Diff	t-test
	n	mean	SD	959	% CI	sign	n	mean	SD	95%	6 CI	sign -	n	mean	SD	959	% CI	sign		sign		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<0.005; 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.

									MEI	V								
							ВІ	ood	pressure d	rug tı	reatn	nent						
	1	998-2	2002		2	008-	2012	2		2	2018-	2019)			18-2019 998-2002		.8-2019 008-2012
Educational level	n	%	95%	Chi-squared test within period CI sign	n	%	95%	6 CI	Chi-squared test within period sign	n	%	95%	s cı	Chi-squared test within period sign ns	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	1249 1730	19 20	16 18	21 22	1183 1018	26 26	23 24	28 29	lis	725 303	26 24	23 19	29 29	115	7	** ns	0.2	ns ns
								Ra	ised blood	pres	sure							
	1	998-2	2002		2	008-	2012	2		2	2018-	2019)			18-2019 998-2002		.8-2019 008-2012
Educational level	n	%	95%	Chi-squared test within period Cl sign	n	%	95%	6 C I	Chi-squared test within period sign	n	%	95%	s cı	Chi-squared test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education	1249 1730	49 52	46 50	ns 52 55	1183 1018	36 44	33 41	39 47	**	725 303	28 34	25 29	31 39	ns	-21 -18	***	-8 -10	**
									Hyperte	nsion								
	1	998-2	2002	Chi-squared	2	008-	2012	2	.,,			2019)			18-2019		8-2019
Educational level	n	%	95%	test within period sign	n	%	959	6 CI	Chi-squared test within period sign	n	%	95%	s cı	Chi-squared test within period sign		chi- squared sign	Diff	chi- squared sign
Higher education	1249 1730	53 56	50 54	55 59	1183 1018	49 53	46 50	52 56	ns	725 303	43	40 40	47 52	ns	-9 -10	***	-6 -7	*
								Undi	agnosed h	vnert	ensid	on						
	1	998-2	2002		2	008-	2012					2019	,			18-2019 998-2002		.8-2019 008-2012
Educational level				Chi-squared test within					Chi-squared test within period					Chi-squared test within period		chi- squared	Diff	chi- squared
Eddeatonanever	n	%	95%	period CI sign ns	n	%	959	6 CI	sign .ns	n	%	95%	s CI	sign ns	J	sign	5	sign
Higher education Lower education	621 1063	53 53	49 50	57 56	555 610	36 39	32 35	40 43	""	314 168	36 38	31 31	41 46	713	-17 -15	***	-0.2 -1	ns ns
						D	iagn	osed	but untre	ated	hype	rtens	ion					
	1	998-2	2002		2	008-	2012	2		2	2018-	2019)			18-2019 998-2002		.8-2019 008-2012
Educational level	n	%	95%		n	%	95%	6 CI	Chi-squared test within period sign	n	%	95%	s CI	Chi-squared test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	621 1063	16 15	13 12	ns 19 17	555 610	19 16	16 13	22 18	ns	314 168	13 15	10 10	17 21	ns	-2 1	ns ***	-6 -0.1	* ns
								Uncc	ontrolled h	ypert	ensid	on						
	1	998-2	2002	Chid	2	008-	2012	2	Chi-squared	2	2018-	2019)	Chi-squared		18-2019 998-2002		.8-2019 008-2012
Educational level	n	%	95%		n	%	95%	6 C I	test within period sign	n	%	95%	s CI	test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	621 1063	25 26		ns 29 28	555 610	22 30	19 26	26 33		314 168	21 26	17 19	26 33	ns	-4 0.5	ns ***	-1 -4	ns ns
								Cor	trolled hy	perte	nsio	1						
	1	998-2	2002		2	008-	2012	2		2	2018-	2019)			18-2019 998-2002		8-2019 008-2012
Educational level	n	%	95%	Chi-squared test within period CI sign	n	%	95%	6 CI	Chi-squared test within period sign	n	%	95%	s CI	Chi-squared test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	621 1063	6	4 5	ns 8 8	555 610	22 15	19 12	26 18	**	314 168	30 20	24 14	35 26	*	23 13	***	7 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.

										WON	1EN								
								В	ood	pressure d	lrug t	reat	men	t		2000			
	1	998-	2002			20	008-	2012	!		2	2018	2019	9			18-2019 998-2002		18-2019 108-2012
Educational level	n	%	95%	Chi-squa test with period CI sign ***	in	n	%	95%	6 CI	Chi-squared test within period sign ***	n	%	959	% CI	Chi-squared test within period sign **	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	1052 1887	16 24		19 25		167 017	19 26	17 24	21 29		725 339	19 27	16 22	22 31		2	ns ns	-0.4 0.4	ns ns
									D.	aised bloo	daro	cour							
	1	998-	2002		ī	20	008-	2012		aiseu bioot			-2019	9			18-2019 998-2002		18-2019 108-2012
				Chi-squa						Chi-squared					Chi-squared		chi-		chi-
ducational level	n	%	95%	test with period color sign		n	%	95%	6 C I	test within period sign ***	n	%	959	6 CI	test within period sign	Diff	squared sign	Diff	squared sign
ligher education ower education	1052 1887	35 42		38 44		167 017	22 30	20 27	24 32		725 339	14 21	11 16	16 25		-21 -21	***	-8 -9	***
		- -	0.000							Hyperte									
	1	000	2002			20	nne	2012)	нурегте			-2019			20	18-2019	202	8-2019
	-	JJ6-	2002	Chi-squa		- 21	008-	2012		Chi-squared		.010	-201:		Chi-squared	vs 1	998-2002	vs 20	008-2012
ducational level	n	%	95%	test with	in	n	%	95%	6 CI	test within period sign	n	%	959	% CI	test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
ligher education	1052	40		43		167	32	29	34	***	725	27	24	30	**	-13	***	-5	*
ower education	1887	47	45	49	10	017	41	38	44		339	38	33	43		-9		-3	ns
				-						iagnosed h						20	18-2019	201	8-2019
	1	998-	2002	Chi saua		20	-800	2012		Chi sausrad	2	2018	-2019	9	Chi-squared		998-2002		008-2012
ducational level	n	%	95%	Cl Sign	in	n	%	95%	6 CI	Chi-squared test within period sign	n	%	959	% CI	test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
ligher education ower education	337 1037	47 43		ns 52 46		311	36 25	30 21	41 28	**	192 172	28 31	21 24	34 38	ns	-19 -12	***	-8 6	ns ns
							-	Diagn	nsan	l but untre	ated	hyne	artar	sion					
	1	998-	2002			20		2012		but untre			-2019				18-2019		8-2019
	-			Chi-squa						Chi-squared		.010			Chi-squared	vs 1	998-2002 chi-	vs 20	008-2012 chi-
ducational level	n	%	95%	test with period cl sign		n	%	95%	6 C I	test within period sign ns	n	%	959	% CI	test within period sign ns	Diff	squared sign	Diff	squared sign
ligher education ower education	337 1037	19 15	14 13	23	_	311 534	15 16	11 13	19 19	713	192 172	17 13	12 8	23 18	,,,,	-1 -2	ns ***	2 -3	ns *
									Unce	ontrolled h	yper	tensi	ion						
	1	998-	2002			20	008-	2012			2	2018	-2019	9			18-2019 998-2002		18-2019 108-2012
ducational level	n	%	95%	Chi-squa test with period	in	n	%	95%	6 CI	Chi-squared test within period sign	n	%	959	% CI	Chi-squared test within period sign		chi- squared sign	Diff	chi-
ligher education	337	24	19	28	3	311	23	18	27	*	192	14	9	19	ns	-9	*	-8	*
ower education	1037	32	29	34	5	534	29	25	33		172	17	11	22		-15	***	-12	ns
										ntrolled hy						20	18-2019	201	8-2019
	1	998-	2002			20	008-	2012			2	2018	-2019	9			998-2002		008-2012
ducational level	n	%	95%	Chi-squa test with period	in	n	%	95%	6 C I	Chi-squared test within period sign	n	%	959	% CI	Chi-squared test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
ligher education	337	11 10	7 8	ns 14 12		311	27 30	22 26	31 34	ns	192	40	33 32	47 47	ns	30 29	***	14	**
Lower education	1037	10	8	12	5	534	30	26	34		172	40	32	41		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	1 and 2
		title or the abstract	
		(b) Provide in the abstract an informative and balanced summary of	2
		what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation	4
		being reported	
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	5
C		of recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of	5
		selection of participants	
Variables	7	Clearly define all outcomes, exposures, predictors, potential	5 and 6
		confounders, and effect modifiers. Give diagnostic criteria, if	
		applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of	5 and 6
measurement		methods of assessment (measurement). Describe comparability of	
		assessment methods if there is more than one group	
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	5 and 6
		applicable, describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control	6
		for confounding	
		(b) Describe any methods used to examine subgroups and	6
		interactions	
		(c) Explain how missing data were addressed	6
		(d) If applicable, describe analytical methods taking account of	5
		sampling strategy	
		(\underline{e}) Describe any sensitivity analyses	na
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg	6 and in al
		numbers potentially eligible, examined for eligibility, confirmed	tables
		eligible, included in the study, completing follow-up, and analysed	
		(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,	6 and table
		clinical, social) and information on exposures and potential	s1
		confounders	
		(b) Indicate number of participants with missing data for each	6 and in al
		variable of interest	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-	6-12 and in
		adjusted estimates and their precision (eg, 95% confidence interval).	all tables
		Make clear which confounders were adjusted for and why they were	
		included	
		(b) Report category boundaries when continuous variables were	6-12 and in
		categorized	related
			tables
		(c) If relevant, consider translating estimates of relative risk into	na
		absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and	6-12 and in
		interactions, and sensitivity analyses	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	14
		potential bias or imprecision. Discuss both direction and magnitude	
		of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering	14-15
		objectives, limitations, multiplicity of analyses, results from similar	
		studies, and other relevant evidence	
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	18
		study and, if applicable, for the original study on which the present	
		article is based	

^{*}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.

BMJ Open

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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Primary Subject Heading :	Epidemiology								
Secondary Subject Heading:	Public health								
Keywords:	Epidemiology < TROPICAL MEDICINE, Hypertension < CARDIOLOGY, PUBLIC HEALTH								

SCHOLARONE*

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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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Word count: 4735

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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 chisquare 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 \pm SD: men 55 \pm 11, women 54 \pm 11), 2218 men and 2204 women (mean age \pm SD: men 55 \pm 11, women 55 \pm 11),

and 1031 men and 1066 women (mean age \pm SD: men 55 \pm 11, women 55 \pm 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				2	2018- n=1	2019			2018-20 vs 1998-2		2018-2019 vs 2008-2012			
	mean	SD	95%	6 CI	mean	nean SD95%		% CI	mean	SD <u>95% CI</u>		% 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	***	***	
Transition (Beauty per Immute)											-								
									chi-		1		chi-	1!-4!-					
	%	95	% CI		%	95% CI		%	95% CI		Diff	squared sign^	Logistic sign^^	Diff	squared sign^	Logistic sign^^			
								•						J	J		J	J	
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																	
				2008	-2012		2	2018-	2019			2018-20	019	2018-2019				
				n=2	204			n=1	066			vs 1998-2	2002	vs 2008-2012				
	mean	SD	95%	% CI	mean	mean SD <u>95% CI</u>		mean	SD	95%	6 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	<i>78</i>	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		% <u>95% CI</u>		% <u>95% CI</u>		chi- squared Logistic Diff sign^ 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	<i>37</i>		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 20		-0,4	ns ***	**	-0,4	ns **	ns **
Uncontrolled Controlled	30 10	27 9	32 12		26 27	23 24	29 30		16 41	13 36	20 46		-13 31	***	***	-10 14	***	***
Controlled	10	3	12		4 1	24	30		41	30	40		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 < 0.001; *** p < 0.01; ** p < 0.05; ns not significant p-value. Raised blood pressure ≥90 mmHg or diastolic blood pressure ≥90 mmHg. Hypertension: systolic blood pressure ≥10 mmHg or diastolic blood pressure ≥90 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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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 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.

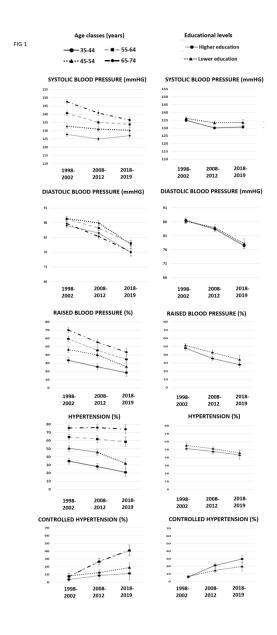


Figure 1. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident men aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019.

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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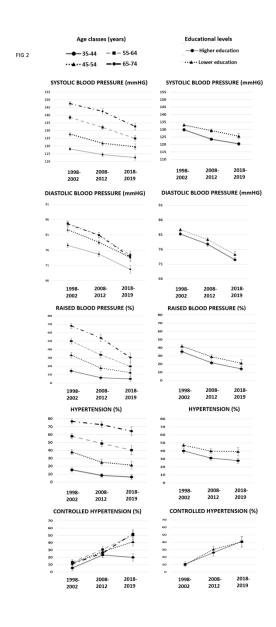


Figure 2. Mean of blood pressure and prevalence of raised blood pressure, hypertension and controlled hypertension based on measurements, by age class, educational level, and period. Italian resident women aged 35-74 years, the CUORE Project Surveys 1998-2002, 2008-2012, and 2018-2019.

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)

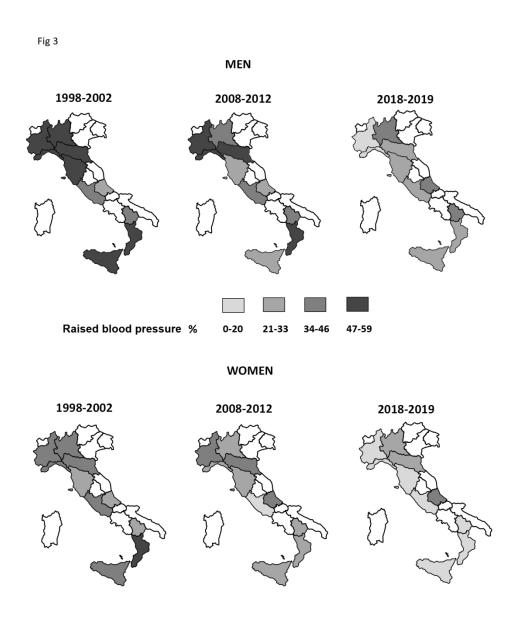


Figure 3. Prevalence of raised blood pressure based on measurements, by sex, Regions, and period.

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)

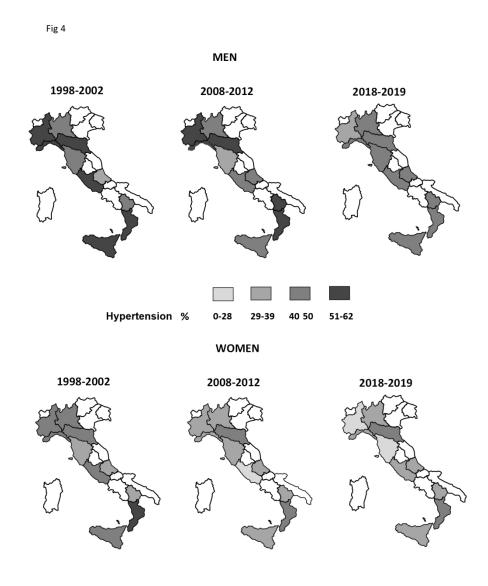


Figure 4. Prevalence of hypertension based on measurements, by sex, Regions, and period. Italian resident men and women aged 35-74 years, the CUORE Project Surveys 1998–2002, 2008–2012, and 2018–2019. Italian Regions: Piedmont, Lombardy, Liguria, Emilia Romagna, Tuscany, Lazio, Abruzzo, Basilicata, Calabria, 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.

			ME	N		
	1998-	2002	2008-	2012	2018-	2019
Age class (years)		0/		0/		0/
25.44	n 717	% 24	n 530	% 24	n 248	% 24
35-44						
45-54	752 704	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
			WON	ΛEN		
	1998-	2002	WON 2008-		2018-	2019
	1998-	2002			2018-	2019
	1998-	2002			2018-	2019
Age class (years)			2008-	2012		
	n	%	2008- n	2012 %	n	%
35-44	n 715	% 24	2008- n 514	2012 % 23	n 237	% 22
35-44 45-54	n 715 769	% 24 26	2008- n 514 577	2012 % 23 26	n 237 271	% 22 25
35-44 45-54 55-64	n 715 769 778	% 24 26 26	2008- n 514 577 584	% 23 26 27	n 237 271 280	% 22 25 26
35-44 45-54	n 715 769	% 24 26	2008- n 514 577	2012 % 23 26	n 237 271	% 22 25
35-44 45-54 55-64	n 715 769 778	% 24 26 26	2008- n 514 577 584	% 23 26 27	n 237 271 280	% 22 25 26
35-44 45-54 55-64 65-74	n 715 769 778	% 24 26 26	2008- n 514 577 584	% 23 26 27	n 237 271 280	% 22 25 26
35-44 45-54 55-64 65-74	n 715 769 778 693	% 24 26 26 23	2008- n 514 577 584 529	% 23 26 27 24	n 237 271 280 278	% 22 25 26 26

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.

												ME	N									
										Systo	olic blo	ood pre	essur	e (mm	Hg)							
		19	998-2	2002		ANOVA within		20	08-2	012		ANOVA within		20	18-2	019		ANOVA within	2018- vs 1998	·2019 8-2002	2018 vs 200	
Age class (years)	n	mean	DS	95%	s CI	period sign ***	n	mean	DS	95%	а	period sign	n	mean	DS	95%	6 CI	period sign	Diff	t-test sign	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 65-74	784 732	141 148	20	139 146	142 149		564 536	135 141	17 18	134 139	136 142		277 258	134 136	14 17	132 134	135 138		-7 -11	***	-1 -4	ns **
03-74	732	140	20	140	143		330	141	10			ood pr				104	130		-11			
		19	998-2	2002		ANOVA		20	08-2			ANOVA	essu	•	18-2	019		ANOVA	2018-		2018	-2019
					•	within			-			within						within	vs 199		vs 200	
Age class (years)	n	mean	DS	95%	s CI	period sign	n	mean	DS	95%	cı	period sign	n	mean	DS	95%	6 CI	period sign	Diff	t-test sign	Diff	t-test sign
25.44	717	85	11	84	86	***	530	83	10	82	83	***	248	76	10	 75	77	**	•	***	-7	***
35-44 45-54	752	87	11	87	88		588	86	10 10	85	87		248	76 79	11	73 77	80		-9 -9	***	-7 -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	***
							9	Systoli	c blo	od pre	ssure	not un	der d	lrug tro	eatm	ent (n	nmHg)					
		19	998-2	2002		ANOVA		20	08-2	012		ANOVA		20	18-2	019		ANOVA	2018-		2018	
						within						within						within	vs 199		vs 200	
Age class (years)	n	mean	DS	95%	s CI	period sign ***	n	mean	DS	95%	cı	period sign	n	mean	DS	95%	6 CI	period sign ***	Diff	t-test sign	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
							L	Diastol	ic blo	ood pre			ider (drug tr	eatn	nent (ı	nmHg		2018-	2010	2018	-2019
		19	998-2	2002		ANOVA within		20	08-2	012		ANOVA within		20	18-2	019		ANOVA within	vs 199		vs 200	
Age class (years)	n	mean	DS	95%	s CI	period sign **	n	mean	DS	95%	а	period sign	n	mean	DS	95%	6 CI	period sign	Diff	t-test sign	Diff	t-test sign
35-44	682	85	10	84	85		504	82	10	81	83		237	75	10	74	77	ns	-9	***	-7	***
45-54	640	86	11	86	87		481	85	10	84	86		212	77	10	76	78		-9	***	-8	***
55-64	581 454	86	10 10	85 83	87 85		370 252	84 81	10 10	83 80	85 82		170 125	78 77	9 11	77 75	79 79		-8	***	-6	***
65-74	454	84	10	03	65		232	01	10	60	02		123	77	''	73	79		-8	***	-4	
										Hea	rt rate	e (beat	s pei	minu	te)							
		19	998-2	2002		ANOVA within		20	08-2	012		ANOVA within		20	18-2	019		ANOVA within	2018- vs 1998	2019 8-2002	2018 vs 200	
Age class (years)	n	mean	DS	95%	s c ı	period sign	n	mean	DS	95%	а	period sign	n	mean	DS	95%	6 CI	period sign	Diff	t-test sign	Diff	t-test sign
	745				67	ns	F00					ns				70	70	ns		***		***
35-44 45-54	715 750	66 66	10 11	65 65	67 67		530 588	68 69	9 10	67 68	69 70		248 248	72 72	12 11	70 71	73 74		6 6	***	4 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<0.001; ** 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.

65-74

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.

										Systoli	ic bloo	d press	ure ((mmHg)							
		19	98-2	002		ANOVA within		20	08-2	012		ANOVA within		2018	3-201	.9	ANOVA within		-2019 <u>8-2002</u>	2018 vs 200	-2019 <u>8-2012</u>
ge class						period						period					period	Diff	t-test	Diff	t-test
(years)	n	mean	DS	95%	6 CI	sign - ***	n	mean	DS	95%	6 CI	sign ***	n	mean	DS	95% CI	sign ***		sign	-	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	***
									[Diasto	lic bloc	od pres	sure	(mmHg	;)						
		19	98-2	002		ANOVA		20	08-2	012		ANOVA		2018	3-201	.9	ANOVA		-2019 8-2002	2018 vs 200	-2019 8-2012
ge class						within period						within period					within period		t-test		t-test
(years)	n	mean	DS	95%	6 CI	sign	n	mean	DS	95%	6 CI	sign	n	mean	DS	95% CI	sign	Diff	sign	Diff	sign
25 44	715	78	10	77	78	***	514	75	9	74	75	***	237	70	10	68 71	***		***	_	***
35-44 45-54	769	83	11	82	83		577	79	9	7 4 78	79		271	70 74	11	72 75		-8 -9	***	-5 -5	***
55-64	778	85	10	84	85		584	81	10	80	82		280	74	11	73 76		-10	***	-3 -7	***
65-74	693	85	10	84	85		529	81	10	80	82		278	74	11	72 75		-11	***	-7	***
							Sy:	stolic k	lood	press	ure no	ot unde	r dru	g treat	ment	t (mmHg)					
		19	98-2	002		ANOVA		20	08-2	012		ANOVA		2018	3-201	.9	ANOVA		-2019 8-2002	2018 vs 200	-2019
ge class						- within period						within period					within period		t-test		t-test
years)	n	mean	DS	95%	6 CI	sign - ***	n	mean	DS	95%	6 CI	sign ***	n	mean	DS	95% CI	sign · ***	Diff	sign	Diff	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	539 374	134 142	18 18	132 140	135 144		401 244	128	17 20	126 135	130 140		203 122	123 127	17 16	121 126 124 130		-10	***	-4	**
65-74	3/4	142	10	140	144			138										-15		-10	
							Dia	stolic	blood	d pres	sure n	ot und	er dru	ug treat	men	t (mmHg		2019	-2019	2010	-2019
		19	98-2	002		ANOVA within		20	08-2	012		ANOVA within		2018	3-201	.9	ANOVA within		8-2002	vs 200	
ge class						period						period					period	Diff	t-test	Diff	t-test
years)	n	mean	DS	95%	6 CI	sign - ***	n	mean	DS	95%	6 CI	sign ***	n	mean	DS	95% CI	sign **		sign		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	t rate ((beats	oer m	ninute)							
		19	98-2	002		ANOVA within		20	08-2	012		ANOVA within		2018	3-201	.9	ANOVA within		-2019 8-2002	2018 vs 200	-2019 8-2012
ge class						period						period					period	Diff	t-test	Diff	t-tes
	n	mean	DS	95%	6 CI	sign	n	mean	DS	95%	6 CI	sign	n	mean	DS	95% CI	sign		sign		sign
years)						**						ns ns					ns				
35-44	711	71	11	70	72	**	514	72	9	71	72	ns	237	74	11	73 75	ns	3	**	2	**
years) 35-44 45-54 55-64		71 70 69	11 10 10	70 69 68	72 71 70	**	514 577 584	72 71 71	9 9 9	71 70 70	72 71 72	ns	237 271 280	74 73 72	11 10 10	73 75 72 74 71 73	ns	3 3 3	** ***	2 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.

D 4	n.
IV	ı

											Ν	1EN										
								Sy	/sto	lic bl	ood	pressur	e (m	mHg)								
		1998	-20	02		ANOVA		2008	2-20	112		ANOVA		201	8-2 (119		ANOVA)18-)19		018- 019
Educational level		1336	-20	<u> </u>		within period		2000	J-20	,12		within period		201	0-20	,13		within period		t-test		t-test
Educational level	n	mean	DS_	95%	6 CI	sign ***	n	mean	DS	95%	6 CI	sign ***	n	mean	DS _	95%	6 CI	sign ***	Diff	sign	Diff	sign
Higher education	1249	135		134 135			1183	130		129	131		725	131		130			-4	***	1	ns
Lower education	1730	136	10	135	137		1018			132			303			132	135		-3	4.4	0.2	ns
								Di	asto	olic b	lood	pressu	re (n	nmHg	,				20	18-	20)18-
		1998	-20	02		ANOVA within		2008	3-20)12		ANOVA within		201	8-20)19		ANOVA within	20	019	20	019
Educational level	n	mean	DS	95%	k CI	period sign	n	mean	DS	95%	% CI	period sign	n	mean	DS	95%	4 CI	period sign	Diff	t-test sign	Diff	t-test sign
Higher education	1249	87	11	86	87	ns	1183		10	83	84	ns	725	77	10	77	78	ns	-9	***	-6	***
Lower education	1730	86	11	86	87		1018		10	83	85		303	78	10	77	79		-8	***	-6	***
						Sys	tolic b	lood r	res	sure	not	under c	lrug	treatn	nen	t (m	mHg)					
		4000				ANOVA						ANOVA		204		٠	Ū.	ANOVA		18-		018-
		1998	-200	02		within		2008	3-2L)12		within		201	8-20)19		within	20	019		019
Educational level	n	mean	DS _	95%	6 CI	period sign ***	n	mean	DS	95%	6 CI	period sign ***	n	mean	DS _	95%	6 CI	period sign ***	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
						Dias	tolic k	olood	pre	ssure	not	under	drug	treat	mer	ıt (m	mHg	:)				
		1998	-20	02		ANOVA		2008	3-20)12		ANOVA		201	8-20)19		ANOVA)18-)19)18-)19
Educational level						within period						within period						within period		t-test		t-test
Eddodional level	n	mean	DS _	95%	6 CI	sign ns	n	mean	DS	95%	6 CI	sign ns	n	mean	DS _	95%	6 CI	sign ns	Diff	sign	Diff	sign
Higher education	1046	86	10	85	86	5	913	83	10	82	83		537	77	10	76	78	5	-9	***	-6	***
Lower education	1305	85	10	85	86		680	83	10	83	84		205	77	9	76	78		-8	***	-6	***
								H	lea	rt rat	te (be	eats pe	r mir	ute)								
		1998	-20	02		ANOVA		2008	3-20)12		ANOVA		201	8-20)19		ANOVA)18-)19		018- 019
Educational level						within period						within period						within period		t-test		t-test
		mean	-		6 CI	sign ns	n	mean				sign ns	n	mean	"			sign **		sign		sign
Higher education	1244	66	11	65	67		1183	68	9	68	69		725	71	11	70	72		5	***	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<0.001; *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.

74 12 73 76

1018 68 10 68 69

66 11 *65 67*

Lower education

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

,											WOI	/IEN										
								Sys	toli	c blo	od pr	essure	(mm	Hg)								
		1998	8-20	02		ANOVA		2008	-201	12		ANOVA within		201	8-20)19		ANOVA within)18-)19)18-)19
Educational level	n	mean	std	95%		period sign ***	n	mean	std	95%	6 CI	period sign	n	mean	std	959	% CI	period sign	Diff	t-test sign	Diff	t-test sign
Higher education Lower education	1052 1887	130 133	16 18	129 132	131 134		1167 1017	124 129		123 128	124 130		725 339	120 126		119 124	122 127		-9 -7	***	-3 -4	***
								Dia			od p	ressure		nHg)								
		1998	200	02		ANOVA		2008			•	ANOVA	•	201	0 20	110		ANOVA)18-)19)18-)19
Educational level	n	mean		95%		within - period sign ***	n	mean		95%	6 CI	within period sign	n	mean		959	% CI	within period sign	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	***
						Syste	olic bl	ood pi	essi	ure n	ot ur	nder dr	ug tr	eatme	nt (mml	Hg)					
		1998	Sys: ANOVA within					2008	-201	12		ANOVA within		201	8-20	019		ANOVA within)18-)19)18-)19
Educational level	n	mean	std	95%	% CI	period sign ***	n	mean	std _	95%	6 CI	period sign	n	mean	std	959	% CI	period sign	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	*
						Diast	olic b	ood p	ress	ure	not u	nder dı	rug tr	eatm	ent	(mm	Hg)					
		1998	R_20	0 2		ANOVA		2008	-201	12		ANOVA		201	8-2 (119		ANOVA)18-)19)18-)19
Educational level	n	mean		959		within period sign	n	mean		95%	s cı	within period sign	n	mean		-	% CI	within period sign	Diff	t-test sign		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	***
								Н	eart	rate	(bea	ts per i	minu	te)								
	1998-2002					ANOVA within		2008			• • • • • • • • • • • • • • • • • • • •	ANOVA within		201	8-20)19		ANOVA within)18-)19)18-)19
Educational level	n	mean	std	95%	% CI	period sign	n	mean	std	95%	 6 CI	period sign	n	mean	std	959	% CI	period sign	Diff	t-test sign	Diff	t-test sign
Higher education Lower education	1047 1884	69 70	11 11	69 69	70 70	ns	1167 1017	71 71	9 10	70 71	72 72	ns	725 339	73 73	10 11	72 72	73 74	ns	3	***	2 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<0.001; *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.

•	_	0-2()12 ai					N	1EN							
							Bl	ood pressure	drug	treat	ment					
	1	1998-2	2002	Chi-squared test within	2	2008-2	2012	Chi-squared test within	2	018-2	2019	Chi-squared test within		18-2019 998-2002		8-2019 08-2012
Age class				period				period				period	Diff	chi- squared	Diff	chi- squared
(years)	n	%	95% CI	sign -	n	%	95%		n	%	95% CI	sign		sign		sign
35-44	717	5	3 6	***	530	5	3	***	248	4	2 7	***	-0.4		-0.5	
45-54	752	15	12 17		588	18		21	248	15	10 19		-0.4	ns ns	-4	ns ns
55-64	784	26	23 29		564	34		38	277	39	33 44		13	***	4	ns
65-74	732	38	34 41		536	53	49 5	57	258	52	45 58		14	**	-1	ns
								Raised blo	od pr	essur	е					
	1	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019	Chi-squared		18-2019 998-2002		8-2019 08-2012
Age class				test within period				test within period				test within period		chi-		chi-
(years)			100000	sign				sign				sign	Diff	squared sign	Diff	squared
	n	%	95% CI	***	n	%	95%	<u>***</u>	n	%	95% CI	***		sign		sign
35-44	717	33	30 37		530	26	22 2	29	248	19	14 23		-15	***	-7	*
45-54	752	46	43 50		588	40	36 4	14	248	26	20 31		-21	***	-14	***
55-64	784	59	56 63		564	46		50	277	35	29 40		-25	***	-11	**
65-74	732	70	67 73		536	55	51 6	50	258	43	37 49		-27	***	-12	**
								Нуре	tensio	on						
	1	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019	Chi-squared		18-2019 998-2002		8-2019 08-2012
Age class				test within period				test within period				test within period	V3.1	chi-	V3 20	chi-
(years)		%	05% 61	sign		%	05%	sign		%	05% 61	sign	Diff	squared	Diff	squared
	n	70	95% CI	***	n	70	95%	***	n	/0	95% CI	**		sign		sign
35-44	717	35	31 38		530	28	24 3	32	248	21	16 26		-14	* * *	-7	*
45-54	752	51	47 54		588	46		50	248	32	26 38		-19	***	-14	**
55-64	784	64	61 68		564	62		56	277	58	53 64		-6	ns	-3	ns
65-74	732	76	72 79		536	76		30	258	74	69 79		-2	ns	-2	ns
								Undiagnosed	hype	rtens	ion					
	1	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019	Chi-squared		18-2019 998-2002		8-2019 08-2012
Age class				test within period				test within period				test within period		chi-		chi-
(years)	n	%	95% CI	sign	n	%	95%	sign	n	%	95% CI	sign	Diff	squared sign	Diff	squared sign
		,,,	3370 CI	**		,	3370	***		,,,	3370 CI	***		5		8
35-44	249	67	62 73		149	54	46	52	52	62	48 75		-6	ns	8	ns
45-54	380	52	47 57		269	40		16	79	35	25 46		-16	**	-4	ns
55-64	505	48	44 52		349	32		37	162	23	17 30		-25	***	-8	ns
65-74	553	39	35 43		407	25	20 2		191	21	16 27		-18		-3	ns
							Diagn	osed but unt	reate	d hyp	ertensio	on			201	
	1	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019	Chi-squared		18-2019 998-2002		8-2019 08-2012
Age class				test within period				test within period				test within period	D.11	chi-	D	chi-
(years)	n	%	95% CI	sign	n	%	95%	sign	n	%	95% CI	sign	Diff	squared sign	Diff	squared sign
				***				***				ns				
35-44	249	18	14 23		149	29		36	52	17	7 28		-1	ns	-12	ns
45-54 55-64	380 505	19 12	15 23 9 14		269 349	20 13	16 2	?5 !6	79 162	19 10	10 28 6 15		0.0	ns ns	-1 -2	ns ns
65-74	553	10	8 13		407	6		8	191	9	5 13		-1 -1	ns	-2 3	ns
	200		- 13		,											3
								Uncontrolled	hype	rtens	ion					
	1	1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019	Chi-squared		18-2019 998-2002		8-2019 08-2012
Age class				test within period				test within period				test within period		chi-		chi-
(years)	n	%	95% CI	sign	n	%	95%	sign	n	%	95% CI	sign	Diff	squared sign	Diff	squared sign
		,,	33/0 CI	***		,,	33/0	***		,,,	3370 01	ns				
35-44	249	10	7 14		149	9		!3	52	10	2 18		-1	ns	1	ns
45-54	380	21	17 25		269	27	22 3		79	27	17 36		5	ns	-1	ns
55-64	505	32	28 37		349	29		34	162	25	19 32		-7	ns **	-4	ns **
65-74	553	43	39 47		407	43	38 4	10	191	28	22 35		-15	**	-14	7.7
								Controlled	hyper	tensio	on					
		1998-2	2002	Chi-squared	2	2008-2	2012	Chi-squared	2	018-2	2019	Chi-squared		18-2019		8-2019
				test within				test within				test within	vs 1	998-2002 chi-	vs 20	08-2012 chi-
Age class (years)				period sign				period sign		100000		period sign	Diff	squared	Diff	squared
.,	n	%	95% CI	- ns	n	%	95%	CI***	n	%	95% CI	- ***		sign		sign
35-44	249	4	1 6	113	149	9	4		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 3	31	162	41	33 48		33	***	14	**
65-74	553	7	5 9		407	27	23 3	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.

/3 1330	-20	UZ,	, 20	00-2	012 and	20.	10-	2013	,.	WOMEN								
							-	Blood	pres	sure drug	trea	tme	nt					
	1	1998	B- 20 0	02	Chi-squared test within		200	8-201	2	Chi-squared test within		201	8-201	19		18-2019 998-2002		18-2019 008-2012
Age class (years)					period sign		0.6			period sign					Diff	chi- squared	Diff	chi- squared
	n	%		% CI	***	n	%	95%		***	n	%		6 CI		sign	123	sign
35-44 45-54	715 769	2 15	1 12	3 17		514 577	3 12	9	4		237 271	1	0	3 16	-1 -2	ns ns	-2 1	ns
55-64	778	31	27 42	34 50		584	31	28 50	35 58		280		22 50	33 62	-3 10	ns **	-4 2	ns
65-74	693	46	42	30		529	54			l blood pre	278		30	02	10		2	ns
	1	009	8-200	12			200	8-201					8-201	10	20	18-2019	20:	18-2019
Age class	-		5-200	, <u> </u>	Chi-squared test within period		200	0-201		Chi-squared test within period		201	0-20.		vs 1	998-2002 chi-	vs 2	008-2012 chi-
(years)	n	%	959	% CI	sign	n	%	95%	6 CI	sign	n	%	959	6 CI	Diff	squared sign	Diff	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		15	25	-30	***	-14	***
65-74	693	68	65	72		529	54	50	58		278	31	25	36	-38	***	-23	offer order order
									H	ypertensio	n				20	18-2019	20.	18-2019
	1	1998	8-200	02	Chi-squared test within		200	8-201	.2	Chi-squared test within		201	8-201	19		998-2002		008-2012
Age class (years)					period sign					period sign					Diff	chi- squared	Diff	chi- squared
(years)	n	%	959	% CI	***	n	%	95%	6 CI	***	n	%	959	% CI		sign		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 65-74	778 693	58 77	55 74	61 80		584 529	49 73	45 69	53 76		280 278	40 64	35 59	46 70	-18 -12	***	-8 -8	*
	030	-				525								,,,			_	
								Und	liagno	osed hype	rtens	sion	1		20	18-2019	20.	18-2019
	1	1998	8-200	02	Chi-squared test within		200	8-201	2	Chi-squared test within		201	8-201	L9		998-2002		008-2012
Age class (years)					period sign					period sign					Diff	chi- squared	Diff	chi- squared
(years)	n	%	959	% CI	***	n	%	95%	6 CI	***	n	%	959	% CI		sign		sign
35-44	110	62	53	71		43	40	25	54		15	47	21	72	-15	ns	7	ns
45-54	292		40	51			39	31	47		58	29	18	41	-16	*	-10	ns
55-64 65-74	451 532		29 28	38 36		285 384	24	19 16	28 23		113 179	21 11	14 6	29 15	-12 -22	***	-2 -9	ns **
									d but	untreated			onsio	n				
	4		8-200	12				8-201					8-201		20	18-2019	20:	18-2019
	-	1996	5-200)Z	Chi-squared test within		200	8-201	.2	Chi-squared test within		201	0-20.	1.9	vs 1	998-2002 chi-	vs 2	008-2012 chi-
Age class (years)	n	%	959	% CI	period sign	n	%	95%	6 CI	period sign	n	%	959	% CI	Diff	squared sign	Diff	squared sign
		,,,	33,	o C1	***		-	337		**		,,,	33,			Sigii		Sign
35-44 45-54	110 292			31 21		43 144	26	13 9	39 20		15 58	33 14	9	57 23	11 -3	ns ns	-1	ns ns
55-64	451		10	17		285		8	16		113		5	16	-3	ns	-2	ns
65-74	532	8	6	10		384	6	4	9		179	2	0	4	-6	***	-4	***
								Unc	ontro	olled hyper	rten	sion	1					
	1	1998	8-200	02	Chi-squared		200	8-201	2	Chi-squared		201	8-201	19		18-2019 998-2002		18-2019 008-2012
Age class					test within period					test within period						chi-		chi-
(years)	n	%	959	% CI	sign	n	%	95%	6 CI	sign	n	%	959	6 CI	Diff	squared sign	υш	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		35	44		285		28	39		113		11	25	-22	***	-16	**
65-74	532	49	45	53		384	48	43	53		179		28	42	-14		-14	
								Со	ntrol	led hypert	ensi	on				10 2015		10 2012
	1	199	8-200	02	Chi-squared test within		200	8-201	2	Chi-squared test within		201	8-201	19		18-2019 998-2002		18-2019 008-2012
Age class					period sign					period sign					Diff	chi- squared	Diff	chi- squared
(years)	n	%	959	% CI	ns	n	%	95%	6 CI	ns	n	%	959	% CI		sign		sign
35-44	110		1	10			23	11	36		15	20	0	40	15	*	-3	ns
45-54 55-64	292 451		8 10	16 17		144 285		20 26	35 36		58 113	41 50	29 41	54 60	29 37	***	14 20	ns **
65-74	532		8	14		384		21	30		179		45	60	41	***	27	*
																0		

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.

									D.I.	M		•						
	19	998-	2002		-2.07700.	2	008-	201		pressure			2019			18-2019		8-2019
icational level	n	%	95%	cı	Chi-squared test within period sign	n	%		5% CI	Chi-squared test within period sign	n	%	95% CI	Chi-squared test within period sign		chi- squared sign		chi- squared sign
gher education wer education	1249 1730	18 19	16 18	20 21	ns	1183 1018	24 25	22		ns	725 303	26 24	23 29 19 29	ns	8	*** ns	2 -1	ns ns
									F	aised bloo	d pre	ssur	e					
	19	998-	2002		Chi-squared test within	2	008-	201	.2	Chi-squared test within	2	2018-	2019	Chi-squared test within		18-2019 998-2002 chi-		8-2019 008-2012 chi-
ucational level	n	%	95%	CI	period sign	n	%	95	5% CI	period sign	n	%	95% CI	period sign	Diff	squared sign	Diff	squared sign
gher education wer education	1249 1730	48 51	45 49	51 54	ns	1183 1018	35 43	33 40			725 303	28 34	25 31 29 39	ns	-20 -17	***	-7 -9	**
										Hypert	ensio	n						
	19	998-	2002		Chi-squared	2	008-	201	.2	Chi-squared	2	2018-	2019	Chi-squared		18-2019 998-2002		.8-2019 08-2012
lucational level	n	%	95%	CI	test within period sign	n	%	95	5% CI	test within period sign	n	%	95% CI	test within period sign		chi- squared sign	25.00	chi- squared sign
igher education ower education	1249 1730	51 55	49 53	54 58	*	1183 1018	48 51	45 48		ns	725 303	43 46	40 47 40 52	ns	-8 -9	**	-4 -5	ns ns
									Und	liagnosed l	hyper	tens	ion					
	19	998-	2002		Chi-squared test within	2	008-	201	.2	Chi-squared test within	2	2018-	2019	Chi-squared test within		18-2019 998-2002 chi-		8-2019 008-2012 chi-
ducational level	n	%	95%	CI	period sign ns	n	%	95	5% CI	period sign ns	n	%	95% CI	period sign - ns	Diff	squared sign	Diff	squared sign
igher education ower education	621 1063	53 54	49 51	57 57	,,,	555 610	38 40	34 36			314 168	36 38	30 41 30 45	,,,,	-18 -16	***	-2 -2	ns ns
								Diag	gnose	d but untre	eated	hyp	ertension	1				
	19	998-	2002		Chi-squared test within	2	008-	201	2	Chi-squared test within	2	2018-	2019	Chi-squared test within		18-2019 998-2002		8-2019 08-2012
lucational level	n	%	95%	CI	period sign	n	%	95	5% CI	period sign	n	%	95% CI	period sign	Diff	chi- squared sign	Diff	chi- squared sign
igher education ower education	621 1063	16 15	13 13	19 17	ns	555 610	20 16	17 13		ns	314 168	13 16	10 17 10 21	ns	-3 1	ns ***	-6 -0.4	* ns
									Und	ontrolled	hyper	tens	ion					
	19	998-	2002		Chi-squared test within	2	008-	201	.2	Chi-squared test within	2	2018-	2019	Chi-squared test within		18-2019 998-2002		8-2019 08-2012
ducational level	n	%	95%	CI	period sign	n	%	95	5% CI	period sign	n	%	95% CI	period sign	Diff	chi- squared sign	Diff	chi- squared sign
igher education ower education	621 1063	24 25	21 22	28 27	ns	555 610	21 29	18 25		**	314 168	21 26	17 26 20 33	ns	-3 2	ns ***	0.1	ns ns
									Co	ntrolled h	ypert	ensi	on					
	19	998-	2002		Chi-squared test within	2	008-	201	.2	Chi-squared test within	2	2018-	2019	Chi-squared test within		18-2019 998-2002 chi-		8-2019 008-2012 chi-
ducational level	n	%	95%	CI	period sign ns	n	%	95	5% CI	period sign **	n	%	95% CI	sign •	Diff	squared sign	Diff	squared sign
igher education ower education	621 1063	6 7	4 5	8		555 610	21 15	18 12			314 168	30 20	25 35 14 26		24 13	**	8 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.

								Blo	od p	ressure dr	ug tre	eatm	ent						
	19	998-2	2002			2	008-	2012	<u>S</u>		2	018-	2019)			18-2019 998-2002		8-2019 08-2012
tional level					Chi-squared test within period sign					Chi-squared test within period sign					Chi-squared test within period sign		chi- squared sign	Diff	chi- squared
	n	%	95%	CI	***	n	%	95%	6 CI	***	n	%	95%	6 CI	**				
lucation ucation	1052 1887	16 23	14 22	19 25		1167 1017	19 26	16 23	21 28		725 339	19 27	17 23	22 32		3	ns ns	1 2	ns ns
									Rai	sed blood	press	ure							
	1	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	2018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
onal level					test within period sign					test within period sign					test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
	n	%	95%	CI	**	n	%	95%	6 CI	***	n	%	95%	6 CI	**		sign		sign
ation ation	1052 1887	35 42	32 40	38 44		1167 1017	22 29	19 26	24 32		725 339	14 21	12 17	17 25		-21 -21	***	-7 -8	***
										Hyperter	nsion								
	1	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	2018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
al level					test within period sign					test within period sign					test within period sign		chi- squared sign		chi- squared sign
	n	%	95%	CI	**	n	%	95%	6 CI	***	n	%	95%	6 CI	**		3igii		Jigii
ducation ducation	1052 1887	40 47	37 45	43 49		1167 1017	31 40	28 37	34 43		725 339	28 39	25 34	31 44		-12 -8	***	-3 -1	ns ns
								u	Jndia	gnosed hy	perte	nsio	n						
	19	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
ional level	n	%	95%	C	test within period sign	n	%	95%	(C)	test within period sign	n	%	95%	(CI	test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
					ns					**					ns				
education education	337 1037	47 43	42 40	53 46		311 534	36 25	31 21	42 28		192 172	27 29	21 23	34 36		-20 -14	***	-9 5	ns
							Di	agno	sed	but untrea	ted h	yper	tens	ion					
	19	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
onal level	п	%	95%	í CI	test within period sign	п	%	95%	á CI	test within period sign	п	%	95%	á CI	test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
			2001		ns					ns					ns				
ucation ucation	337 1037	19 15	14 13	23 18		311 534	15 17	11	19 20		192 172	16 13	8	22 18		-2 -3	ns ***	1 -4	ns *
								U	Jnco	ntrolled hy	perte	nsio	n						
	19	998-2	2002		Chi-squared test within	2	008-	2012		Chi-squared test within	2	2018-	2019)	Chi-squared test within		18-2019 998-2002		8-2019 108-2012
onal level					period sign					period sign					period sign	Diff	chi- squared	Diff	chi- squared
	n	%	95%		**	n	%	95%		ns	n	%	95%		ns		sign		sign
lucation lucation	337 1037	23 31	19 29	28 34		311 534	22 28	18 25	27 32		192 172	15 17	10 12	20 23		-8 -14	***	-7 -11	ns *
									Cont	trolled hyp	erten	sion							
	19	998-2	2002		Chi-squared	2	008-	2012		Chi-squared	2	018-	2019)	Chi-squared		18-2019 998-2002		8-2019 08-2012
					test within period sign					test within period sign					test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
tional level		01											_						
onal level	n	%	95%	CI	ns	n	%	95%	6 CI	ns	n	%	95%	6 CI	ns		oig.i		-

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

									М	EN								
		Syst		ood pres nHg)	sure	Dias		ood pres nHg)	ssure		ised blo pressure		Ну	pertens	ion	_	ontrolle pertensi	-
Italian Region	n	mean	SD	95	%CI	mean	SD	959	%CI	%	95%	s CI	%	95%	6 CI	%	95%	i 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	<i>75</i>	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	<i>57</i>	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	<i>75</i>	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

		Syst		od pres nHg)	sure	Dias		ood pres nHg)	sure		ised blo pressure		Ну	pertens	ion		ontrolle pertensi	
Italian Region	n	mean	SD	959	%CI	mean	SD	959	%CI	%	95%	6 CI	%	95%	S CI	%	95%	S CI
Abruzzo	104	122	17	118	125	73	10	71	<i>7</i> 5	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	<i>57</i>
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		2	2008	-2012	2	2	018	2019)	201	8-2019	201	8-2019
		n=2985				n=2	218			n=1	031		vs 19	98-2002	vs 20	08-2012
	mean	SD	959	% CI	mean	SD	959	% CI	mean	SD	959	6 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	***
														chi-		chi-
	%	959	% CI		%	959	% CI		%	959	% CI		Diff	squared p-value	Diff	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-			2008-2012 n=2185				2	018 n=1	- 201 9			8-2019 98-2002		8-2019 08-2012
	mean	SD	959	% CI	mean	SD	959	6 CI	mean	SD	959	% 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	***
													Diff	chi- squared	Diff	chi- squared
	%	959	% CI		%	95	% CI		%	95	% CI			p-value		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									2.11							
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	***

MOMEN

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.

		and										MEN										
										Systo	lic bloo	d press	ure (mmHg	g)							
		199	98-20	002		ANOVA		20	08-2	012		ANOVA		20	18-2	2019		ANOVA		-2019 8-2002		-2019 8-2012
ational level	n	mean	SD _	95%	% CI	within period sign	F			within period sign	n	mean	SD_	95%	s CI	within period sign	Diff	t-test sign	Diff	t-test sign		
er education er education	1249 1730	135 137	17 18	135 136	136 138		1183 1018	131 134	15 17	130 133	131 135		725 303	131 134	14 16	130 132	132 135		-5 -3	***	0.1 -0.3	ns ns
										Diasto	olic bloo	od pres	sure ((mmH	g)							
		199	98-20	002		ANOVA		20	08-2	012		ANOVA		20	18-2	2019		ANOVA		-2019 8-2002		-2019 8-2012
onal level	n	mean	SD _	95%	% CI	within period sign	n	mean	SD_	95:	% CI	within period sign	n	mean	SD_	95%	s CI	within period sign	Diff	t-test sign	Diff	t-test sign
education education	1249 1730	87 86	11 11	86 86	87 87	ns	1183 1018	83 84	10 10	83 83	84 84	ns	725 303	77 78	10 10	77 77	78 79	ns	-9 -8	***	-6 -6	***
							Sys	tolic b	loo	d pres	sure no	ot unde	r dru	g trea	tmei	nt (mn	nHg)					
		199	98-20	002		ANOVA		20	08-2	012		ANOVA		20	18-2	2019		ANOVA		-2019 8-2002		-2019 8-2012
tional level	n	mean	SD_	95%	% CI	within period sign	n	mean	SD_	95	% CI	within period	n	mean	SD_	95%	s CI	within period	Diff	t-test sign	Diff	t-test sign
education education	1046 1305	134 134	16 17	133 133	135 135	***	913 680	129 132	15 16	128 131	130 133	***	537 205	130 133	13 15	129 131	131 135	***	-4 -1	*** ns	1	ns ns
adoution.												ot unde							-	113	-	113
		199	98-20	002		ANOVA		20	08-2	012		ANOVA		20	18-2	2019		ANOVA		-2019 8-2002		-2019 8-2012
ional level	n	mean	SD_	95%	% CI	within period sign	n	mean	SD	95	% CI	within period sign	n	mean	SD_	95%	s CI	within period sign	Diff	t-test sign	Diff	t-test sign
education	1046	86	10	85 85	86 86	ns	913	83	10	82 83	83 84	ns	537	77	10	76 76	78 78	ns	-9	***	-6	***
education	1305	85	10	00	00		680	83	10			(haata u	205	77 :	9	70	70		-8		-6	
		100	20.20	002				20	00.0		t rate	(beats p	oer m			010				-2019		-2019
ional level		19:	98-20	002		ANOVA within period		20	08-2	.012		_ ANOVA within period		20	18-2	2019		_ ANOVA within period	Diff	t-test	Diff	t-test
aducation	n 1244	mean 66	SD _	95 %	67	sign ns	n 1183	mean 66	SD _	95 :	% CI 67	sign ns	n 725	mean	SD_	95% 70	71	sign **	5	sign ***	-	sign ***
education education	1730	66	11	65	67		1018	66	12	66	67		303	74	12	73	76		8	***	5 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<0.001; **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.

											V	VOMEN	ı									
									S	ystoli	c bloo	d press	ure (mmHg	;)							
		199	8-20	02		ANOVA		200	8-20	112		ANOVA	A 2018-2019					ANOVA	2018 vs 199			-2019 8-2012
		1990	5-20	02		within period		200	10-20	12		within period		201	8-20	19		within period	V3 133	t-test	V3 200	t-test
Educational level	n	mean	SD	959	% CI	sign	n	mean	SD	959	% CI	sign	n	mean	SD	95%	s CI	sign	Diff	sign	Diff	sign
Higher education	1052	130	16		131	***	1167	124	15	123	125	***	725	120	15	119		***	-10	***	-4	***
Lower education	1887	133	18		134		1017	130	18	129	131		339	125	17		127		-8	***	-4	***
									D	iastol	ic bloc	d press	sure (mmH	g)							
		1998	8-20	02		ANOVA		200	8-20	12		ANOVA		201	8-20	19		ANOVA	2018 vs 199			-2019 8-2012
Educational level						within - period						within period						within period	Diff	t-test	Diff	t-test
Educational level	n	mean	SD	959	% CI	sign ***	n	mean	SD	95%	% CI	sign - ***	n	mean	SD	95%	S CI	sign **	Dill	sign	Dill	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	***
							Sys	tolic b	ood	press	ure no	t unde	r dru	g treat	men	t (mr	nHg)					
		199	8-20	02		ANOVA		200	8-20	12		ANOVA		201	8-20	19		ANOVA	2018 vs 199			-2019 8-2012
Educational level						within - period						within period						within period	Diff	t-test	Diff	t-test
	n	mean	SD	959	% CI	sign ***	n	mean	SD	95%	6 CI	sign - ***	n	mean	SD	95%	S CI	sign ***		sign		sign
Higher education	928	128	16	127	129		992	122	14	121	122		593	119	15	117			-9	***	-3	***
Lower education	1331	129	16	129	130		651	127	16	126	128		203	123	16	121	125		-6	***	-4	**
							Dias	tolic b	lood	press	ure no	ot unde	r dru	g trea	tmer	nt (m	mHg)					
		199	8-20	02		ANOVA		200	8-20	12		ANOVA		201	8-20	19		ANOVA	2018 vs 199			-2019 8-2012
Educational level						within = period						within period						within period	Diff	t-test	Diff	t-test
	n	mean	SD	959	% CI	sign ***	n	mean	SD	95%	6 CI	sign ***	n	mean	SD	95%	s CI	sign *		sign		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 p	er m	inute)								
		1998	8-20	02		ANOVA		200	8-20	12		ANOVA		201	8-20	19		ANOVA	2018 vs 199			-2019 8-2012
Educational level						within ⁻ period						within period						within period	Diff	t-test	Diff	t-test
Educational level	n	mean	SD	959	% CI	sign	n	mean	SD	95%	% CI	sign -	n	mean	SD	95%	s CI	sign	UIIT	sign	DIII	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<0.005; 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												
							Blo	od I	pressure d	rug tı	eatn	nent						
	1	998-2	2002		2	.008-	2012			2	2018-	2019)			18-2019 998-2002		.8-2019 .08-2012
Educational level	n	%	95% CI	Chi-squared test within period sign	n	%	95%	CI	Chi-squared test within period sign ns	n	%	95%	6 CI	Chi-squared test within period sign ns	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	1249 1730	19 20	16 21 18 22	113	1183 1018	26 26	23 28 24 29		113	725 303	26 24	23 19	29 29	713	7	** ns	0.2	ns ns
								Ra	ised blood	pres	sure							
	1	998-2	2002		2	.008-	2012			2	2018-	2019)			18-2019 998-2002		.8-2019 008-2012
Educational level	n	%	95% CI	Chi-squared test within period sign	n	%	95%	cı	Chi-squared test within period sign	n	%	95%	6 CI	Chi-squared test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education	1249 1730	49 52	46 52 50 55	ns	1183 1018	36 44		39 47	**	725 303	28 34	25 29	31 39	ns	-21 -18	***	-8 -10	**
									Hyperte	nsion								
	1	998-2	2002	Chi-squared	2	.008-	2012		Hyperte			2019)			18-2019		8-2019
Educational level	n	%	95% CI	test within period sign	n	%	95%	CI.	Chi-squared test within period sign	n	%	95%	6 CI	Chi-squared test within period sign		chi- squared sign	Diff	chi- squared
Higher education	1249 1730	53 56	50 55 54 59	*	1183 1018	49 53	46	52 56	ns	725 303	43 46	40	47 52	ns	-9 -10	***	-6 -7	*
								Indi	agnosed h			nn						
	1	998-2	2002		2	008-	2012	1101	-			2019)			18-2019		8-2019
				Chi-squared					Chi-squared test within period					Chi-squared test within period		998-2002 chi-		008-2012 chi-
Educational level	n	%	95% CI	test within period sign ns	n	%	95%	CI	sign	n	%	95%	6 CI	sign	Diff	squared sign	Diff	squared sign
Higher education Lower education	621 1063	53 53	49 57 50 56		555 610	36 39		40 43		314 168	36 38	31 31	41 46		-17 -15	***	-0.2 -1	ns ns
						D	iagno	sed	but untrea	ated	hype	rtens	sion					
	1	998-2	2002		2	008-	2012			2	2018-	2019)			18-2019 998-2002		.8-2019 .08-2012
Educational level	n	%	95% CI	Chi-squared test within period sign	n	%	95%	cı	Chi-squared test within period sign	n	%	95%	6 CI	Chi-squared test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	621 1063	16 15	13 19 12 17	ns	555 610	19 16		22 18	ns	314 168	13 15	10 10	17 21	ns	-2 1	ns ***	-6 -0.1	* ns
							U	Inco	ntrolled h	ypert	ensid	n						
	1	998-2	2002	Chi-squared	2	008-	2012		Chid	2	2018-	2019)	Chi-squared		18-2019 998-2002		.8-2019 .08-2012
Educational level	n	%	95% CI	test within period sign	n	%	95%	CI	Chi-squared test within period sign **	n	%	95%	6 CI	test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	621 1063	25 26	22 29 23 28	ns	555 610	22 30		26 33		314 168	21 26	17 19	26 33	ns	-4 0.5	ns ***	-1 -4	ns ns
								Con	trolled hyp	erte	nsior	1						
	1	998-2	2002	Car year make	2	008-	2012		1365 CONSTRU	2	2018-	2019)	eggperatura la		18-2019 998-2002		8-2019 008-2012
Educational level	n	%	95% CI	Chi-squared test within period sign	n	%	95%	CI	Chi-squared test within period sign	n	%	95%	6 CI	Chi-squared test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education Lower education	621 1063	6 7	4 8 5 8	ns	555 610	22 15		26 18	**	314 168	30 20	24 14	35 26	*	23 13	***	7 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.

										WON	IEN								
								ВІ	ood	pressure d	lrug t	reati	ment	1					
	19	998-2	2002			2	008-	2012			2	2018-	2019)			18-2019 998-2002		18-2019 008-2012
Educational level	n	%	95%	s cı	Chi-squared test within period sign ***	n	%	95%	s cı	Chi-squared test within period sign ***	n	%	95%	í CI	Chi-squared test within period sign **	Diff	chi- squared sign	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
									Ra	aised blood	pres	ssure	•						
	19	998-2	2002			2	008-	2012	!		2	2018-	2019)			18-2019 998-2002		18-2019 008-2012
ducational level	n	%	95%	s cı	Chi-squared test within period sign	n	%	95%	s cı	Chi-squared test within period sign	n	%	95%	s cı	Chi-squared test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education	1052 1887	35 42	32 40	38 44	**	1167 1017	22 30	20 27	24	***	725 339	14 21	11 16	16 25	**	-21 -21	***	-8 -9	***
ower education	1007	42	40	77		1017	30	21	32				70	25		-21		-9	
										Hyperte						20	18-2019	201	18-2019
	19	998-2	2002			2	008-	2012			2	2018-	2019)			998-2002		008-2012
Educational level	n	%	95%	cı	Chi-squared test within period sign	n	%	95%	s CI	Chi-squared test within period sign	n	%	95%	s CI	Chi-squared test within period sign	Diff	chi- squared sign	Diff	chi- squared sign
Higher education	1052	40	37	43	**	1167	32	29	34	***	725	27	24	30	**	-13	***	-5	*
ower education	1887	47	45	49		1017	41	38	44		339	38	33	43		-9	**	-3	ns
									Und	iagnosed h	yperl	tensi	on						
	19	998-	2002			2	008-	2012			2	2018-	2019)			18-2019 998-2002		18-2019 008-2012
ducational level	n	%	95%	c cı	Chi-squared test within period sign	n	%	95%	s cı	Chi-squared test within period sign	n	%	95%	s cı	Chi-squared test within period sign		chi- squared sign		chi- squared sign
	207		40	50	ns	044		20	44	**	400		04	24	ns		***		
ligher education ower education	337 1037	47 43	42 40	52 46		311 534	36 25	30 21	41 28		192 172	28 31	21 24	34 38		-19 -12	**	-8 6	ns ns
								Diagn	osed	but untre	ated	hype	erten	sion					
	19	998-	2002			2		2012					2019				18-2019		18-2019
ducational level	n	%	95%		Chi-squared test within period	n	%	95%	· •	Chi-squared test within period	n	%	95%	· 61	Chi-squared test within period		chi- squared	Vs 20	chi- squared
				002000	ns				2012	sign ns			22.75.41	220000	sign ns				
ligher education ∟ower education	337 1037	19 15	14 13	23 18		311 534	15 16	11 13	19 19		192 172	17 13	12 8	23 18		-1 -2	ns ***	-3	ns *
									Unce	ontrolled h	vneri	tensi	on						
	10	998-	2002			2	008-	2012		one one o			2019	,			18-2019		18-2019
					Chi-squared					Chi-squared				,	Chi-squared	vs 1	998-2002 chi-	vs 20	008-2012 chi-
ducational level	n	%	95%	s CI	test within period sign **	n	%	95%	s CI	test within period sign *	n	%	95%	s CI	test within period sign ns	Diff	squared sign	Diff	squared sign
ligher education ower education	337 1037	24 32	19 29	28 34		311 534	23 29	18 25	27 33		192 172	14 17	9	19 22		-9 -15	*	-8 -12	* ns
ower education	1037	32	29	34		554	29	25						22		-13		-12	115
										ntrolled hy	perte	nsio	n			20	18-2019	201	18-2019
	19	998-2	2002			2	008-	2012			2	2018-	2019)			998-2002		008-2012
					Chi-squared test within					Chi-squared test within					Chi-squared test within	Diff	chi- squared	Diff	chi- squared
ducational level	n	%	95%	ci Ci	period sign ns	n	%	95%	s CI	period sign ns	n	%	95%	s CI	period sign ns		sign		sign

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	1 and 2
		title or the abstract	
		(b) Provide in the abstract an informative and balanced summary of	2
		what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation	4
		being reported	
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	5
C		of recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of	5
		selection of participants	
Variables	7	Clearly define all outcomes, exposures, predictors, potential	5 and 6
		confounders, and effect modifiers. Give diagnostic criteria, if	
		applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of	5 and 6
measurement		methods of assessment (measurement). Describe comparability of	
		assessment methods if there is more than one group	
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	5 and 6
		applicable, describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control	6
		for confounding	
		(b) Describe any methods used to examine subgroups and	6
		interactions	
		(c) Explain how missing data were addressed	6
		(d) If applicable, describe analytical methods taking account of	5
		sampling strategy	
		(\underline{e}) Describe any sensitivity analyses	na
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg	6 and in al
		numbers potentially eligible, examined for eligibility, confirmed	tables
		eligible, included in the study, completing follow-up, and analysed	
		(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,	6 and table
		clinical, social) and information on exposures and potential	s1
		confounders	
		(b) Indicate number of participants with missing data for each	6 and in al
		variable of interest	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-	6-12 and in
		adjusted estimates and their precision (eg, 95% confidence interval).	all tables
		Make clear which confounders were adjusted for and why they were	
		included	
		(b) Report category boundaries when continuous variables were	6-12 and in
		categorized	related
			tables
		(c) If relevant, consider translating estimates of relative risk into	na
		absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and	6-12 and in
		interactions, and sensitivity analyses	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	14
		potential bias or imprecision. Discuss both direction and magnitude	
		of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering	14-15
		objectives, limitations, multiplicity of analyses, results from similar	
		studies, and other relevant evidence	
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	18
		study and, if applicable, for the original study on which the present	
		article is based	

^{*}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.