Blood pressure control in Italy: analysis of clinical data from 2005–2011 surveys on hypertension

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Introduction: Blood pressure (BP) control is poorly achieved in hypertensive patients, worldwide.

Aim: We evaluated clinic BP levels and the rate of BP control in hypertensive patients included in observational studies and clinical surveys published between 2005 and 2011 in Italy.

Methods: We reviewed the medical literature to identify observational studies and clinical surveys on hypertension between January 2005 and June 2011, which clearly reported information on clinic BP levels, rates of BP control, proportions of treated and untreated patients, who were followed in different clinical settings (mostly in general practice, and also in outpatient clinics and hypertension centres).

Results: The overall sample included 158 876 hypertensive patients (94 907 women, mean age 56.6 ± 9.6 years, BMI 27.2 ± 4.2 kg/m^2, known duration of hypertension 90.2 ± 12.4 months). In the selected studies, average SBP and DBP levels were 145.7 ± 15.9 and 87.5 ± 9.7 mmHg, respectively; BP levels were higher in patients followed in hypertension centres (n = 10 724, 6.7%; 146.5 ± 17.3/88.5 ± 10.3 mmHg) than in those followed by general practitioners (n = 148 152, 93.3%; 143.5 ± 13.9/84.8 ± 8.9 mmHg; $P < 0.01$). More than half of the patients were treated (n = 91 318, 57.5%); among treated hypertensive patients, only 31 727 (37.0%) had controlled BP levels.

Conclusion: The present analysis confirmed inadequate control of BP in Italy, independently of the clinical setting. Although some improvement was noted compared with a similar analysis performed between 1995 and 2005, these findings highlight the need for a more effective clinical management of hypertension.

Keywords: blood pressure control, global cardiovascular risk, hypertension, hypertension surveys

Abbreviations: ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; BP, blood pressure

INTRODUCTION

Over the last decades, large observational studies have consistently reported a persistently inadequate level of blood pressure (BP) control in hypertensive patients [1,2]. Insufficient BP control has dramatic consequences for Public Health. In turn, effective BP reduction by means of pharmacological intervention is one of the most powerful and successful ways to reduce the incidence of cardiovascular morbidity and mortality [3,4].

Randomized clinical trials, in fact, have consistently demonstrated significant benefits by lowering high BP levels in hypertensive patients in different conditions, including high cardiovascular risk [5–7], coronary disease [8,9], stroke [10,11] or diabetic nephropathy [12,13]. A closer analysis of these interventional trials, however, showed that effective BP control (i.e. BP levels <140/90 mmHg for hypertensive patients and <130/80 mmHg in high-risk hypertensive patients with diabetes or renal disease) was achieved only in a few of these randomized clinical trials [14,15], thus confirming how challenging it is to achieve adequate BP control.

Poor BP control rates have been reported also by large observational studies and clinical surveys, performed in different clinical settings and in different countries. Indeed, our previous meta-survey of observational studies between 1995 and 2005, and involving about 53 000 diagnosed hypertensive patients in Italy, showed that only 22% of the patients had their BP levels below the recommended targets (<140/90 mmHg), whereas about 39% persisted in stage 1 hypertension and almost one-third had stage 2 hypertension, despite antihypertensive therapy [16]. A more

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recent international survey, which documented the clinical profile of more than 20 000 patients with arterial hypertension and cardiovascular risk factors, confirmed that only 22% of diagnosed hypertensive outpatients achieved the recommended BP control in Italy [17].

In recent years, many observational studies addressing the issue of BP control have been performed in Italy. This gave us the unique opportunity to achieve an updated appraisal of the clinical management of hypertension, focusing on high BP treatment and control in Italy. Thus, in the present article, we analysed the results of observational studies and clinical surveys to evaluate clinic BP levels and rates of BP control based on a large, representative hypertensive population in Italy. The main aim of our analysis was to report mean BP levels and to determine the rate of BP control according to the most recent sets of European guidelines on hypertension [18], that is, to determine how many patients had BP values less than 140 mmHg for systolic and/or less than 90 mmHg for diastolic, in different clinical settings.

METHODS

Data search and study selection

The methodology of our analysis has been previously described [19]. Briefly, we reviewed the medical literature to identify recent observational studies and clinical surveys conducted on hypertensive patients in Italy.

In this perspective, a computerized literature search was carried out using the *PubMed*, *MEDLINE*, *OVID* and *EMBASE* databases from January 2005 to June 2011. Only articles published in English language in peer-reviewed journals and clinical studies performed in adults (more than 18 years of age) were considered. For study searching, the following key words were applied: 'blood pressure', 'hypertension', 'observational study' and 'Italy'. Once identified, clinical studies were carefully revised by two investigators (G.T. and M.V.) to be considered for the present analysis according to the predefined criteria.

We considered the following inclusion criteria: observational studies or clinical surveys performed in individuals of both sexes, aimed at evaluating prevalence and/or clinical characteristics of hypertensive patients, which were carried out and published between 2005 and 2011; inclusion of hypertensive patients recruited in Italy; clear information on average levels of SBP and DBP in each population sample; and absence of any prospective pharmacological or nonpharmacological interventions in the study protocol (interventional, randomized clinical trials). Hypertensive patients have been evaluated and clinic BP levels have been measured in all patients included in the analysis during time intervals predefined in the individual studies. All clinical data have been collected by the investigators of the various studies during the observational periods. On the contrary, we considered the following exclusion criteria: interventional trials or clinical studies, aimed at evaluating the antihypertensive efficacy of any pharmacological or nonpharmacological strategy compared with placebo or active treatment; study population in which hypertensive patients represented only a minority (with a cut-off value that was arbitrarily considered by less than 30% of the population sample); patients included in national or local registry for evaluating the efficacy, safety and tolerability of antihypertensive agents or any other cardiovascular drugs and/or for administrative purposes.

Clinic blood pressure values and antihypertensive therapy

Although different criteria were used in the selected studies, particularly in those published before 2007, BP control was uniformly regarded as clinic BP values below 140 mmHg for SBP and/or below 90 mmHg for DBP [18].

In each study, absolute prevalence of treated and untreated hypertensive patients, as well as prevalence of controlled and uncontrolled individuals among treated hypertensive patients were calculated, when available. In this regard, proportions of treated patients on major antihypertensive drug class [including ACE inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, calcium-channel blockers and diuretics] were also reported.

Cardiovascular risk profile characterization

Sex distribution, mean values of age, BMI, heart rate and prevalence of cardiovascular major risk factors such as smoking, hypercholesterolemia and diabetes were collected for each survey included in the analysis. Information on hypertension-related organ damage and associated clinical conditions was also collected, when available.

Data analysis

According to the study protocol applied to our previous analysis [19], even in this population sample of hypertensive patients, the BP control was estimated according to types of studies (population surveys or clinical studies) and type of clinical setting (hypertension centres or general practitioners) to which patients were referred.

Because of the descriptive nature of the results, no statistical test was applied to the collected data. Data are expressed as mean ± SD and/or as percentage, when appropriate.

RESULTS

Study selection

Flowchart for study selection is reported in Fig. 1. Among the 61 studies initially selected for the analysis, 27 were excluded because of partial or missing information on BP levels and 15 because they were already considered in our previous analysis [19]. Four observational studies were excluded because they did not provide clear data on BP levels [20–23]. Two additional studies were omitted because they were published [24] or concluded [25] before 2005. Finally, two studies were not considered because they primarily focused on patients with metabolic syndrome [26] or otherwise healthy individuals [27] rather than on hypertension. Thus, on the basis on a strict selection approach and according to the predefined inclusion and exclusion criteria, a total of 11 observational studies or clinical surveys on hypertension in Italy were included the present analysis

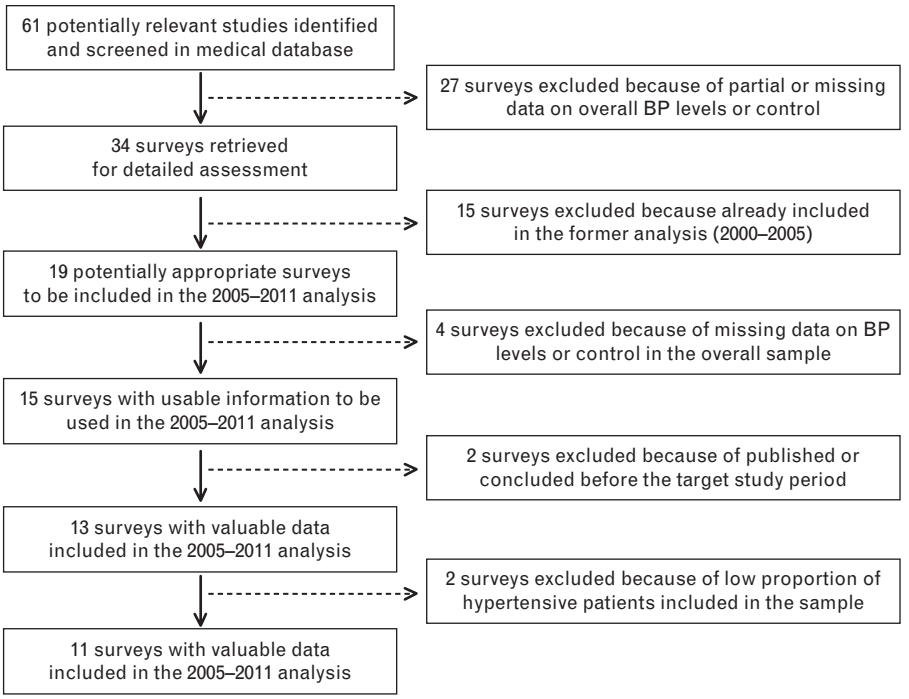

FIGURE 1 Flowchart for study selection.

[28–38]. A list of these studies with acronyms is reported in Acknowledgements section.

General characteristics of clinical studies

Table 1 reports the main characteristics of observational studies and clinical surveys considered for the analysis, including sample size, year of publication, observational period, geographical area, type of referring centre (general practitioners, hypertension clinics, outpatient clinics), type of population (outpatients or general population) and type of data collection (single centre or multicentre).

These studies enrolled a total of 158 876 hypertensive patients, a vast majority of whom were followed by general practitioners ($n = 148\,152$, 93.3%) [28,32,37–39] and only a minority by specialized centres (mostly hypertension centres) ($n = 10\,724$, 6.7%) [29–31,33,35,36,39]; in addition, almost all patients were included in multicentre studies ($n = 158\,021$, 99.5%) [28–32,36–39], whereas the proportion of patients included in single-centre studies was negligible ($n = 855$, 0.5%) [33,35].

Cardiovascular risk profile

General characteristics of the overall population and hypertensive patients, which were stratified according to the type of clinical referrals, are reported in Table 2.

In the overall population, 63 622 (40.0%) were men and 94 907 (60.0%) were women. Patients followed by general practitioners were predominantly women (about 60%), whereas a more balanced sex distribution was observed in outpatients followed by hypertension centres. Mean age was 56.6 ± 9.6 years, BMI was $27.2 \pm 4.2\,kg/m^2$ and heart rate was 73.2 ± 9.8 beats/min; all these parameters

TABLE 1. General characteristics of observational studies and clinical surveys on hypertension, performed in Italy between 2005 and 2010

Clinical survey	Population (*n*)	Publication (year)	Observational period (years)	Area	Type of referring centre	Type of population	Study design
SIMONA	18 326	2005	n.a.	Italy	GP	General population	Multicentre
APROS-Diadys	2 545	2007	n.a.	Italy	HC	Outpatient clinic	Multicentre
HYPER-PRACT	211	2008	2006 (March) to 2007 (March)	Lombardy	HC	Outpatient clinic	Multicentre
IPERDIA	1 397	2008	2001 (March 1 to October 31)	Italy	HC	Outpatient clinic	Multicentre
GP survey	119 065	2009	2005	Italy	GP	General population	Multicentre
MAGIC	400	2009	2002 (January) to March (2007)	Genoa	HC	Outpatient clinic	Single centre
EFFECTUS	9 904	2009	2006 (May)	Italy	HC, DC, GP	Outpatient clinic	Multicentre
REDHY	455	2010	n.a.	Palermo	HC	Outpatient clinic	Single centre
IDEMAND	3 534	2010	n.a.	Italy	HC	Outpatient clinic	Multicentre
MARTE	1 768	2010	2005 (July) to 2006 (November)	Italy	GP	General population	Multicentre
MIRACLES	1 271	2011	2007 (May) to 2008 (May)	Italy	GP	General population	Multicentre
OVERALL	158 876						

HC, hypertension centre; GP, general practitioner.

TABLE 2. General characteristics of hypertensive patients included in observational studies and clinical surveys on hypertension

Clinical survey	Male [*n* (%)]	Female [*n* (%)]	Age (years)	BMI	HR (beats/min)	Smoking	Dyslipidemia	Diabetes
Total centres = 158 876								
Hypertension centres (*n* = 10 724, 6.7%)								
APROS-Diadys	1248 (49.0)	1297 (51.0)	70.3 ± 4.5	26.0 ± 2.6	70.1 ± 8.6	n.a.	1364 (61.0)	404 (19.4)
HYPER-PRACT	111 (52.6)	100 (47.4)	56.4 ± 13.8	26.6 ± 3.8	73.2 ± 11.7	47 (22.5)	n.a.	21 (9.9)
IPERDIA	690 (49.4)	707 (50.6)	59.0 ± 8,0	28.0 ± 4.5	73.0 ± 10.0	n.a.	n.a.	242 (17.3)
MAGIC	260 (65.0)	140 (35.0)	47.0 ± 9.0	26.4 ± 3.5	n.a.	108 (27.0)	n.a.	0 (0.0)
EFFECTUS – Cardiology	5300 (53.5)	4604 (46.5)	67.0 ± 9.0	28.0 ± 5.0	n.a.	510 (23.4)	861 (59.0)	444 (37.0)
REDHY	246 (54.1)	209 (45.9)	48.3 ± 14.4	28.7 ± 4.8	n.a.	141 (31.0)	n.a.	n.a.
IDEMAND	1908 (54.0)	1626 (46.0)	61.5 ± 11.6	28.5 ± 4.8	n.a.	1484 (42.0)	2156 (61.0)	1308 (37.0)
Total	5184 (48.3)	5540 (51.7)	58.5 ± 10.0	27.5 ± 4.1	72.1 ± 10.1	2291 (21.4)	4381 (40.8)	2418 (22.6)
General practice (*n* = 148 152, 93.3%)								
SIMONA	0.0 (0.0)	18 326 (100.0)	52.8 ± 4,0	25.1 ± 4.2	75.0 ± 9.4	3848 (21.0)	4582 (25.0)	861 (4.7)
EFFECTUS – GPs	4129 (53.5)	3593 (46.5)	67.0 ± 9.0	28.0 ± 5.0	n.a.	2537 (32.9)	4402 (59.0)	2454 (37.0)
GP survey	52 788 (44.3)	66 017 (55.4)	n.a.	n.a.	n.a.	n.a.	n.a.	11 114 (16.6)
MARTE	843 (47.7)	925 (52.3)	61.1 ± 12.0	27.7 ± 4.3	74.6 ± 9.5	256 (14.5)	660 (37.4)	246 (13.9)
MIRACLES	724 (57.0)	547 (43.0)	43.0 ± 9.7	n.a.	n.a.	292 (25.0)	465 (36.6)	166 (13.1)
Total	58 484 (39.5)	89 408 (60.3)	56.0 ± 8.7	26.9 ± 4.5	74.8 ± 9.5	6933 (4.7)	10 109 (6.8)	14 841 (10.0)
Overall	63 668 (40.4)	94 948 (59.8)	56.6 ± 9.6	27.2 ± 4.2	73.2 ± 9.8	9501 (6.0)	15 099 (9.5)	18 043 (11.4)

Since both EFFECTUS [34] and MIRACLES [38] studies included patients followed in different clinical settings, in this table, only those data from hypertensive patients followed by GPs in the EFFECTUS [34] and by hypertension centres in the EFFECTUS [34] and MIRACLES [38] studies were reported. In the GP Survey [32], sex was not reported for 264 individuals. GP, general practitioner.

tended to be higher in patients followed by hypertension centres rather than in those followed by general practitioners.

In the overall sample, 6.0% of the patients were smokers, 9.5% had hypercholesterolemia and 11.4% had diabetes. Of note, and as an index of a greater complexity of patients, the prevalence of all these risk factors was substantially higher in the subgroup of patients followed in hypertension centres as compared with those followed by general practitioners, as illustrated in Fig. 2.

Blood pressure levels and control rates

As shown in Table 3, in the overall sample, mean SBP and DBP levels were 145.7 ± 15.9 and 87.5 ± 9.7 mmHg, respectively. In the majority of the selected studies, SBP levels exceeded the normal threshold of 140 mmHg, whereas DBP levels were more frequently below 90 mmHg, as represented in Fig. 3. Mean BP values were higher in patients followed in hypertension centres (146.5 ± 17.3/88.5 ± 10.3 mmHg) than in those followed by general practitioners (143.5 ± 13.9/84.8 ± 8.9 mmHg; $P < 0.01$) (Fig. 4). In addition, average BP levels were higher in single-centre studies than in multicentre studies (155.0 ± 18.0/96.0 ± 12.0 versus 143.7 ± 15.4/85.6 ± 9.2 mmHg; $P < 0.01$). In some selected studies which provided information on BP stratification ($n = 42\,845$) [32–34], the vast majority of the patients had grade I ($n = 30\,456$, 71.1%) or grade II–III ($n = 9340$, 21.8%) hypertension and only 2.8% ($n = 1182$)

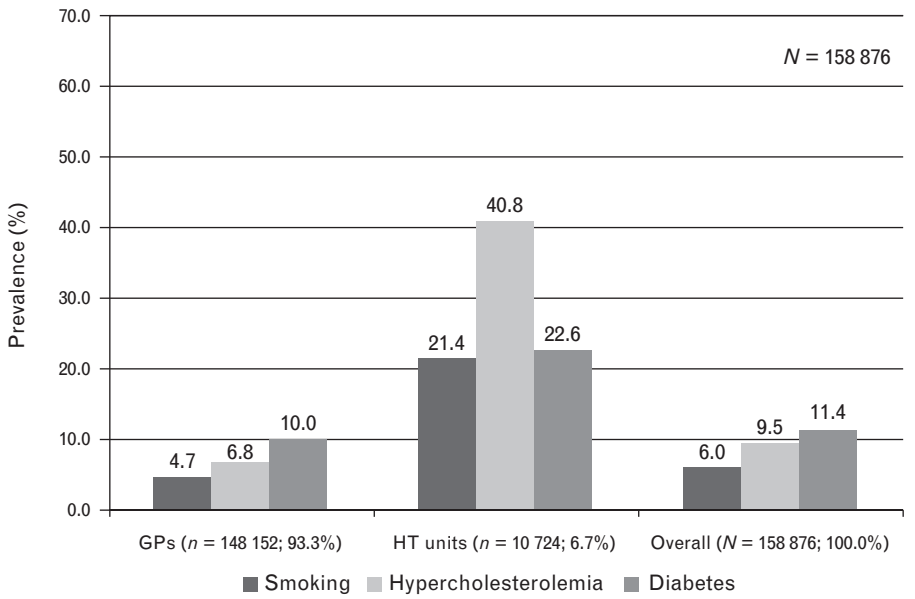

FIGURE 2 Distribution of major cardiovascular risk factors among hypertensive patients according to referring centres in Italy.

TABLE 3. Clinic SBP and DBP levels and proportions of treated and untreated patients in observational studies and clinical surveys on hypertension

Clinical survey	Clinic BP levels (mmHg)		Antihypertensive therapy (% among overall population)	
	SBP	DBP	Treated	Untreated
Hypertension centres ($n = 10\,724$, 6.7%)				
APROS-Diadys	145.2 ± 15.9	84.7 ± 8.5	2393 (94.0)	152 (6.0)
HYPER-PRACT	145.7 ± 19.7	89.1 ± 10.7	168 (79.6)	43 (20.4)
IPERDIA	145.0 ± 16.0	88.0 ± 9.0	1347 (96.4)	50 (3.6)
MAGIC	156.0 ± 15.0	100.0 ± 8.0	0 (0.0)	400 (100.0)
EFFECTUS – Cardiology	138.0 ± 14.0	81.0 ± 8.0	6025 (78.0)	1697 (22.0)
REDHY	154.0 ± 21.0	92.0 ± 16.0	345 (75.8)	110 (24.2)
IDEMAND	139.4 ± 16.6	83.8 ± 9.7	3237 (91.6)	297 (8.4)
Total	146.5 ± 17.3	88.5 ± 10.3	8658 (80.7)	2066 (19.3)
General practice ($n = 148\,152$, 93.3%)				
SIMONA	136.6 ± 17.6	83.0 ± 10.0	6066 (33.1)	12 260 (66.9)
EFFECTUS – GPs	140.0 ± 17.0	82.0 ± 10.0	1168 (53.5)	1014 (46.5)
MARTE	144.0 ± 15.8	85.8 ± 9.6	1768 (100.0)	0 (0.0)
MIRACLES	135.6 ± 12.5	83.4 ± 7.5	1243 (97.8)	28 (2.2)
Total	143.5 ± 13.9	84.8 ± 8.9	81 989 (55.3)	66 163 (44.7)
OVERALL	145.7 ± 15.9	87.5 ± 9.7	91 318 (57.5)	67 558 (42.5)

When available [32–34,37], SBP and DBP levels were always within the high-normal values in treated hypertensive patients (135.1 ± 12.0/81.1 ± 7.6 mmHg), whereas they were in stage 2 hypertension thresholds in untreated hypertensive patients (150.0 ± 12.8/89.6 ± 8.5 mmHg), with the only exception of the EFFECTUS study [34], in which both treated and untreated BP levels were reported in the high-normal thresholds. BP, blood pressure.

had high-normal BP values, the remaining proportions were of patients with normal or optimal BP thresholds ($n = 2317$, 4.3%).

About half of the overall patients were treated ($n = 91\,318$, 57.5%). The proportion of treated patients, however, was higher in those followed in hypertension centres ($n = 8658$, 80.7%) than in those followed by general practitioners ($n = 81\,989$, 55.3%). BP control rates among treated hypertensive patients were reported in three surveys performed by general practitioners ($n = 30\,801$, 40.6%) [32,37,38] and only in one study performed in hypertension centres ($n = 526$, 10.7%) [29], with an overall

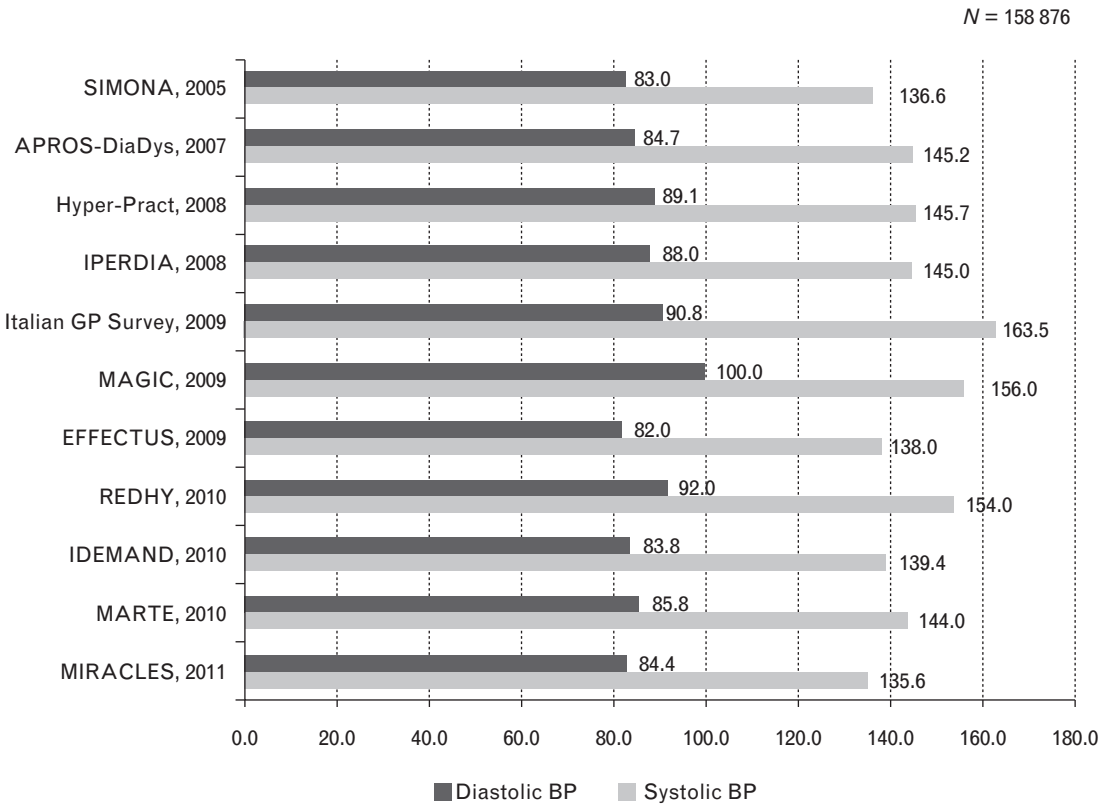

FIGURE 3 Clinic blood pressure levels in hypertensive patients included in observational studies or clinical surveys on hypertension between 2005 and 2011 in Italy. Histograms represent average SBP and DBP levels in each study included in the analysis. Data are expressed as mean ± SD.

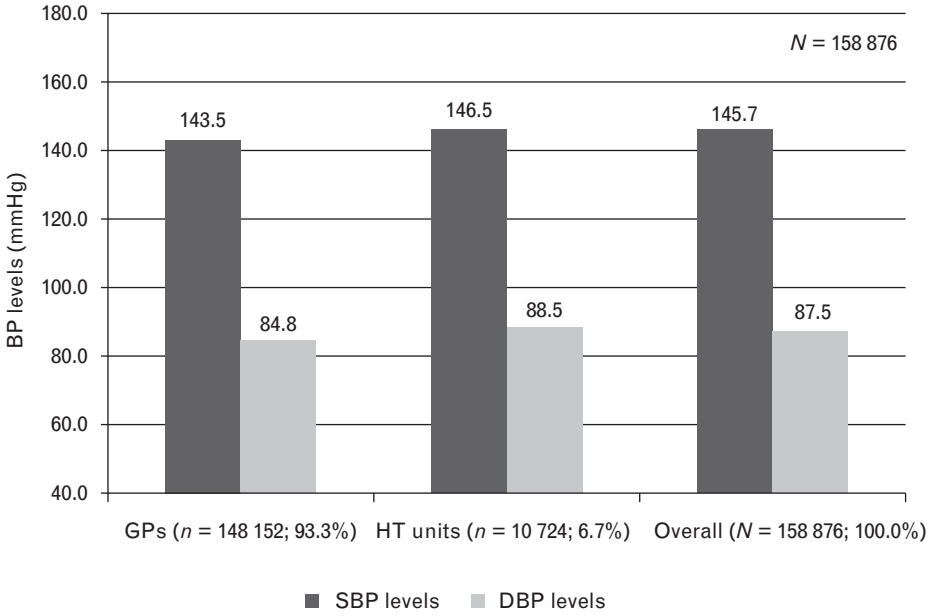

FIGURE 4 Clinic blood pressure levels in the overall population sample and in subgroups of patients followed by general practitioners or in hypertension centres. Data are expressed as mean ± SD.

BP control rate of 37.0% ($n = 31.727$) among treated hypertensive patients.

Drugs inhibiting the renin–angiotensin system were the most common therapy prescribed in the overall population sample, either as a monotherapy or in combination therapy with thiazide diuretics ($n = 41\,089$, 48.5% among treated hypertensive patients); in particular, 25 150 (29.7%) hypertensive patients were treated with ACE inhibitors and 13 289 (15.7%) with ARBs. In addition, 21 376 (25.2%) hypertensive patients were treated with calcium antagonists, 18 973 (22.4%) with diuretics and 17 790 (21.0%) with beta-blockers (Table 4).

DISCUSSION

The present analysis provides one of the largest, updated and comprehensive available database on the extent to which BP is controlled by treatment in hypertensive patients or the hypertensive fraction of general populations. This large population sample derives from hypertensive patients included in observational and clinical studies performed in Italy and whose results were published between 2005 and 2011 in Italy. From the large number of findings provided by the present analysis, we discuss below some of the main aspects.

First of all, BP control by antihypertensive treatment was achieved in a relatively small fraction of hypertensive patients. In fact, among treated hypertensive patients, about 37% achieved the recommended BP values, the others remaining in the abnormal range of BP. This result is in line with that of our previous analysis, which collected data on BP levels reported in clinical studies made available between 2000 and 2005 in Italy [19]. This is also in line with other large observational surveys performed in both European [17,40] and North American [2,41–43] countries, which reported a disappointingly low rate of BP control among treated hypertensive patients. Our previous analysis, however, reported that only 19% ($n = 6698$) of treated hypertensive patients ($n = 34596$) achieved effective BP control [19], compared with the relatively higher proportion (37%) observed in the present analysis. A similar improvement in BP control rates was reported in several

TABLE 4. Proportions of treated hypertensive patients assuming different antihypertensive drugs in observational studies and clinical surveys on hypertension

Clinical survey	RAS blockers	ACEi	ARB	CCB	BB	AB	Diuretics
APROS-Diadys	1896 (79.2)	1113 (46.5)	783 (32.7)	971 (40.6)	634 (26.5)	258 (10.8)	288 (12.0)
IPERDIA	1029 (76.4)	711 (52.8)	318 (23.6)	520 (38.6)	359 (26.7)	180 (13.4)	604 (44.8)
GP survey	26 134 (39.1)	17 209 (25.7)	8925 (13.3)	16 705 (25.0)	13 778 (20.6)	0 (0.0)	12526 (18.7)
MAGIC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
EFFECTUS	7011 (89.2)	4825 (61.4)	2186 (27.8)	2335 (29.7)	2138 (27.2)	0 (0.0)	3192 (40.6)
IDEMAND	2650 (81.9)	n.a.	n.a.	n.a.	n.a.	n.a.	1414 (43.7)
MARTE	1343 (76.0)	797 (45.1)	546 (30.9)	532 (30.1)	563 (31.8)	169 (9.6)	808 (45.7)
MIRACLES	1026 (82.5)	495 (39.8)	531 (42.7)	313 (25.2)	318 (25.6)	0 (0.0)	141 (11.3)
Total	41 089 (48.5)	25 150 (29.7)	13 289 (15.7)	21 376 (25.2)	17 790 (21.0)	607 (0.7)	18 973 (22.4)

The MAGIC study [33] included untreated hypertensive patients, thus information on antihypertensive drug therapies at baseline cannot be produced. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta-blocker; CCB, calcium-channel blocker; GP, general practitioner; RAS, renin–angiotensin system.

Italian surveys [44–46]. As an example, in the Gubbio study [45], the overall BP control rate increased from 10% reported in the 1980s to 20% in the 1990s to about 40% in the early 2000s; this was paralleled with consistent reductions in both all-cause and cardiovascular death during the observational period. Several potential explanations may be advocated in an attempt to explain this poor BP control rate, including the relatively high risk of the study population, the concomitant presence of associated clinical conditions, the low proportions of treated patients with diagnosed hypertension and the use of certain antihypertensive drug therapies (or dosages). However, the observational nature of our study did not allow us to provide such explanations.

Second, BP levels and control of treated hypertensive patients were substantially better in population surveys than in hypertensive patient-based study. This observation seems to confirm the hypothesis that these hypertensive patients have more difficult-to-treat hypertension, which may be at least, in part, due to the relatively higher prevalence of cardiovascular risk factors (obesity, smoking, dyslipidemia, diabetes) reported in the former than in the latter group. However, it also differs from the results of our previous analysis [19], in which BP control was somewhat better in patients seen by specialists than in those seen by general practitioners. In this latter regard, when comparing average BP levels between our previous [19] and current analyses, we observed a substantial reduction in BP levels only in the subgroup of patients followed by general practitioners (from 154.1/90.9 to 143.5/84.8 mmHg), whereas no relevant difference was observed in outpatients followed by hypertension clinics (from 147.2/89.6 to 146.5/88.5 mmHg). Several explanations may be advocated for explaining these apparently contrasting results. Among these, the different proportions of hypertensive patients followed by specialized physicians (which was lower in the current than in the former analysis), the availability of new sets of guidelines [18,47] and several interventional clinical trials [6,48–53] (which further emphasize the importance of strict BP control both in the general hypertensive population and in specific subgroups of patients) during the observational period of our analysis can be cited. In addition, the larger use of electronic support [54] and automated 24-h and home BP monitoring devices [55,56] (which may help in promoting hypertension awareness, treatment and control among treated and untreated hypertensive patients) may also have an impact on our results.

Third, the different rates of BP control reported in hypertensive patients followed by hypertension centres compared with that reported by general practitioners may be at least, in part, due to relatively higher prevalence of additional cardiovascular risk factors and higher cardiovascular risk profile in the former than in the latter group. This is of particular relevance for the healthcare policies in Italy, because it may imply a proper selection of high-risk hypertensive patients from general practice towards hypertension clinics, in which challenging hypertension should be referred.

Fourthly, to our knowledge, this is the first and largest analysis on hypertension, which include a considerably higher proportion of female rather than male individuals. Among other observations made in Italy, only one study, in fact, was specifically designed and carried out in postmenopausal women, aimed at evaluating high BP prevalence and control [28]. In view of the largest and updated population sample, the analysis allows us to provide a current appraisal of the BP treatment and control of a gender-balanced population sample in Italy.

On the basis of these findings, the analysis allows us to conclude that in Italy effective treatment of hypertension continues to remain largely unsuccessful, because the overall percentage of treated hypertensive patients is small, particularly among general practitioners.

Several other aspects deserve to be discussed. First of all, data included in the analysis were collected over the entire Italian territory, which means that the conclusion on the unsatisfactory rates of BP control, particularly for the SBP levels, may reflect the overall situation of Italy.

BP control is much more rarely achieved for SBP than for DBP values. This is particularly the case for hypertensive patients followed by hypertension centres than for those followed by general practitioners, despite the smaller sample size and the larger use of antihypertensive drug therapies in the former than in the latter group. This result confirms that there is a generally greater difficulty to effectively lower SBP levels, as also reported by other independent analyses performed on interventional randomized clinical trials [15,57], which calls for research and clinical efforts focused on this specific issue. This may also imply that acting on physicians' information and motivation and treatment approach holds promise for improvement.

Our results substantially confirm that also in Italy hypertension rarely comes as an isolated risk factor. In this regard, 11% of the patients had diabetes mellitus and about 10% had dyslipidemia; in addition, about 20% had evidence of left ventricular hypertrophy, 30% had metabolic syndrome and 15% had microalbuminuria. With regard to associated clinical conditions (when available), about 12% had history of coronary artery disease, 6% previous myocardial infarction and 5% stroke. This means that the possibility of a high-risk condition in hypertensive patients seen in the clinical practice should not be lightly dismissed. It also implies that search for associated risk factors as well as for markers of organ damage should be implemented. It finally means that efforts towards a more rigorous control of BP should be even more stringent because of the greater event-saving effect of BP control when the cardiovascular risk is high.

Potential limitations

The present study is based on a cross-sectional, descriptive analysis of large observational studies and clinical surveys and, as such, it can only identify associations but cannot provide insights into causation. In view of the relatively large sample size of our study, even the possibility of sampling bias has to be considered, although proven methods were applied to avoid this. The large sample size and different distribution of involved physicians may also mean that the views expressed by respondents may not be fully representative of opinions of the wider physician community in Italy. In most clinical studies, dependence on physician self-reporting throughout standardized questionnaires, rather than more objective measures or quantifications, may also create potential biases. Our analysis

cannot provide information about whether physicians' practices were located in rural or urban areas. Access to medical healthcare in rural areas may be more difficult than in urban areas, and this aspect should be acknowledged when considering the higher prevalence of major cardiovascular risk factors, including diabetes, and associated clinical conditions in different areas of Italy. At the same time, we cannot provide data on the socio-economic position of individual patients. The relatively low prevalence of smoking in this hypertensive high-risk population is probably due to the lack of this information in several studies considered in our analysis. Also, information on home or 24-h ambulatory BP levels, as well as those on the proportions of treated hypertensive patients on combination therapy, was not available in the selected clinical surveys or observational studies. Finally, because of the different type of the studies and the different outpatients populations included in the present analysis, no statistical analyses were performed in comparisons with data provided from our previous analysis of Italian surveys on hypertension [19].

In conclusion, our analysis of the most large, representative and updated sample of hypertensive patients derived from the most recent observational studies available in Italy over the last 5 years confirmed inadequate control of BP in Italy, independently of the clinical setting. This analysis may have major implications for public health because of the severe impact of uncontrolled BP levels on the increased risk of cardiovascular diseases in terms of morbidity, mortality and socio-economic burden. Our findings also underline the need for more effective and comprehensive actions to control BP in hypertensive patients in Italy.

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Conflicts of interest

This work has been endorsed by the Italian Society of Hypertension (SIIA) and Italian Society of Cardiovascular Prevention (SIPREC).

No conflict of interest about the work reported in this paper has been declared by any of the authors.

Appendix: acronyms of surveys include in the analysis

SIMONA: Study on hypertension prevalence in menopause in the Italian population [28]. APROS-Diadys: assessment of prevalence observational study of diastolic dysfunction [29]. HYPER-PRACT: hypertrophy in clinical practice [30]. IPERDIA: *Ipertensione* and *diabete* study [31]. General Practice survey on hypertension [32]. MAGIC: Microalbuminuria: A Genoa Investigation on Complications [33]. EFFECTUS: Evaluation of Final Feasible Effect of Control Training and Ultra Sensitisation [34]. REDHY: Renal dysfunction in hypertension [35]. IDEMAND: Italy developing education and awareness on microalbuminuria in patients with hypertensive disease [36]. MARTE: Monitoraggio della Pressione Arteriosa nella Medicina Territoriale [37]. MIRACLES: migraine and hypertension relationship: comorbidity and risk of cerebrovascular events [38].

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Reviewers' Summary Evaluations

Reviewer 1

Blood pressure control is known to be too low in Europe and worldwide. The present paper illustrates that this is also the case in Italy. Among treated hypertensive patients, only 37% were under control. Unfortunately, no data are given whether this insufficient control is confirmed by ambulatory or home blood pressure. In any way, the question today is no longer ''how to control blood pressure'', but rather ''How to ensure that patients get antihypertensive treatment and remain compliant to it?''

Reviewer 2

This study is a meta-analysis of published literature between 2005 and 2011 on the treatment of hypertension in Italy. Out of 61 potentially relevant studies, the authors selected 11 surveys with adequate data. These surveys comprised over 150,000 patients, thereby representing one of the largest cohorts studied thus far. In this cohort, control of BP was inadequate in the great majority of the patients. The studies are based on intention-to-treat principles rather than actual measurement of drug use. The data should be judged in the light of the notoriously low adherence of patients to antihypertensive drug use.