




May Measure Month 2022 in Italy: A Focus on Fixed-dose Combination, Therapeutic Adherence, and Medical Inertia in a Nationwide Survey

Rita Del Pinto¹ · Claudia Agabiti Rosei² · Claudio Borghi³ · Franco Cipollini⁴ · Santina Cottone⁵ · Giuseppe Antonio De Giorgi⁶ · Antonino Di Guardo⁷ · Maurizio Dugnani⁸ · Bruno Fabris⁹ · Cristina Giannattasio¹⁰ · Gilberta Giacchetti¹¹ · Pietro Minuz¹² · Giuseppe Mulè⁵ · Pietro Nazzaro¹³ · Gianfranco Parati^{14,15} · Marcello Rattazzi¹⁶ · Francesca Saladini¹⁷ · Massimo Salvetti¹⁸ · Riccardo Sarzani¹⁹ · Carmine Savoia²⁰ · Giuliano Tocci²⁰ · Franco Veglio²¹ · Massimo Volpe²² · Vito Vulpis²³ · Gianluca Baldini¹ · Claudio Ferri¹  · Maria Lorenza Muiesan²

Received: 29 February 2024 / Accepted: 4 April 2024 / Published online: 3 June 2024
© The Author(s) 2024

Abstract

Introduction Hypertension is the main risk factor for cardiovascular diseases (CVD). Notably, only about half of hypertensive patients manage to achieve the recommended blood pressure (BP) control. Main reasons for the persistence of uncontrolled BP during treatment are lack of compliance on the patients' side, and therapeutic inertia on physicians' side.

Methods During the global BP screening campaign “May Measure Month” (MMM) (May 1st to July 31st, 2022), a nationwide, cross-sectional, opportunistic study endorsed by the Italian Society of Hypertension was conducted on volunteer adults ≥ 18 years to raise awareness of the health issues surrounding high BP. A questionnaire on demographic/clinical features and questions on the use of fixed-dose single-pills for the treatment of hypertension was administered. BP was measured with standard procedures.

Results A total of 1612 participants (mean age 60.0 ± 15.41 years; 44.7% women) were enrolled. Their mean BP was $128.5 \pm 18.1/77.1 \pm 10.4$ mmHg. About half of participants were sedentary, or overweight/obese, or hypertensive. 55.5% individuals with complete BP assessment had uncontrolled hypertension. Most were not on a fixed-dose combination of antihypertensive drugs and did not regularly measure BP at home. Self-reported adherence to BP medications was similar between individuals with controlled and uncontrolled BP (95% vs 95.5%).

Conclusions This survey identified a remarkable degree of therapeutic inertia and poor patients' involvement in the therapeutic process and its monitoring in the examined population, underlining the importance of prevention campaigns to identify areas of unsatisfactory management of hypertension, to increase risk factors' awareness in the population with the final purpose of reducing cardiovascular risk.

Keywords Hypertension · Blood pressure · Therapeutic inertia · Prevention campaigns

1 Introduction

By affecting approximately 30% of the world's adult population of all ethnic groups, hypertension is the main risk factor for cardiovascular disease (CVD) [1]. According to a recent World Health Organization (WHO) report, high blood pressure (BP) was the cause of 51% of stroke deaths and 45% of overall cardiovascular deaths [2].

Classical and emerging cardiovascular risk factors, such as smoking habits, unhealthy diet, inflammatory conditions, including common periodontitis and gout, and early menopause, occur in association with arterial hypertension and its poor control [3–6]. Indeed, non-pharmacological strategies for hypertension control represent a mainstay of cardiovascular prevention, both before the initiation of and during any antihypertensive treatment. However, BP remains elevated in approximately 50% of treated hypertensive patients [5]. Relevant reasons that contribute to the persistence of uncontrolled BP values during treatment are lack of compliance on the patients' side, and clinical inertia on physicians' side.

Rita Del Pinto and Claudia Agabiti Rosei equal contribution.

Extended author information available on the last page of the article

Nonadherence to medications can depend on several factors, including treatment complexity and poor patients' involvement in the therapeutic process, especially in terms of education regarding indications and benefits of treatment [7]. Clinical inertia is not only the lack of increase in the number of antihypertensive drugs that are prescribed, but also the failure to replace the same drugs when ineffective and failure to exploit all the available pharmacological classes and their combinations according to guidelines recommendations [8]. Reducing therapeutic inertia is necessary and possible and requires a therapeutic alliance grounded on effective patient-centered communication and mutual engagement in the healthcare team to overcome clinician- and patient-level factors involved in the failure to achieve treatment goals. In this context, national, preventive population screening campaigns have a fundamental role both in raising awareness regarding the risks of uncontrolled cardiovascular risk factors and in educating to the good practices for a healthy lifestyle [9]. In this nationwide survey, we assessed BP profile, management, control, and relevant associated risk factors among Italian participants of the 2022 edition of the May Measure Month (MMM).

2 Methods

2.1 Study Design

The May Measure Month (MMM) is an international, annual BP screening campaign initiated by the International Society of Hypertension (ISH) in 2017 to raise the awareness of health issues related to high BP. During the extended MMM 2022 survey (May 1st to July 31st, 2022), the Italian Society of Hypertension participated in the campaign by endorsing a nationwide, cross-sectional, opportunistic study aimed at raising awareness of BP in the Italian general population. Volunteer adults aged 18 years, or more, were recruited at local sites by medical staff from the participating hospitals and general practitioners' offices in 23 Italian cities using convenience sampling. Staff at participating sites received specific training on BP measurements and administered a predefined questionnaire (Supplementary material) on major demographic and clinical characteristics, including BP-related features (personal history of hypertension, whether on antihypertensive medications, number of antihypertensive drug classes, compliance with antihypertensive treatment, timing of last BP assessment), integrated with questions for the assessment of periodontal health status (diagnosed periodontitis, bleeding on brushing, elongated teeth, loose teeth) and use of fixed-dose single-pill for the treatment of hypertension (2-drug or 3-drugs single-pill combinations).

2.2 BP Measurement

BP measurements were performed using automated, validated sphygmomanometers [10]. After a 5-min rest in the sitting position, with back and arm supported and feet flat on the floor, participants underwent a minimum of one single BP measurement up to three consecutive assessments at 1-minute intervals. For each participant, all the available BP readings were recorded. Automatically displayed pulse rates were also recorded.

2.3 Definitions

Hypertension was defined as a self-reported diagnosis or being currently treated for high BP. Untreated hypertension was defined as BP ≥ 140 and/or 90 mmHg in the absence of antihypertensive medications. Among individuals who received antihypertensive medications, uncontrolled hypertension was defined as BP $\geq 130/80$ mmHg if < 70 years of age and $\geq 140/80$ mmHg if ≥ 70 years [11].

Non-compliance to antihypertensive medications and related reasons (unavailability, forgetfulness, "on demand" use, excessive costs, side effects) was assessed based on a self-reported questionnaire.

2.4 Ethical Clearance

The survey was conducted in conformity with the Helsinki Declaration [12] and the European General Data Protection Regulation (EU GDPR), article 89 [13]. For each participating site, a coordinator was identified to take the responsibility of acquiring ethical clearance for the survey, if required. Data were anonymized at enrolment, making the identification of participants not possible.

2.5 Statistical analysis

Data were entered on pre-prepared paper forms that were centralized at the Italian Society of Hypertension coordinating centre, where they were transferred to a spreadsheet.

All analyses were performed using R (v 4.2.1). Unpaired Student's *t* test and Chi-squared test were used to detect differences in quantitative (mean \pm standard deviation [SD]) and qualitative (N, %) data, respectively (statistical significance: $p < 0.05$). BP was used as a continuous (mmHg) and categorical variable. When available, the average of the 2nd and 3rd readings was calculated; otherwise, the first measurement alone was used for descriptive statistics, and BP ≥ 140 and/or 90 mmHg was considered as high BP.

BP profile and hypertension prevalence and classification (normal BP, newly diagnosed hypertension; controlled/

uncontrolled hypertension) overall and after stratification based on sex were assessed based on the mean of the 2nd and 3rd BP readings in the subset of individuals undergoing all three BP measurements who reported complete information on hypertension history and treatment. Individuals with newly diagnosed hypertension were considered unaware of their condition.

Multiple response analysis was performed to assess the frequency of different combinations of variables (including male sex, age ≥ 70 years, overweight/obesity, smoke, physical inactivity, non-use of fixed-dose single-pill combinations, diabetes, periodontitis, alcohol use) in the entire sample and in the subset of individuals with uncontrolled hypertension. The relative UpSet plot, showing intersections in a matrix whose rows correspond to given factors and the columns to the intersections between the same factors, was generated with the dedicated R package.

Data were analyzed as recorded, without imputation for missing data. Comparisons were not performed for variables with missing data exceeding 20%.

3 Results

3.1 Overall Findings

A total of 1612 participants (mean age 60.0 ± 15.4 years; 44.7% women) took part in the survey. Their clinical and demographic features are reported in Table 1. Screening mostly occurred in outdoors public areas or in hospitals/clinics and pharmacies. Participants were mostly white, highly educated, non-diabetic, non-smoker individuals; 7.7% declared having participated in previous MMM campaigns. In the overall sample 51.4% participants were overweight or obese, 44.3% self-declared being hypertensive, 9.8% were diabetics, and 5.3% and 2.3% reported a history of heart attack and stroke, respectively; about 1 in 10 individuals reported a previous diagnosis of periodontitis, and bleeding on brushing was more frequently reported by women. Overweight/obesity, diabetes, and history of heart attack were more commonly reported by males. In terms of lifestyle habits, nearly half participants were sedentary, one in three individuals reported regular (daily or most days/week) alcohol use, and one in 5 was an active smoker. Women were less likely than men to drink alcohol and to smoke cigarettes (Table 1). All participants underwent at least one BP reading; 84.9% individuals underwent a second and third BP reading, with a mean BP of $128.5 \pm 18.1 / 77.1 \pm 10.4$ mmHg (Table 1). Interestingly, overweight/obesity and sedentary lifestyle were, together with male sex, the combination of traits most frequently observed among individuals with high BP on their first reading (measured BP ≥ 140 and/or 90 mmHg) (Fig. 1, panel a).

In terms of medication history, 26.8% and 16.7% reported being on a statin and on aspirin, respectively. Of those individuals who reported taking antihypertensive pills, most (47%) reported being on a single drug class, and nearly 40% reported being on at least 2 drug classes, but only 11.9% participants were taking a single pill combination. Most participants (94.9%) reported taking medications regularly. Interestingly, some participants were not able to tell whether they were taking statin, aspirin, or antihypertensive medications, or whether their BP pill was a combination of multiple drugs.

3.2 BP Profile and Control

Globally, 636 participants (39.5% of total; 41.8% women) underwent all three BP measurements and provided complete information on hypertension history and treatment (S Table 1 and Table 2).

Nearly 9 in 10 of them reported being hypertensive, and 85.7% declared taking antihypertensive medications (S Table 1). Based on their history and the average of the second and third BP readings, more than half participants (55.5%) had uncontrolled hypertension; only 1 in 3 (35.4%) showed levels within the predefined therapeutic goals; 7.1% had normal BP values; and 2.0% were in the BP range of newly diagnosed hypertension. Mean BP was lower in women than men (S Table 1); however, no sex-based difference in BP profile was recorded (Table 2).

Most treated participants took 1 to 2 drug classes for hypertension treatment, but only 1 in 6 was taking single-pill combinations; individuals with controlled hypertension were on a similar number of BP medication classes as compared with participants with uncontrolled hypertension (S Table 1). In terms of adherence to BP medications, the majority (95.0%) reported regular drug use, while about 4% declared taking medications “as needed” or forgetting to take them (S Table 1). Even more interestingly, no difference in antihypertensive medications adherence ($p = 0.936$) nor in the use of fixed-dose combinations of antihypertensive drugs ($p = 0.518$ for use vs non-use) was reported between controlled and uncontrolled hypertensive individuals (Figs. 2, 3). However, the combination of features most frequently observed among individuals with uncontrolled hypertension included male sex, overweight/obesity, sedentary lifestyle, and not being on a fixed-dose combination of antihypertensive drugs (Fig. 1, panel b).

Most participants who reported not measuring BP in the previous 12 months had BP values compatible with newly diagnosed hypertension, and individuals with controlled BP were more likely to have had their BP measured within the past 12 months compared with uncontrolled hypertensives (Table 2). Women reported more frequently than men to having had their BP measured in

Table 1 Demographic and clinical features of the Italian participants in the MMM 2022 campaign

Variable	Overall	Female	Male	p value	Missing
n	1612	721	891		
Age, years [mean (SD)]	59.99 (15.41)	60.09 (15.03)	59.91 (15.72)	0.817	0
Ethnicity (%)					
Non-White	47 (2.9)	18 (2.5)	29 (3.3)	0.445	0.6
White	1555 (97.1)	700 (97.5)	855 (96.7)		
BMI [mean (SD)]	25.82 (5.05)	24.50 (5.14)	26.88 (4.72)	< 0.001	15.8
BMI category (%)					
Underweight	54 (4.0)	44 (7.3)	10 (1.3)	< 0.001	15.8
Normal	605 (44.6)	330 (54.6)	275 (36.5)		
Overweight	451 (33.2)	145 (24.0)	306 (40.6)		
Obese	247 (18.2)	85 (14.1)	162 (21.5)		
Alcohol use (%)					
1–3 times per month	230 (14.7)	93 (13.2)	137 (15.9)	< 0.001	3
1–6 times per week	294 (18.8)	88 (12.5)	206 (23.9)		
Daily	143 (9.1)	31 (4.4)	112 (13.0)		
Never/rarely	897 (57.4)	490 (69.8)	407 (47.2)		
Tobacco smoke (%)					
Never	570 (36.3)	278 (39.4)	292 (33.7)	0.055	2.5
Previous	701 (44.6)	304 (43.1)	397 (45.8)		
Current	301 (19.1)	124 (17.6)	177 (20.4)		
Exercise (%)	771 (52.6)	341 (52.5)	430 (52.6)	0.99	9
Education (%)					
0	14 (1.0)	5 (0.8)	9 (1.2)	0.24	14.4
1–6 years	231 (16.7)	111 (18.2)	120 (15.6)		
7–12 years	602 (43.6)	250 (40.9)	352 (45.8)		
Over 12 years	533 (38.6)	245 (40.1)	288 (37.5)		
Diabetes (%)	129 (9.8)	44 (7.3)	85 (11.9)	0.007	18.1
Diagnosed hypertension (%)	712 (44.3)	303 (42.1)	409 (46.1)	0.128	0.3
Heart attack (%)	81 (5.3)	25 (3.6)	56 (6.7)	0.01	4.8
Stroke (%)	39 (2.6)	15 (2.2)	24 (2.9)	0.471	5.2
Previous pregnancy (%)	51 (7.6)	51 (7.9)	NA	NA	58.4
Diagnosed periodontitis (%)	169 (11.6)	79 (12.0)	90 (11.3)	0.756	9.7
Gingival bleeding on brushing (%)	206 (12.8)	112 (15.5)	94 (10.5)	NA	87.2
Mobile teeth (%)	102 (6.3)	43 (5.9)	59 (6.6)	NA	93.7
Long teeth (%)	26 (1.6)	10 (1.4)	16 (1.8)	NA	98.4
Screening site (%)					
Hospital/clinic/pharmacy	503 (31.2)	231 (32.0)	272 (30.5)	0.737	0
Public area (indoors)	84 (5.2)	39 (5.4)	45 (5.1)		
Public area (outdoors)	1025 (63.6)	451 (62.6)	574 (64.4)		
Previous MMM campaigns (%)	109 (7.7)	46 (7.2)	63 (8.1)	0.595	12.1
Last BP measurement (%)					
Never	55 (3.6)	20 (2.9)	35 (4.1)	0.304	4
Over 12 months ago	304 (19.6)	130 (18.8)	174 (20.3)		
Within the last 12 months	1189 (76.8)	542 (78.3)	647 (75.6)		
Mean SBP [mean (SD)]	128.51 (18.08)	125.11 (18.43)	131.26 (17.33)	< 0.001	15.1
Mean DBP [mean (SD)]	77.04 (10.44)	75.28 (9.95)	78.48 (10.61)	< 0.001	15.1
Mean HR [mean (SD)]	74.02 (11.40)	75.62 (10.55)	72.73 (11.89)	< 0.001	17.4
HTN drug classes (%)					
0	102 (13.3)	43 (13.2)	59 (13.4)	NA	52.5
1	360 (47.0)	163 (50.2)	197 (44.7)		
2	213 (27.8)	92 (28.3)	121 (27.4)		

Table 1 (continued)

Variable	Overall	Female	Male	p value	Missing
3	61 (8.0)	20 (6.2)	41 (9.3)		
4	16 (2.1)	5 (1.5)	11 (2.5)		
5 or more	6 (0.8)	0 (0.0)	6 (1.4)		
Don't know	8 (1.0)	2 (0.6)	6 (1.4)		
Single-pill combinations (%)					
2-Drug single pill	154 (11.0)	73 (11.3)	81 (10.7)	0.08	12.8
3-Drug single pill	12 (0.9)	2 (0.3)	10 (1.3)		
No	1222 (86.9)	567 (87.6)	655 (86.3)		
Don't know	18 (1.3)	5 (0.8)	13 (1.7)		
BP medications regularly (%)					
I do	617 (94.9)	260 (92.9)	357 (96.5)	NA	59.7
I forget	5 (0.8)	0 (0.0)	5 (1.4)		
Not easily available	6 (0.9)	4 (1.4)	2 (0.5)		
Only take them when I need them	20 (3.1)	14 (5.0)	6 (1.6)		
Side effects	1 (0.2)	1 (0.4)	0 (0.0)		
Too expensive	1 (0.2)	1 (0.4)	0 (0.0)		
Statin (%)					
Don't know	21 (1.4)	7 (1.1)	14 (1.8)	0.058	9.5
No	1047 (71.8)	496 (74.7)	551 (69.3)		
Yes	391 (26.8)	161 (24.2)	230 (28.9)		
Aspirin (%)					
Don't know	35 (2.4)	15 (2.3)	20 (2.5)	0.041	10.2
No	1170 (80.9)	548 (83.7)	622 (78.5)		
Yes	242 (16.7)	92 (14.0)	150 (18.9)		

p-Values indicate female-male comparisons; comparisons were not performed for variables with missing data exceeding 20%

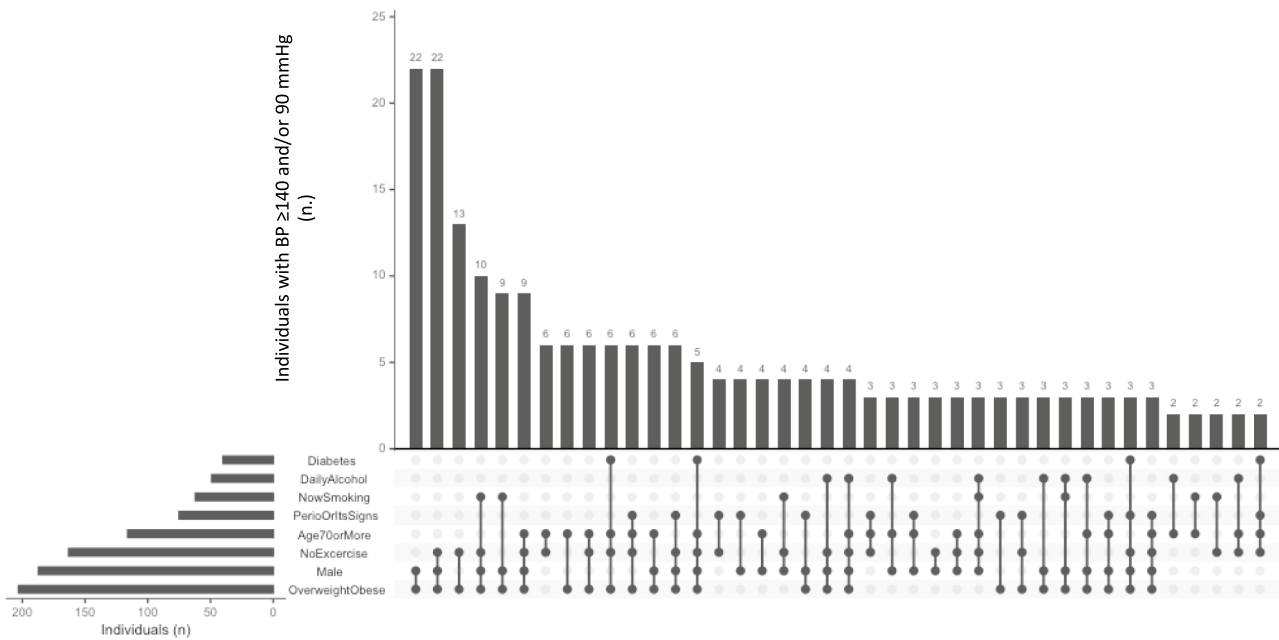
the previous year (S Table 1). Interestingly, 9.8% individuals with controlled hypertension versus 6.6% with uncontrolled hypertension reported participation in previous MMM campaigns, while none of those with new hypertension ever did (Table 2).

No significant differences in terms of prevalent diabetes, previous heart attack, or previous stroke, nor in the use of statin or aspirin, was observed based on sex or BP category (S Table 1, Table 2). Mean body weight progressively increased, with a parallel tendency to increased BMI, from individuals with normal BP to those with controlled hypertension and new/uncontrolled hypertension (Table 2). Individuals with new hypertension reported more frequently being current smokers and making regular alcohol use (from once weekly to daily consumption; Table 2). In parallel, a large proportion of normotensive individuals reported regular exercise and high education, although the finding was not significant as compared to individuals with hypertension. A large percentage of individuals with newly diagnosed hypertension declared signs of periodontal disease or a previous diagnosis of periodontitis (Table 2).

4 Discussion

The findings of this pragmatic, nationwide, cross-sectional BP survey of Italian adults indicate a high prevalence of adverse cardiometabolic features in the examined population, with about one in two participants declaring being sedentary, or suffering from exceeding body weight, or hypertension. Importantly, more than one in two individuals with complete BP assessment had uncontrolled hypertension, and male sex, overweight/obesity, sedentary lifestyle, and not being on a fixed-dose combination of antihypertensive drugs were the most common cluster of features in this setting. In addition, individuals with uncontrolled hypertension measured their BP less often than those with controlled hypertension, reflecting poor education to this practice that translates into scarce BP status awareness. However, adherence to BP medications was similar between individuals with controlled and uncontrolled BP (95% vs 95.5%). Altogether, these findings indicate a certain degree of therapeutic inertia and poor patients' involvement in the therapeutic process and its monitoring.

A



B

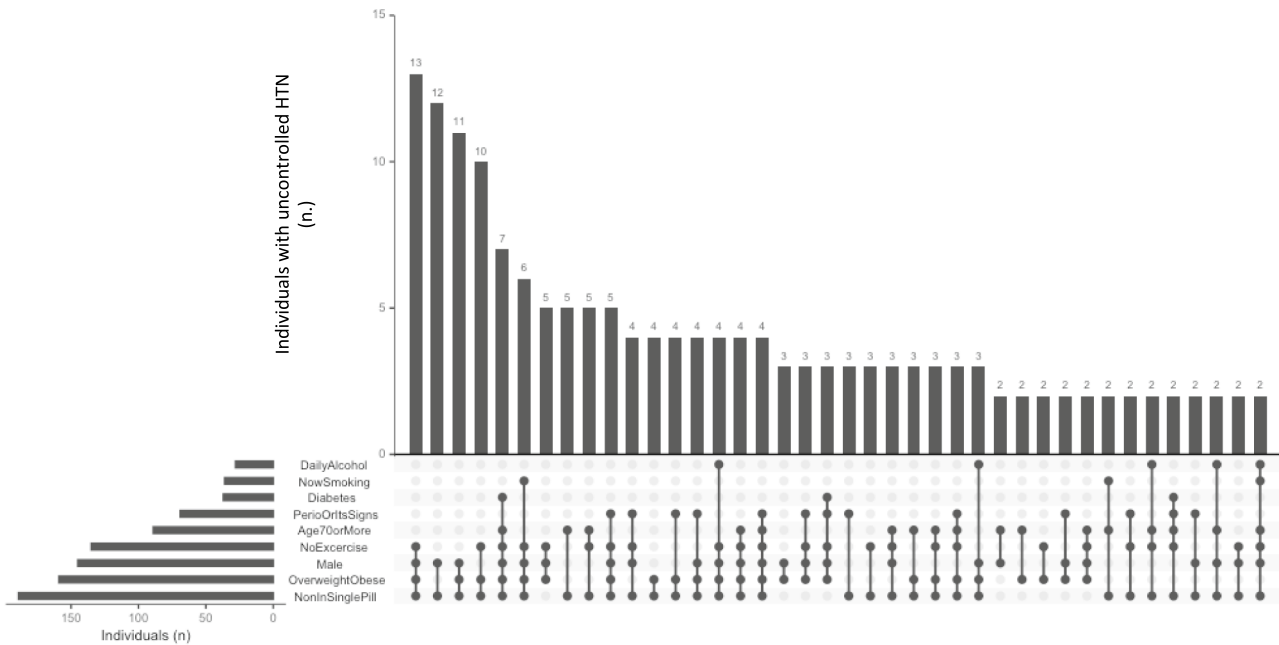


Fig. 1 Upset plot showing intersections of factors (overweight-obesity, male sex, sedentary lifestyle, older age, self-reported diagnosis of periodontitis and its signs, tobacco smoking, daily alcohol use, and diabetes) in individuals with BP ≥ 140 and/or 90 mmHg on their first

BP assessment (panel **a**) and in the subset of individuals with uncontrolled hypertension (panel **b**). The rows of the matrix correspond to the factors, and the columns to the intersections between these factors

Table 2. Demographic and clinical features of participants based on their BP profile.

Variable	Controlled HTN	New HTN	Normal BP	Uncontrolled HTN	p-Value	Missing (%)
n	225	13	45	353		
Age (mean, SD)	68.60 (11.53)	68.08 (10.90)	46.51 (15.52)	66.01 (11.51)	<0.001	0
White ethnicity (%)	220 (97.8)	12 (92.3)	45 (100.0)	339 (96.9)	0,399	0,5
Women (%)	107 (47.6)	3 (23.1)	21 (46.7)	135 (38.2)	0,066	0
Weight, kg (mean, SD)	73.49 (13.68)	74.54 (12.43)	71.73 (16.08)	78.27 (15.66)	0,001	2,2
BMI category (%)						
Underweight	10 (5.2)	0 (0.0)	4 (8.9)	6 (1.9)	0,026	11,5
Normal	62 (32.0)	6 (46.2)	20 (44.4)	97 (31.2)		
Overweight	80 (41.2)	2 (15.4)	10 (22.2)	119 (38.3)		
Obese	42 (21.6)	5 (38.5)	11 (24.4)	89 (28.6)		
Tobacco smoke (%)						
Never	89 (40.3)	5 (41.7)	23 (51.1)	127 (36.6)	<0.001	1,7
No—but did in the past	100 (45.2)	0 (0.0)	9 (20.0)	168 (48.4)		
Yes	32 (14.5)	7 (58.3)	13 (28.9)	52 (15.0)		
Alcohol (%)						
1–3 times per month	27 (12.1)	0 (0.0)	12 (26.7)	33 (9.5)	0,003	1,1
1–6 times per week	34 (15.2)	2 (16.7)	5 (11.1)	57 (16.3)		
Daily	20 (9.0)	4 (33.3)	0 (0.0)	39 (11.2)		
Never/rarely	142 (63.7)	6 (50.0)	28 (62.2)	220 (63.0)		
Diabetes (%)	33 (16.8)	1 (9.1)	6 (14.6)	46 (15.0)	0,881	12,6
Diagnosed hypertension (%)	223 (99.1)	0 (0.0)	0 (0.0)	348 (98.6)	<0.001	0
Heart attack (%)	22 (10.3)	1 (7.7)	2 (4.4)	29 (8.5)	0,629	3,8
Stroke (%)	11 (5.1)	0 (0.0)	0 (0.0)	14 (4.1)	0,383	3,8
Diagnosed periodontitis (%)	32 (15.3)	4 (30.8)	6 (13.3)	45 (13.8)	0,389	6,8
Bleeding on brushing (%)	40 (17.7)	3 (23.1)	3 (6.6)	54 (15.3)	NA	84,3
Mobile teeth (%)	29 (12.9)	2 (15.4)	2 (4.4)	18 (5.1)	NA	92
Long teeth (%)	7 (3.1)	0 (0)	0 (0)	7 (1.9)	NA	97,8
Exercise (%)	87 (41.2)	5 (41.7)	20 (46.5)	145 (43.8)	0,901	6,1
Education (%)						
0	2 (1.1)	0 (0.0)	0 (0.0)	3 (0.9)	0,618	11,6
1–6 years	45 (23.9)	3 (25.0)	3 (7.0)	71 (22.3)		
7–12 years	82 (43.6)	6 (50.0)	23 (53.5)	144 (45.1)		
Over 12 years	59 (31.4)	3 (25.0)	17 (39.5)	101 (31.7)		
Last BP measurement (%)						
Never	2 (0.9)	3 (23.1)	3 (6.7)	2 (0.6)	<0.001	1,3
Over 12 months ago	17 (7.7)	6 (46.2)	16 (35.6)	42 (12.1)		
Within the last 12 months	203 (91.4)	4 (30.8)	26 (57.8)	304 (87.4)		
HTN drug classes (%)						
0	10 (4.4)	13 (100.0)	45 (100.0)	23 (6.5)	<0.001	0
1	114 (50.7)	0 (0.0)	0 (0.0)	184 (52.1)		
2	71 (31.6)	0 (0.0)	0 (0.0)	98 (27.8)		
3	16 (7.1)	0 (0.0)	0 (0.0)	37 (10.5)		
4	8 (3.6)	0 (0.0)	0 (0.0)	6 (1.7)		
5 or more	3 (1.3)	0 (0.0)	0 (0.0)	2 (0.6)		
Don't know	3 (1.3)	0 (0.0)	0 (0.0)	3 (0.8)		
Statin (%)						
Don't know	7 (3.3)	0 (0.0)	0 (0.0)	7 (2.1)	<0.001	5,2
No	112 (53.3)	12 (92.3)	41 (93.2)	203 (60.4)		
Yes	91 (43.3)	1 (7.7)	3 (6.8)	126 (37.5)		
Aspirin (%)						

Table 2. (continued)

Variable	Controlled HTN	New HTN	Normal BP	Uncontrolled HTN	p-Value	Missing (%)
Don't know	6 (2.9)	0 (0.0)	0 (0.0)	7 (2.1)	0,036	5,8
No	148 (70.5)	10 (76.9)	41 (93.2)	224 (67.5)		
Yes	56 (26.7)	3 (23.1)	3 (6.8)	101 (30.4)		
Mean SBP [mean (SD)]	119.37 (10.48)	158.54 (11.34)	114.16 (11.80)	141.94 (15.86)	<0.001	0
Mean DBP [mean (SD)]	69.50 (6.14)	87.96 (10.33)	72.54 (8.62)	82.89 (8.78)	<0.001	0
Mean HR [mean (SD)]	71.30 (11.06)	77.81 (9.53)	72.80 (11.36)	74.41 (11.96)	0,009	3,9
Previous MMM campaigns (%)	20 (9.8)	0 (0.0)	1 (2.4)	21 (6.6)	0,212	9,4

Participants with complete information on hypertension history and treatment and undergoing all three BP measurements (n. 636) are included. p-Values indicate between-groups comparisons; comparisons were not performed for variables with missing data exceeding 20%

Therapeutic inertia, a multifactorial condition where lack of treatment intensification leads to failure to achieve treatment goals [14], is considered an obstacle to effective BP control in clinical practice [15]. Indeed, the lack of antihypertensive treatment intensification is a major contributing factor to poor BP control [16]. Findings of a retrospective cohort study conducted before the SPRINT era on 7253 hypertensive patients undergoing at least 4 visits and who had at least one measured BP compatible with uncontrolled BP indicate that antihypertensive therapy was intensified at only 13% of visits with uncontrolled BP, i.e. roughly one in 10 encounters [16]. Despite current hypertension guidelines recommend a BP target set at values lower than ever before, which should have prompted intensification of treatment as early as during its initiation and during follow-up until the achievement of target BP, still less than 25% of treated patients achieve their BP target, according to recent reports [17]. Factors found to be inversely correlated with medication escalation include older age, comorbidities, number of antihypertensive medications, visit frequency, and near-target BP, while conditions like kidney and heart failure are inversely related to inertia [18–20]. Interestingly, a cohort study on 6400 individuals with uncontrolled BP on one or two BP-lowering drugs found that the first reason why general practitioners did not intensify therapy was their consideration of office BP measurements as non-representative, determining the postponement of the decision to undertake any therapeutic change to the following BP measurement [15]. A recent Monte Carlo simulation study further expanded on this point by investigating the impact of measurement error on BP control in the presence of therapeutic inertia [20]. The authors found an inverse relationship between measurement error and controlled BP, suggesting an attitude towards reduced therapeutic inertia in relation to perceived accurate BP measurement [20]. In clinical practice, a strategy to minimize measurement error and provide an understanding of real BP values could be achieved through repeated BP measurements in the same individual. This is

in line with our findings that individuals with uncontrolled hypertension reported measuring their BP less often, and were therefore less aware of their BP status, than those with controlled hypertension.

The same simulation study also found that a strategy like treatment initiation with a dual antihypertensive therapy was likely to improve long-term BP control irrespective of BP measurement technique [20]. Indeed, real-world data on 13196 treated hypertensive individuals (mean age 73.2 ± 7.5 years, 55.5% women) suggest that simplified treatment strategies and use of fixed-dose combinations improve adherence to antihypertensive therapy and BP control [7]. Similarly, evidence indicates that adherence decreases with each pill added [21]. These observations are in line with our findings that not being on a fixed-dose combination of antihypertensive drugs was a common feature of individuals with uncontrolled hypertension. Beside increasing persistence and adherence to antihypertensive medication, thereby leading to an improvement in BP control, fixed-dose combinations were also reported to reduce adverse drug-related effects [23–25], which is particularly relevant during complex therapeutic regimens for cardiovascular and metabolic prevention. Finally, fixed-dose combinations may also improve hypertension control [25].

Notably, only 6.6% of individuals with uncontrolled BP reported participation in previous MMM campaigns, while none of those with new hypertension ever did, supporting the usefulness of periodical screening campaigns to increase awareness of risk factors and improve their control. As the most recent recommendations in hypertension indicate [26], it is mandatory to educate on correct lifestyles as non-pharmacological strategies for BP control. Such an approach includes dietary measures, regular physical activity, smoking cessation, as well as effective oral hygiene practices to control for periodontal disease, a non-traditional cardiovascular risk factor found to be independently linked to hypertension and target organ damage, possibly by means of low-grade systemic inflammation [27]. In accordance with this, a large percentage of individuals with newly diagnosed

BP medications regularly?

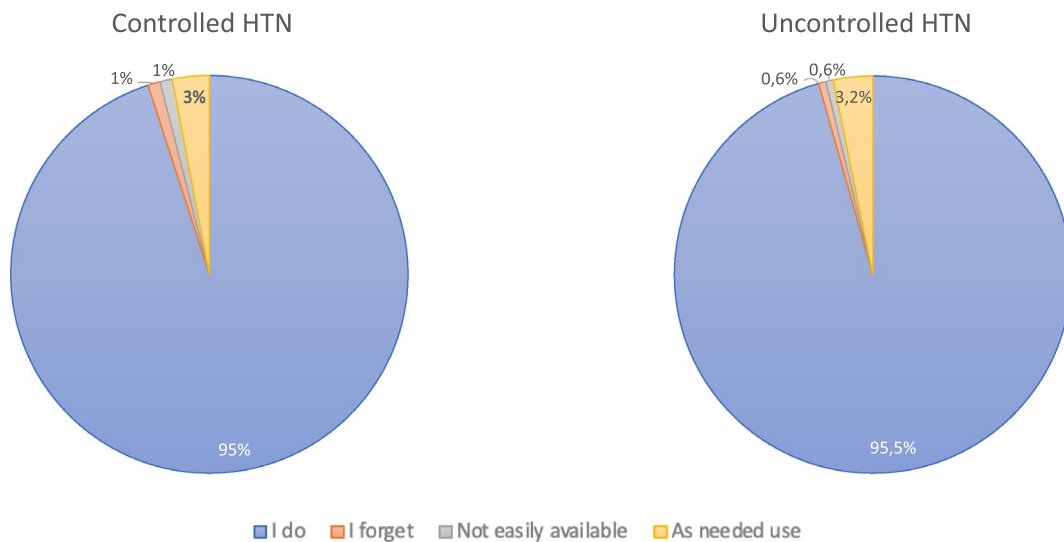


Fig. 2 Attitude towards use of antihypertensive drugs (regular use, forgetfulness, unavailability, and as needed use) among participants with controlled (left) and uncontrolled (right) hypertension. Percentages of individuals for each category are reported

Fixed-dose combinations of BP drugs

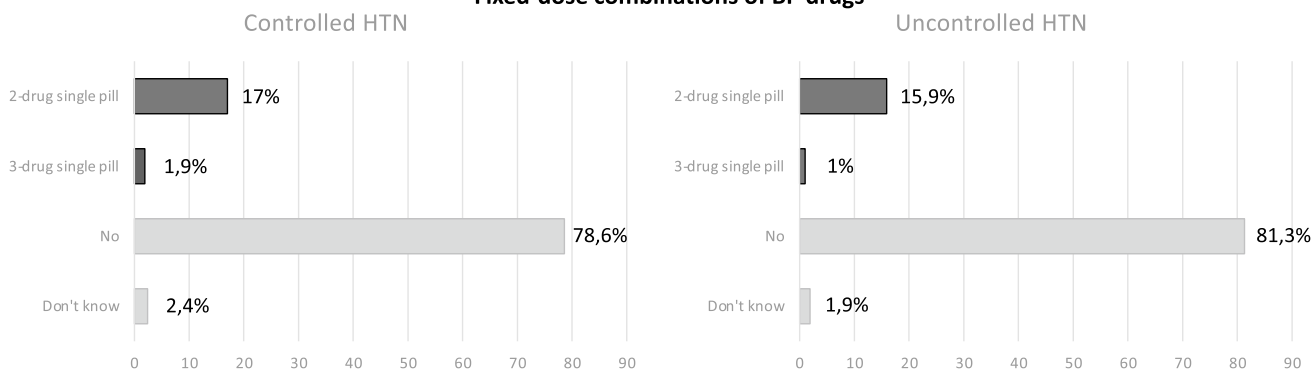


Fig. 3 Individuals (%) on a fixed-dose combination of antihypertensive drugs among participants with controlled (left) and uncontrolled (right) hypertension. Percentages of individuals for each category are reported

hypertension in this survey declared a previous diagnosis of periodontitis or signs of periodontal disease. Periodontitis is also a common finding and an exacerbating factor in individuals with diabetes [28]. Thus, greater awareness of traditional and emerging cardiovascular risk factors at the population level is mandatory to reduce the risk of death related to CVD [29], and screening campaigns could serve as a valuable means to achieve this goal [30].

This study has some limitations. Data, including medications type/combinations and compliance with treatment, were mostly self-reported. No information on antihypertensive medications dosage was available. Orthostatic BP changes were not assessed. Most participants underwent a single onsite BP measurement, which should be cautiously

considered when interpreting the related results. However, to overcome this issue, the assessment of the BP status was performed only on those participants who underwent complete BP measurements according to the study procedure.

In conclusion, this pragmatic, nationwide survey identified a high prevalence of cardiometabolic disorders and uncontrolled hypertension in the examined sample of the Italian population, indicating a remarkable degree of therapeutic inertia and poor patients' involvement in the therapeutic process and its monitoring, thereby underlining the importance of prevention campaigns to increase risk factors awareness and reduce cardiovascular risk. In addition, the study identified a low use of fixed-dose combinations in single-pill and thus a persistently low adherence to the

recommendations of the most recent Guidelines for the management of hypertension.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s40292-024-00642-4>.

Acknowledgements The authors would like to acknowledge the work of all the pharmacists who collected the data during the Italian campaign. The full list of collaborators to the MMM2022 global campaign is available here: <https://maymeasure.org/supporters/>. RDP acknowledges the PROMOTE-BP grant from Eklund Foundation (2022), the NIH/ORWH (3R01DK042191-30S1, administrative supplement for Research on Sex/Gender Differences) and the Crohn's & Colitis Foundation (882725, Clinical Research Investigator-Initiated Award (CRIA)-Senior Research Award (SRA)). RDP and CAR are Young Investigators of the Italian Society of Hypertension. MLM is President of the Italian Society of Hypertension. MV is supported by a grant of the Italian Ministry of Health.

Author Contributions RDP and CAR contributed equally to this work. RDP, CF, MLM conceived the study, carried out its design and interpreted the results. All authors participated to data collection. RDP performed statistics and data visualization. RDP, CAR, GB drafted the first manuscript. RDP, MLM, CF, MV, GP contributed to the interpretations of the findings and the critical revision of the manuscript. All authors agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.

Funding Open access funding provided by Università degli Studi dell'Aquila within the CRUI-CARE Agreement.

Data availability Data will be made available upon reasonable request to the Corresponding Author.

Declarations

Conflict of interest The authors declare no conflicts of interests. MLM declares travel support from Servier®.


Open Access This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

References

- Zhou B, Carrillo-Larco RM, Danaei G, Riley LM, Paciorek CJ, Stevens GA, Gregg EW, Bennett JE, Solomon B, Singleton RK, Sophiea MK, Iurilli ML, Lhoste VP, Cowan MJ, Savin S, Woodward M, Balanova Y, Cifkova R, Damasceno A, Ezzati M. World-wide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet*. 2021;398(10304):957–80. [https://doi.org/10.1016/S0140-6736\(21\)01330-1](https://doi.org/10.1016/S0140-6736(21)01330-1).
- WHO Global report on hypertension. <https://www.who.int/teams/noncommunicable-diseases/hypertension-report>. Accessed 30 Jan 2024
- Borghetti C, Agnoletti D, Cicero AFG, Lurbe E, Virdis A. Uric ACID and hypertension: a review of evidence and future perspectives for the management of cardiovascular risk. *Hypertension*. 2022;79(9):1927–36. <https://doi.org/10.1161/HYPERTENSIONAHA.122.17956>.
- Honigberg MC, Zekavat SM, Niroula A, Griffin GK, Bick AG, Pirruccello JP, Nakao T, Whitsel EA, Farland LV, Laurie C, Kooperberg C, Manson JE, Gabriel S, Libby P, Reiner AP, Ebert BL, Natarajan P. Premature menopause, clonal hematopoiesis, and coronary artery disease in postmenopausal women. *Circulation*. 2021;143(5):410–23. <https://doi.org/10.1161/CIRCULATIONAHA.120.051775>.
- Surma S, Romańczyk M, Witalińska-Łabuzek J, Czerniuk MR, Łabuzek K, Filipiak KJ. Periodontitis, blood pressure, and the risk and control of arterial hypertension: epidemiological, clinical, and pathophysiological aspects—review of the literature and clinical trials. *Curr Hypertens Rep*. 2021. <https://doi.org/10.1007/s11906-021-01140-x>.
- Del Pinto R, Landi L, Grassi G, Sforza NM, Cairo F, Citterio F, Paolantoni G, D'Aiuto F, Ferri C, Monaco A, Pietropaoli D. Hypertension and periodontitis: a joint report by the Italian Society of Hypertension (SIIA) and the Italian Society of Periodontology and Implantology (SIdP). *High Blood Press Cardiovasc Prev*. 2021. <https://doi.org/10.1007/s40292-021-00466-6>.
- Del Pinto R, Desideri G, Ferri C, Agabiti Rosei E. Real-world antihypertensive treatment patterns, treatment adherence, and blood pressure control in the elderly: an Italian awareness-raising campaign on hypertension by Senior Italia FederAnziani, the Italian Society of Hypertension and the Italian Federation of General Practitioners. *High Blood Press Cardiovasc Prev*. 2021;28(5):457–66. <https://doi.org/10.1007/s40292-021-00465-7>.
- Massimo Volpe con la collaborazione di Giovanna Gallo. (2017) Aderenza e continuità terapeutica nell'ipertensione arteriosa: il problema e le possibili soluzioni. *SPECIALITIES CORNER: Ipertensione Arteriosa. Rivista Società Italiana di Medicina Generale N.5 VOL.24 2017*
- Del Pinto R, Pagliacci S, de Feo M, Grassi D, Ferri C. Prevalence of hypertension and associated cardiovascular risk factors among pharmacists customers: an Italian nationwide epidemiological survey. *Eur J Prev Cardiol*. 2020;27(11):1228–30. <https://doi.org/10.1177/2047487319851301>.
- Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Brady A. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J*. 2018;39(33):3021–104. <https://doi.org/10.1093/eurheartj/ehy339>.
- Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, Benetos A, Biffi A, Boavida J-M, Capodanno D, Cosyns B, Crawford C, Davos CH, Desormais I, di Angelantonio E, Franco OH, Halvorsen S, Hobbs FDR, Hollander M, Williams B. 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J*. 2021;42(34):3227–337. <https://doi.org/10.1093/eurheartj/ehab484>.
- World Medical Association Declaration of Helsinki. *JAMA*. 2013;310(20), 2191. <https://doi.org/10.1001/jama.2013.281053>.
- Article 89 EU GDPR "Safeguards and derogations relating to processing for archiving purposes in the public interest, scientific or historical research purposes or statistical purposes". <https://>

- www.privacy-regulation.eu/en/article-89-safeguards-and-derogations-relating-to-processing-for-archiving-purposes-the-public-interest-scientific-or-hi-gdpr.htm. Accessed 30 Jan 2024
14. Dixon DL, Sharma G, Sandesara PB, Yang E, Braun LT, Mensah GA, Sperling LS, Deedwania PC, Virani SS. Therapeutic inertia in cardiovascular disease prevention. *J Am Coll Cardiol*. 2019;74(13):1728–31. <https://doi.org/10.1016/j.jacc.2019.08.014>.
 15. Ali DH, Kiliç B, Hart HE, Bots ML, Biermans MCJ, Spiering W, Rutten FH, Hollander M. Therapeutic inertia in the management of hypertension in primary care. *J Hypertens*. 2021;39(6):1238–45. <https://doi.org/10.1097/HJH.0000000000002783>.
 16. Okonofua EC, Simpson KN, Jesri A, Rehman SU, Durkalski VL, Egan BM. Therapeutic inertia is an impediment to achieving the healthy people 2010 blood pressure control goals. *Hypertension*. 2006;47(3):345–51. <https://doi.org/10.1161/01.HYP.0000200702.76436.4b>.
 17. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Das SR, Delling FN, Djousse L, Elkind MSV, Ferguson JF, Fornage M, Jordan LC, Khan SS, Kissela BM, Knutson KL, Virani SS. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation*. 2019. <https://doi.org/10.1161/CIR.0000000000000659>.
 18. Redón J, Coca A, Lázaro P, Aguilar MD, Cabañas M, Gil N, Sánchez-Zamorano MÁ, Aranda P. Factors associated with therapeutic inertia in hypertension: validation of a predictive model. *J Hypertens*. 2010;28(8):1770–7. <https://doi.org/10.1097/HJH.0b013e32833b4953>.
 19. Gil-Guillén V, Orozco-Beltrán D, Pérez RP, Alfonso JL, Redón J, Pertusa-Martínez S, Navarro J, Cea-Calvo L, Quirce-Andrés F, Merino-Sánchez J, Carratalá C, Martín-Moreno JM. Clinical inertia in diagnosis and treatment of hypertension in primary care: quantification and associated factors. *Blood Press*. 2010;19(1):3–10. <https://doi.org/10.3109/08037050903350762>.
 20. Augustin A, Coutts L, Zanisi L, Wierzbicki AS, Shankar F, Chowiecnyk PJ, Floyd CN. Impact of therapeutic inertia on long-term blood pressure control. *Hypertension*. 2021;77(4):1350–9. <https://doi.org/10.1161/HYPERTENSIONAHA.120.15866>.
 21. Gupta P, Patel P, Horne R, Buchanan H, Williams B, Tomaszewski M. How to screen for non-adherence to antihypertensive therapy. *Curr Hypertens Rep*. 2016;18(12):89. <https://doi.org/10.1007/s11906-016-0697-7>.
 22. Bahiru E, de Cates AN, Farr MR, Jarvis MC, Palla M, Rees K, Ebrahim S, Huffman MD. Fixed-dose combination therapy for the prevention of atherosclerotic cardiovascular diseases. *Cochrane Database Syst Rev*. 2017. <https://doi.org/10.1002/14651858.CD009868.pub3>.
 23. Gupta AK, Arshad S, Poulter NR. Compliance, safety, and effectiveness of fixed-dose combinations of antihypertensive agents. *Hypertension*. 2010;55(2):399–407. <https://doi.org/10.1161/HYPERTENSIONAHA.109.139816>.
 24. Sherrill B, Halpern M, Khan S, Zhang J, Panjabi S. Single-pill vs free-equivalent combination therapies for hypertension: a meta-analysis of health care costs and adherence. *J Clin Hypertens*. 2011;13(12):898–909. <https://doi.org/10.1111/j.1751-7176.2011.00550.x>.
 25. Parati G, Kjeldsen S, Coca A, Cushman WC, Wang J. Adherence to single-pill versus free-equivalent combination therapy in hypertension: a systematic review and meta-analysis hypertension. *Am Heart Assoc*. 2021;77(2):692–705. <https://doi.org/10.1161/HYPERTENSIONAHA.120.15781>.
 26. Charchar FJ, Prestes PR, Mills C, Ching SM, Neupane D, Marques FZ, Sharman JE, Vogt L, Burrell LM, Korostovtseva L, Zec M, Patil M, Schultz MG, Wallen MP, Renna NF, Islam SMS, Hiremath S, Gyeltshen T, Chia Y-C, Tomaszewski M. Lifestyle management of hypertension: International Society of Hypertension position paper endorsed by the World Hypertension League and European Society of Hypertension. *J Hypertens*. 2024;42(1):23–49. <https://doi.org/10.1097/HJH.0000000000003563>.
 27. Del Pinto R, Landi L, Grassi G, Sforza NM, Cairo F, Citterio F, Paolantoni G, D’Aiuto F, Ferri C, Monaco A, Pietropaoli D. Hypertension and periodontitis: a joint report by the Italian Society of Hypertension (SIIA) and the Italian Society of Periodontology and Implantology (SIdP). *High Blood Press Cardiovasc Prev*. 2021;28(5):427–38. <https://doi.org/10.1007/s40292-021-00466-6>.
 28. Bitencourt FV, Nascimento GG, Costa SA, Andersen A, Sandbæk A, Leite FRM. Co-occurrence of periodontitis and diabetes-related complications. *J Dent Res*. 2023;102(10):1088–97. <https://doi.org/10.1177/00220345231179897>.
 29. Del Pinto R, Viazzi F, Pontremoli R, Ferri C, Carubbi F, Russo E. The URRAH study. *Panminer Med*. 2021. <https://doi.org/10.2373/S0031-0808.21.04357-3>.
 30. De Feo M, del Pinto R, Pagliacci S, Grassi D, Ferri C. Real-world hypertension prevalence, awareness, treatment, and control in adult diabetic individuals: an Italian Nationwide Epidemiological Survey. *High Blood Press Cardiovasc Prev*. 2021;28(3):301–7. <https://doi.org/10.1007/s40292-021-00449-7>.

Authors and Affiliations

Rita Del Pinto¹ · Claudia Agabiti Rosei² · Claudio Borghi³ · Franco Cipollini⁴ · Santina Cottone⁵ · Giuseppe Antonio De Giorgi⁶ · Antonino Di Guardo⁷ · Maurizio Dugnani⁸ · Bruno Fabris⁹ · Cristina Giannattasio¹⁰ · Gilberta Giacchetti¹¹ · Pietro Minuz¹² · Giuseppe Mulè⁵ · Pietro Nazzaro¹³ · Gianfranco Parati^{14,15} · Marcello Rattazzi¹⁶ · Francesca Saladini¹⁷ · Massimo Salvetti¹⁸ · Riccardo Sarzani¹⁹ · Carmine Savoia²⁰ · Giuliano Tocci²⁰ · Franco Veglio²¹ · Massimo Volpe²² · Vito Vulpis²³ · Gianluca Baldini¹ · Claudio Ferri¹  · Maria Lorenza Muiesan²

✉ Claudio Ferri
claudio.ferri@univaq.it

¹ Department of Life, Health and Environmental Sciences, Internal Medicine unit, ESH Excellence Center, S. Salvatore Hospital, University of L’Aquila, L’Aquila, Italy

² ESH Excellence Center, University of Brescia, Spedali Riuniti di Brescia, Italy

³ ESH Excellence Center, Sant’Orsola-Malpighi University Hospital, Alma Mater Studiorum University of Bologna, Bologna, Italy

- 4 San Jacopo Hospital, PIOT San Marcello Pistoiese, Pistoia, Italy
- 5 ESH Excellence Center, P. Giaccone Hospital, University of Palermo, Palermo, Italy
- 6 Outpatients Hypertension clinic, Lecce, Italy
- 7 Outpatients Hypertension clinic, Catania, Italy
- 8 Outpatients Hypertension clinic, Novara, Italy
- 9 Cattinara Hospital, University of Trieste, Trieste, Italy
- 10 ESH Excellence Center, Niguarda Hospital, University of Milano-Bicocca, Milan, Italy
- 11 Azienda Ospedaliero Universitaria delle Marche, Ancona, Italy
- 12 ESH Excellence Center, Policlinico G.B. Rossi, University of Verona, Verona, Italy
- 13 Hypertension clinic A.M.Pirrelli, University of Bari, Bari, Italy
- 14 Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy
- 15 Istituto Auxologico Italiano, IRCCS, St. Luke Hospital, Milan, Italy
- 16 Hypertension clinic, Cà Foncello Hospital, University of Padua, Treviso, Italy
- 17 Hypertension clinic, Cittadella Hospital, Padua, Italy
- 18 Department of Medical and Surgical Sciences, Spedali Civili, University of Brescia, Brescia, Italy
- 19 ESH Excellence Center, IRCCS-INRCA, Università Politecnica delle Marche, Ancona, Italy
- 20 Clinical and Molecular Medicine Department, Sapienza University, Rome, Italy
- 21 Department Medical Sciences, ESH Excellence Center, AOU Città della Salute e della Scienza, University of Turin, Turin, Italy
- 22 IRCCS San Raffaele, Rome, Italy
- 23 Emergency Medicine, Hypertension and Cardiovascular Risk Unit-Policlinico Hospital, Bari, Italy