



UNIVERSITÀ  
DEGLI STUDI  
FIRENZE

## FLORE

# Repository istituzionale dell'Università degli Studi di Firenze

### **Undertreatment of hypertension in community-dwelling older adults: a drug-utilization study in Dicomano, Italy**

Questa è la Versione finale referata (Post print/Accepted manuscript) della seguente pubblicazione:

*Original Citation:*

Undertreatment of hypertension in community-dwelling older adults: a drug-utilization study in Dicomano, Italy / M. DI BARI; F. SALTI; M. NARDI; M. PAHOR; E. TONON; A. UNGAR; R. PINI; G. MASOTTI; N. MARCHIONNI; C. DE FUSCO. - In: JOURNAL OF HYPERTENSION. - ISSN 0263-6352. - STAMPA. - 17:(1999), pp. 1633-1640.

*Availability:*

This version is available at: 2158/308943 since:

*Terms of use:*

Open Access

La pubblicazione è resa disponibile sotto le norme e i termini della licenza di deposito, secondo quanto stabilito dalla Policy per l'accesso aperto dell'Università degli Studi di Firenze (<https://www.sba.unifi.it/upload/policy-oa-2016-1.pdf>)

*Publisher copyright claim:*

(Article begins on next page)

# Undertreatment of hypertension in community-dwelling older adults: a drug-utilization study in Dicomano, Italy

Mauro Di Bari<sup>a,b</sup>, Francesca Salti<sup>a</sup>, Monica Nardi<sup>a</sup>, Marco Pahor<sup>c</sup>, Carmela De Fusco<sup>a</sup>, Elisabetta Tonon<sup>a</sup>, Andrea Ungar<sup>a,b</sup>, Riccardo Pini<sup>a,b</sup>, Giulio Masotti<sup>a,b</sup> and Niccolò Marchionni<sup>a,b</sup>

**Objective** To define: (1) the prevalence of and (2) factors associated with undertreatment of hypertension in older persons; and (3) the prevalence of specific drug regimens and reasons for their selection.

**Participants** Cross-sectional survey of persons aged  $\geq 65$  years living in Dicomano, Italy.

**Main outcome measures** Prevalence of untreated and uncontrolled hypertension, both defined on the basis of two blood pressure (BP) cut-off points ( $\geq 140/90$  and  $\geq 160/90$  mmHg) and of the presence of pharmacological treatment. Predictors of undertreatment were analysed for the higher BP cut-off only.

**Results** Five hundred of 692 (72.3%) and 380/692 (54.9%) participants met the 140/90 and the 160/90 mmHg BP criterion, respectively. Of the latter, 162 (42.6%) were untreated, 119 (31.3%) had uncontrolled and 99 (26.1%) controlled hypertension. Women [odds ratio (OR), 0.4; 95% confidence interval (CI), 0.2–0.7], participants with coronary artery disease (CAD) (OR, 0.2; 95% CI, 0.1–0.6), stroke (OR, 0.3; 95% CI, 0.1–0.7), and preserved cognitive status (Mini Mental State Examination score  $> 21$ : 0.3; 95% CI, 0.2–0.7) were more frequently treated. Uncontrolled hypertension was less likely in women (OR, 0.5; 95% CI, 0.3–1.0) and CAD patients (OR, 0.3; 95% CI, 0.1–0.7). Angiotensin converting enzyme (ACE)-inhibitors (55%),

calcium (Ca)-antagonists (31%) and diuretics (20%) were the drugs most commonly prescribed. ACE-inhibitors were preferred, and diuretics rarely used, in diabetic subjects. Ca-antagonists were used mostly in CAD participants.

**Conclusions** Hypertension is undertreated in the majority of noninstitutionalized older adults, especially in men with impaired cognition and no vascular disease. Drug regimens are mostly based on ACE-inhibitors and Ca-antagonists, as a result of associated clinical conditions, requiring individualized treatment. *J Hypertens* 1999, 17:1633–1640 © Lippincott Williams & Wilkins.

*Journal of Hypertension* 1999, 17:1633–1640

**Keywords:** hypertension, elderly, drug therapy, undertreatment, ICARE Dicomano study

<sup>a</sup>Department of Gerontology and Geriatrics, University of Florence, <sup>b</sup>Azienda Ospedaliera 'Careggi', Florence, Italy and <sup>c</sup>Department of Internal Medicine, Wake Forest University School of Medicine, Winston-Salem, NC, USA.

Sponsored in part by the Italian Ministry of the University and Scientific and Technological Research (National Special Project on Heart Failure), and by the Regional Government of Tuscany. M.P. has received research grants from BMS and Merck, and has received fees for giving talks at meetings sponsored by BMS, Merck, Parke Davis, Boehringer Ingelheim and Bayer.

Correspondence and requests for reprints to Dr M. Di Bari, Department of Gerontology and Geriatrics, University of Florence, via delle Oblate 4, 50141 Florence, Italy.

Tel: +39 055 4279604; fax: +39 055 4223879; e-mail: dibari@cesit1.unifi.it

Received 20 May 1999 Revised 30 June 1999

Accepted 16 July 1999

## Introduction

Since the publication of the results of the European Working Party on Hypertension in the Elderly Program [1] in 1985, evidence on the benefits of drug treatment of hypertension in older persons has been consistently accumulating. Randomized clinical trials [2–4] showed that diuretics and  $\beta$ -blockers, used as first-line antihypertensive medications, reduce the incidence of all-cause and coronary death, stroke, myocardial infarction, and congestive heart failure in the elderly. According to a recent meta-analysis [5], the advantage of treatment is greater in older than in younger patients. More recently, nitrendipine was also shown to reduce the incidence of stroke, of all cardiovascular events [6] and, possibly, of dementia [7] in

older participants in the Systolic Hypertension in Europe (Syst-Eur) trial.

At a population level, mortality and morbidity due to hypertension can be reduced only if evidence-based guidelines are thoroughly and appropriately followed in community medicine. Unfortunately, hypertension still remains largely undiagnosed or untreated, at any age [8] but more frequently in older adults [8,9]. Moreover, the therapeutic regimens usually prescribed are rarely based on diuretics and  $\beta$ -blockers, the only drugs proven effective in the prevention of hypertension-related complications [10] until the recent publication of the Syst-Eur [6] and the Captopril Prevention Project (CAPPP) [11] studies.

Identification of factors associated with undertreatment of hypertension may have major public health impact, providing clues to improve the delivery of effective care and, ultimately, to reduce the burden of the disease in the general population. In countries such as the USA, where universal health care coverage is lacking, the strongest barriers to appropriate treatment are the limited access to health services and the excessive costs of care [12], but it is unlikely that these findings can be generalized to countries with different health care systems. Furthermore, other unidentified factors may play a role, since suboptimal blood pressure control has been reported even among patients who receive regular care [9,13,14].

Therefore, we carried out the present study to define the prevalence of, and factors associated with, undertreatment of older hypertensive persons living in a small town near Florence, Italy; a country where the National Health Service warrants free access to health care and availability of drugs. As a secondary objective, we aimed at identifying specific patterns of treatment, and at verifying whether associated comorbidities, which might require individualized treatment, can explain the choice, by the primary care physicians (PCP), of a therapeutic regimen not based on diuretics and  $\beta$ -blockers. When the data for this study were collected in 1995, the Joint National Committee V (JNC-V) guidelines [10] strongly recommended these drugs as first-line antihypertensive agents, which were also listed first, in terms of proven benefits from mortality-morbidity studies, in the 1993 World Health Organization (WHO)/International Society of Hypertension (ISH) guidelines [15].

## Methods

### Population and protocol of the study

This analysis was carried out using data from a population-based survey on heart failure, enrolling the entire noninstitutionalized, community-dwelling older population living in Dicomano, a small town near Florence, Italy ('Insufficienza Cardiaca negli Anziani Residenti a Dicomano', ICARE Dicomano Study) in April 1995. The general design of the survey has been previously published in detail [16]. Briefly, all community-dwelling citizens aged  $\geq 65$  years recorded in the City Registry Office were considered eligible for multidimensional, geriatric assessment consisting of home interview, laboratory testing and clinical examination. Proxy interviews were obtained in 29 cases with severe cognitive or sensorial impairment. Further clinical information was gathered from the participants' PCP, who answered a structured questionnaire on history and treatment of several clinical conditions, including hypertension.

### Data collection

#### *Blood pressure measurement and diagnosis of hypertension*

Blood pressure (BP) was measured by the study physicians, with the participant in the supine position after a 10-min rest, using a cuff of proper size for arm circumference. A first measure was taken at each arm. Two further readings were thereafter obtained 1–2 min apart, usually at the nondominant arm, except when systolic BP (SBP) differed between the two sides by more than 10 mmHg. In these cases, the side with the highest SBP was chosen. Diastolic BP (DBP) was taken at Korotkoff's phase V. The second and third measures at the selected arm were averaged and mean values were considered as the reference SBP and DBP, respectively.

For descriptive purposes, the prevalence of hypertension was first defined, following commonly accepted criteria, for SBP  $\geq 140$  mmHg or DBP  $\geq 90$  mmHg, or current treatment with antihypertensive drugs, as defined later. However, a higher SBP cut-off ( $\geq 160$  mmHg) was considered more appropriate for the analysis of predictors of undertreatment, since this could minimize the number of subjects falsely defined as uncontrolled hypertensive on the basis of a single set of measures. Indeed, according to both the JNC V [10] and WHO/ISH [15] guidelines, persistently elevated BP values must be verified, and nonpharmacological interventions first attempted, before a drug treatment is started. Moreover, in 1993, BP values  $< 160/90$  mmHg were suggested as a therapeutic goal for older adults [10].

Participants with hypertension, diagnosed according to either threshold, were further classified as: (1) controlled (BP below the diagnostic threshold); (2) uncontrolled (current antihypertensive treatment but BP above the diagnostic threshold); or (3) untreated (no drug therapy).

### Drug history

Medications were investigated with the drug inventory method [17] and recorded using a commercially oriented Italian coding system. Drugs were therefore classified with the international ATC coding [18], a hierarchical classification system grouping pharmacological agents on the basis of their main anatomic (A) site of action, and therapeutic (T) and chemical (C) characteristics. The following ATC codes were considered to represent antihypertensive drugs: C02 (central antiadrenergics), C03A, C03B, C03EA (low-ceiling diuretics, i.e. thiazides and thiazide-like), C07 ( $\beta$ -blockers), C08 [calcium (Ca)-antagonists], and C09 [angiotensin converting enzyme (ACE)-inhibitors]. Many of these drugs can be prescribed for the treatment of diverse clinical conditions. Hence, in case of uncertain

or possibly multiple indications, coding for antihypertensive treatment was definitely assigned only when antihypertensive prescription had been reported in the PCP's questionnaire.

#### **Predictors of undertreatment and of specific therapeutic regimens**

Several variables exploring the traditional areas of multidimensional geriatric assessment [19] (socio-economic status, physical health, comorbidity and functioning, cognition and mood) were considered to be potentially associated with untreated or uncontrolled hypertension.

Socio-economic variables included marital status, household composition, years of formal education, previous occupation, and indirect indicators of poor economic status (self-rated inadequate income and need for regular economic help). Comorbidity was diagnosed from standardized algorithms [16], based on history, physical, laboratory, and instrumental findings directly collected by the study physicians. Diseases assumed to have a potential association (positive or negative) with undertreatment of hypertension were: diabetes (increased fasting glucose, treatment with antidiabetic agents or, in case of uncertainty, increased HbA<sub>1c</sub>), heart failure (McKee's criteria [20]), coronary heart disease (myocardial infarction or angina pectoris, based on ECG, history and Rose's Questionnaire [21]), previous stroke, and indicators of alcohol abuse (positive CAGE questionnaire [22] or associated increase in mean corpuscular volume and  $\gamma$ -glutamyl-transpeptidase [23]). The total number of chronic conditions (including vascular disease such as coronary heart disease, stroke or lower extremity arterial disease, diabetes, heart failure, asthma or chronic bronchitis, chronic liver disease or peptic ulcer) was also taken into account. Disability (need for someone's help in one or more basic activity of daily living-BADL) was evaluated with a modified WHO scale [24,25]. Cognitive impairment, depressive or anxiety symptoms were screened with the Mini Mental State Examination (MMSE) [26], the Geriatric Depression Scale [27] and a brief version of the Hopkins' Symptoms Check List (HSCL) [28,29], respectively. The body mass index was calculated as body weight (kg) divided by height squared (m<sup>2</sup>).

Age, gender and history of diabetes, coronary artery disease, and heart failure were considered as possible predictors of specific therapeutic regimens.

#### **Analytic procedure**

Statistical analysis was carried out using the SPSS for Windows 8.0 package. Mean values are expressed as mean  $\pm$  SEM. The  $\chi^2$  test and the Student's *t* test were

used to compare relative frequencies and mean values, respectively.

Continuous variables were dichotomized using standard cut-off points whenever possible or, otherwise, contrasting one extreme of the population distribution (10th or 90th percentile) to the remaining population. Selection between the 10th and the 90th percentile was supported by the clinical significance of each variable as a potential risk factor for undertreatment. Hence, the MMSE score, which decreases with cognitive impairment, and the HSCL score, which increases with anxiety symptoms, were dichotomized at 21 (10th percentile) and at 1.5 (90th percentile), respectively.

From bivariate comparisons, candidate predictors ( $P < 0.1$ ) of treated hypertension and controlled hypertension were selected and entered into separate logistic regression analysis models, to identify the explanatory variables of each individual outcome. Logistic regression was also used to identify the independent predictors of specific drug regimens (ACE-inhibitors, Calcium antagonists, and diuretics).

$P < 0.05$  was considered statistically significant.

## **Results**

Complete data were available for 692 out of 864 eligible subjects (80.0%). Of the 172 subjects not included, four had died before study onset, 163 refused to participate, and five had missing data. The proportion of men was slightly, but significantly, higher among nonparticipants (23.1%) than participants (17.5%;  $P = 0.040$ ), whereas mean age was comparable ( $74.2 \pm 0.6$  years versus  $74.1 \pm 0.3$  years, respectively;  $P = 0.906$ ). According to the PCPs' reports, the frequency of hypertension was similar between participants and nonparticipants (35.5 versus 37.2%;  $P = 0.607$ ).

#### **Prevalence, treatment and control of hypertension**

Table 1 shows the prevalence of hypertension according to the 140/90 and 160/90 mmHg cut-off, in relation to treatment and BP control. According to the 140/90 mmHg cut-off, the prevalence of hypertension was 72.3% (500/692). When the more restrictive criterion of 160/90 mmHg was considered, 380 participants (54.9%) were definitely hypertensive, of whom 281 were untreated or uncontrolled (Table 1). Therefore, the prevalence of definitively undertreated hypertension in the study population was 40.6% (281 of 692), within a 95% confidence interval (CI) of 36.9–44.3%. Of the 162 cases with untreated hypertension, only 19 (11.7%) had an antihypertensive medication prescribed by their PCP and can therefore be considered as totally noncompliant, whereas the remaining 143 had not been prescribed antihypertensive drugs.

**Table 1** Prevalence of untreated, uncontrolled, and controlled hypertension (HT) by gender, according to two different blood pressure cut-off points

	Men			Women			Total		
	<i>n</i>	% of HT	% of population	<i>n</i>	% of HT	% of population	<i>n</i>	% of HT	% of population
<b>≥ 140/90 mmHg cut-off</b>									
Normotensive	93	—	32.5	99	—	24.4	192	—	27.7
Untreated HT	124	64.2	67.5	158	51.5	75.6	282	56.4	72.3
Uncontrolled HT	60	31.3		117	38.1		177	35.4	
Controlled HT	9	4.7		32	10.4		41	8.2	
Total	286	100	100	406	100	100	692	100	100
<b>≥ 160/90 mmHg cut-off</b>									
Normotensive	137	—	47.9	175	—	43.1	312	—	45.1
Untreated HT	80	53.7	52.1	82	35.5	56.9	162	42.6	54.9
Uncontrolled HT	45	30.2		74	32.0		119	31.3	
Controlled HT	24	16.1		75	32.5		99	26.1	
Total	286	100	100	406	100	100	692	100	100

Percentages do not sum up to 100 due to rounding.

### Predictors of undertreated hypertension

Bivariate predictors of undertreated, either untreated or uncontrolled, hypertension ( $\geq 160/90$  mmHg cut-off) are reported in Table 2, whereas Figures 1 and 2 show the logistic models for multivariate prediction of the two outcomes. Women and participants with associated coronary artery disease, stroke or preserved cognitive status were less likely to be untreated, both in bivariate (Table 2) and in multivariate (Fig. 1) analyses. A bivariate association with current or previous smoking status (Table 2) was not confirmed in the multivariate model (Fig. 1). Among cognitively impaired ( $\text{MMSE} \leq 21$ ) participants, the presence of

a caregiver was not predictive of drug treatment (data not shown). Uncontrolled hypertension was negatively associated with female gender and coexisting coronary artery disease, in both bivariate (Table 2) and multivariate (Fig. 2) comparisons. A borderline association with a lower education (Table 2) was not confirmed in the logistic regression model (Fig. 2).

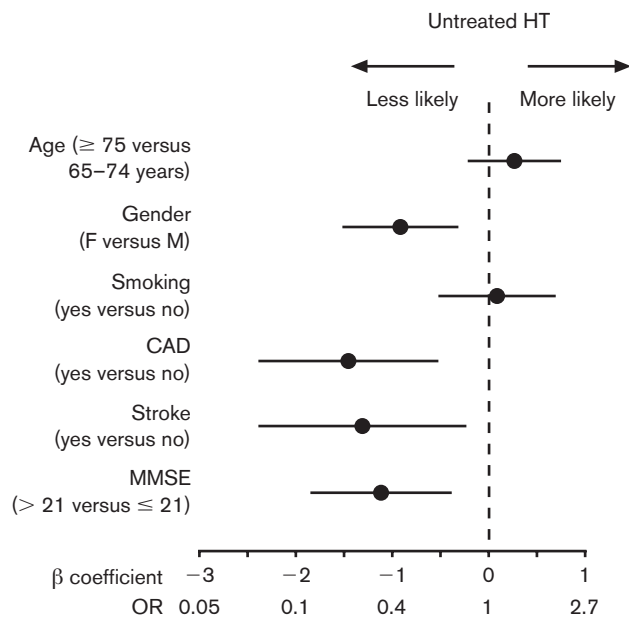
The three largest PCP practices in Dicomano included about 92% of the study population. The prevalence of treated and controlled hypertension was comparable among the three PCP practices (data not shown).

**Table 2** Bivariate predictors of untreated and uncontrolled hypertension (HT) ( $\geq 160/90$  mmHg cut-off)

Factor	Untreated HT ( <i>n</i> = 380)		Uncontrolled HT ( <i>n</i> = 218)	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
<b>Demographic and social variables</b>				
Age $\geq 75$ years	1.4 (1.0–2.2)	0.087	0.8 (0.5–1.4)	0.464
Female sex	0.5 (0.3–0.7)	0.000	0.5 (0.3–0.9)	0.032
Being married	0.9 (0.6–1.4)	0.762	1.0 (0.6–1.8)	0.916
Education $> 6$ years	1.1 (0.5–2.2)	0.817	2.7 (0.9–7.9)	0.054
Poor economic status	1.2 (0.7–2.0)	0.523	1.0 (0.5–2.1)	0.990
Living alone	0.7 (0.4–1.2)	0.214	0.8 (0.4–1.6)	0.615
<b>Health status</b>				
Current or ex-smoking	1.6 (1.4–2.4)	0.033	1.6 (0.9–2.8)	0.115
BMI $\geq 30$ kg/m <sup>2</sup>	0.7 (0.4–1.2)	0.194	0.9 (0.5–1.7)	0.819
Alcohol abuse	1.6 (0.8–3.2)	0.185	1.2 (0.4–3.4)	0.688
Heart failure	0.7 (0.4–1.2)	0.163	0.6 (0.4–1.3)	0.234
Diabetes	0.7 (0.4–1.2)	0.192	0.8 (0.3–1.5)	0.435
Coronary artery disease	0.3 (0.1–0.7)	0.007	0.4 (0.1–0.9)	0.017
Stroke	0.3 (0.1–0.9)	0.022	1.2 (0.5–3.2)	0.431
$\geq 2$ chronic diseases	1.4 (0.9–2.2)	0.114	1.1 (0.6–1.9)	0.806
Disability in $\geq 1$ BADL	1.5 (0.7–3.4)	0.327	2.6 (0.7–9.9)	0.144
<b>Cognition and mood</b>				
MMSE $> 21$	0.4 (0.2–0.7)	0.003	0.5 (0.2–1.4)	0.205
GDS $\geq 14$	0.9 (0.6–1.4)	0.593	0.7 (0.4–1.2)	0.155
HSCL $> 1.5$	1.0 (0.6–1.5)	0.858	1.2 (0.7–2.3)	0.520

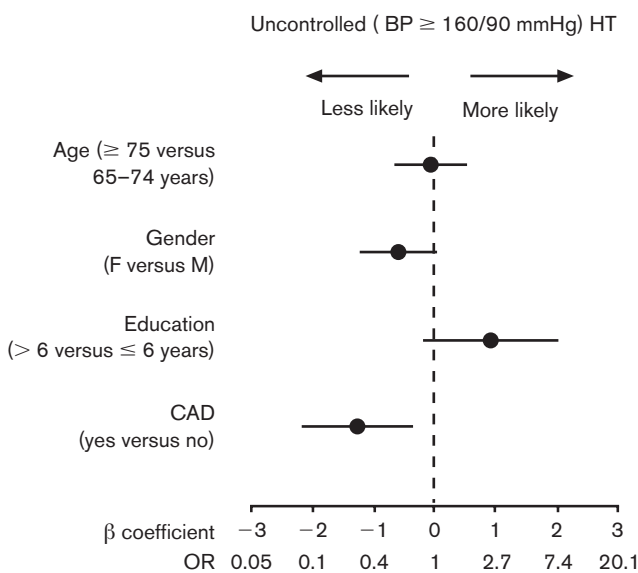
OR, odds ratio; CI, confidence interval; BMI, body mass index; BADL, basic activities of daily living; MMSE, Mini Mental State Examination; GDS, Geriatric Depression Scale; HSCL, Hopkins' Symptoms Check List.

Fig. 1



Logistic regression model of factors associated with untreated hypertension in 380 community-dwelling hypertensive elderly. The 95% confidence interval around the estimate is shown. HT, hypertension; F, female; M, male; CAD, coronary artery disease; MMSE, Mini Mental State Examination; OR, odds ratio.

Fig. 2



Logistic regression model of factors associated with uncontrolled hypertension in 218 community-dwelling treated hypertensive elderly. The 95% confidence interval around the estimate is shown. BP, Blood Pressure; HT, hypertension; F, female; M, male; CAD, coronary artery disease; OR, odds ratio.

### Drug regimens

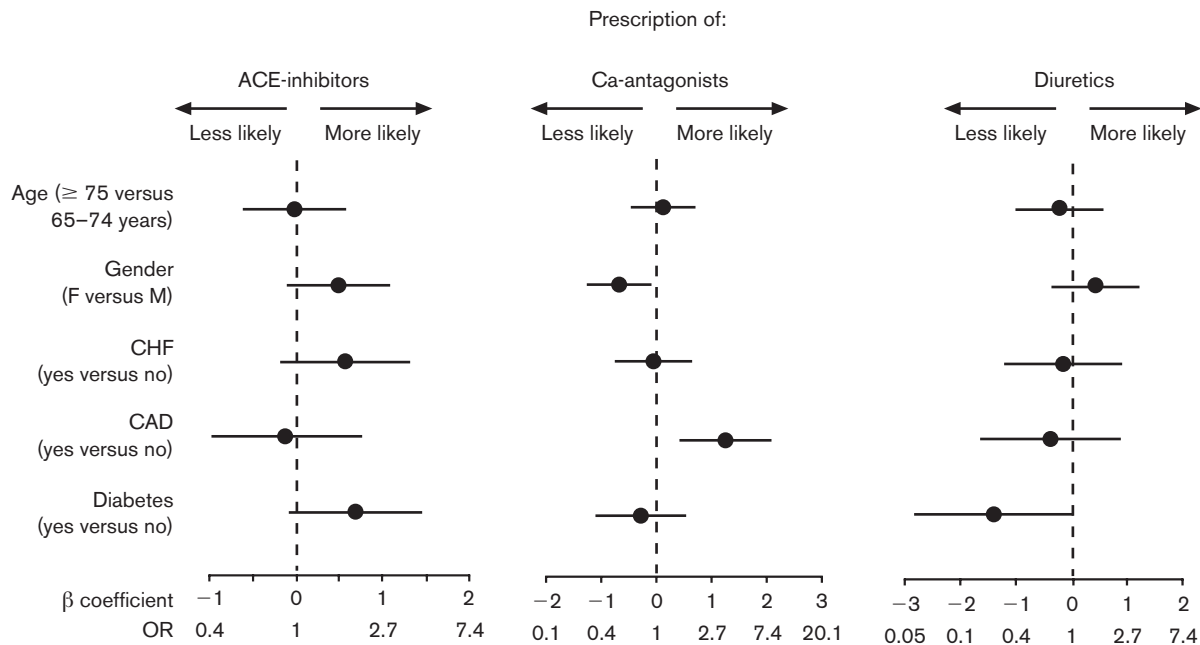
The majority (79.9%) of the 218 treated hypertensive participants was on monotherapy. The most frequently prescribed antihypertensive agents were ACE-inhibitors (119 of 218, 54.6%), followed by Ca-antagonists (71 of 218, 32.6%), low-ceiling diuretics (41/218, 18.8%), central antiadrenergics (18 of 218, 8.3%), and  $\beta$ -blockers (15/218, 6.9%). Age, gender and history of diabetes, coronary artery disease, and heart failure were entered into three separate logistic regression models, testing for their multivariate association with ACE-inhibitors, Ca-antagonists, and low-ceiling diuretics, respectively (Fig. 3). History of diabetes tended to be associated positively with the prescription of ACE-inhibitors and negatively with the use of diuretics, whereas male gender and history of coronary artery disease independently predicted the use of Ca-antagonists (Fig. 3). No therapeutic regimen was significantly associated with a higher prevalence of 'acceptably' ( $< 160/90$  mmHg cut-off) controlled hypertension (data not shown).

### Discussion

In the present study, we assessed the prevalence and found some predictors of definitely undertreated hypertension in the elderly. Major strengths of this study are the evaluation of an entire community of free-living individuals, the accurate collection of medication use, validated with information obtained from the PCP, and the direct assessment of several possible predictors of undertreatment. Since an individual's BP is evaluated more accurately when several measures are taken on different occasions, a possible limitation of the study is that BP was measured in a single occasion, although averaging two out of three readings. Within-person variability of BP measures, which is common, especially at an advanced age, was shown to affect substantially the estimated prevalence of undertreated hypertension in a previous study [30]. However, even a single BP measure accurately predicts clinical events [31–33]. Furthermore, Mancia *et al.* have recently shown that clinic uncontrolled BP is highly predictive of exceedingly elevated average home and 24-h BP [34].

The prevalence of hypertension in the elderly population of Dicomano was higher than in previous Italian series [35]. In particular, the Italian Longitudinal Study on Aging, using BP cut-off values of 140/90 mmHg, found a 67.3 and 59.4% prevalence in women and men, out of a random sample of 5632 subjects aged 65–84 years [36]. A possible source of variation, in the comparison between this and previous studies, is that BP was measured in the supine position. Measures of BP in the supine position have been used both in observational studies [37] and in randomized clinical trials [3], although the sitting position is usually considered as the acknowledged standard [10,15]. However, we argue that this methodological difference should have only a

Fig. 3



Logistic regression models of factors associated with use of angiotensin converting enzyme (ACE)-inhibitors, calcium (Ca)-antagonists, and low-ceiling diuretics in 218 community-dwelling treated hypertensive elderly. The 95% confidence interval around the estimate is shown. F, Female; M, male; CHF, congestive heart failure; CAD, coronary artery disease; OR, odds ratio.

minor impact in surveys of elderly subjects, since the difference between supine and sitting BP has been shown to be not significant for SBP in a broad age range, and trivial for DBP at an advanced age [38]. We therefore believe that our figures truly reflect an exceeding prevalence of hypertension in our study population.

In Italy, the National Health Service warrants each elderly citizen a PCP and a full availability of drugs, with, at most, a minor copayment. In spite of these favorable premises, control of hypertension in our study was far from optimal. Indeed, taking into account the 160/90 mmHg cut-off as a reasonable therapeutic goal for older adults, only 26% of hypertensive participants were acceptably treated, and most were totally undiagnosed and/or untreated. These figures are within the broad range observed in other countries with a government-financed primary health care [37,39-41]. In particular, Bursztyn *et al.* [40] reported that 86% out of 448 70-year-old hypertensive citizens of Jerusalem, Israel, were treated, and 43% had BP values below 160/95 mmHg. Conversely, in a large national random sample in Canada [41], only 16% of hypertensive women, and 13% of men aged 65-74 years had their BP below 140/90 mmHg, whereas an additional 38 and 27%, respectively, were treated but not optimally controlled.

Dicomano is a rural town, whose elderly population has a low level of formal education (> 6 years in only 9.5% of cases). Moreover, many persons live in country houses, isolated and far from the centre of the town [16]. This may represent a nonfinancial barrier in the access to primary care. Therefore, we acknowledge that our results possibly depict a worse-case scenario of the prevalence of undertreated hypertension, rather than a nation-wide representative picture of the Italian elderly population. Even with these limitations in mind, these are the only data available to estimate the need for the prevention of hypertension-related complications in our country, since to our knowledge no other recent population-based survey reported the prevalence of undertreated hypertension in older Italians. If the overall 40.6% (95% CI, 36.9-44.3%) proportion of undertreated hypertension in Dicomano is projected to the 1991 national population [42], more than 3.4 million unselected Italians ≥ 65 years of age can be estimated to be affected (95% CI, 3.1-3.7 million). Finally, it can be calculated that 16%, or about 16 000 cases, of the first-ever strokes annually occurring in aged Italians (population attributable risk) could be prevented with appropriate treatment of hypertension (see Appendix for calculations).

Other findings of this study deserve comment. Unlike previous investigations [12], a more advanced age was not an independent risk factor for undertreatment,

which, conversely, appeared to be definitely more frequent in men. The more favourable control of BP in women, also observed by other authors [12,30,41], probably reflects a more health-oriented behaviour in the female gender. Alcohol abuse and smoking habits were not significant confounders of this association.

Diagnosis of coronary artery disease was a strong predictor of more satisfactory control of hypertension, even after adjusting for gender. Many drugs used for the treatment of hypertension are also prescribed as anti-anginal agents, and in epidemiological studies this might determine a spurious association between the diagnoses of hypertension and coronary artery disease, based on drug history. However, such a misclassification bias in our study is unlikely. Indeed, the presence of antihypertensive drugs was coded by taking into account the information provided by the PCP on the indications to treatment, while the diagnosis of coronary artery disease was based on clinical data independently collected by the study physicians. Confounding by left ventricular systolic dysfunction, as a cause of reduced BP values in formerly hypertensive subjects, is similarly unlikely, since no association was observed with the clinical diagnosis of heart failure. Therefore, we believe that the association between coronary artery disease and a better control of hypertension in our study truly reflects a higher level of medical attention, more frequent contacts with the PCP, and/or a better compliance with treatment in patients with heart disease. This interpretation is further supported by the negative association between untreated hypertension and stroke (Fig. 1), and by similar results reported by other authors [12]. This suggests that community medicine is still poorly oriented to treat individuals at risk before complications of hypertension have become clinically evident.

In this study, as in other populations [12], a poor cognitive status was strongly predictive of untreated hypertension. PCPs must be aware of the increased risk of undertreatment of their older patients with initial cognitive impairment, which can produce a vicious circle. Hypertension is in fact emerging as a risk factor for dementia [43], and antihypertensive treatment may probably reduce the rate of cognitive decline [7].

The more commonly prescribed antihypertensive drugs were ACE-inhibitors and Ca-antagonists. Our findings in this small population reflect changes in prescribing patterns [44], and major market shifts [45], which have been observed on a larger scale. Before the recent publication of the Syst-Eur [6] and the CAPPP [11] studies, diuretics and, although with some controversies [46],  $\beta$ -blockers were the only antihypertensive agents with definitively proven benefits on clinical outcomes [5], and they are the most largely prescribed antihypertensive drugs in England [39]. Thus, the appropriate-

ness of diverging therapeutic attitudes in the medical community has been challenged [45]. Our results suggest that associated comorbidities could at least in part explain the choice of therapeutic regimens not based on these drugs. Indeed, ACE-inhibitors were clearly preferred, and diuretics avoided, in diabetic subjects, whereas the use of Ca-antagonists was strongly associated with a diagnosis of coronary artery disease. However, we cannot exclude that previous standard approaches had been unsuccessfully attempted.

In conclusion, this study confirms that in older persons, hypertension is largely undertreated even in a country, such as Italy, with universal health care coverage. Some risk factors for undertreatment can be identified. Among those, cognitive impairment is noteworthy, since uncontrolled hypertension may accelerate cognitive decline in at-risk individuals. The public health implications of these findings are remarkable. Knowledge of risk factors for undertreatment of hypertension may provide clues to improve the delivery of efficacious therapies to older populations, and ultimately to decrease the burden of mortality, morbidity, and disability that is associated with this common, treatable condition.

## References

- Amery A, Birkenhager W, Brixko P, Bulpitt C, Clement D, Deruyttere M, *et al.* Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly trial. *Lancet* 1985; **i**:1349–1354.
- SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA* 1991; **265**:3255–3264.
- Dahlof B, Lindholm LH, Hansson L, Schersten B, Ekbom T, Wester PO. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension). *Lancet* 1991; **338**:1281–1285.
- Medical Research Council Working Party. Medical Research Council trial of treatment of hypertension in older adults: principal results. *BMJ* 1992; **304**:405–412.
- Psaty BM, Smith NL, Siscovick DS, Koepsell TD, Weiss NS, Heckbert SR, *et al.* Health outcomes associated with antihypertensive therapies used as first-line agents. A systematic review and meta-analysis. *JAMA* 1997; **277**:739–745.
- Staessen JA, Fagard R, Thijs L, Celis H, Arabidze GG, Birkenhager WH, *et al.* Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. *Lancet* 1997; **350**:757–764.
- Forette F, Seux ML, Staessen JA, Thijs L, Birkenhager WH, Babarskiene MR, *et al.* Prevention of dementia in randomised double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) trial. *Lancet* 1998; **352**:1347–1351.
- Joint National Committee. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Arch Intern Med* 1997; **157**:2413–2446.
- Berlowitz DR, Ash AS, Hickey EC, Friedman RH, Glickman M, Kader B, *et al.* Inadequate management of blood pressure in a hypertensive population. *N Engl J Med* 1998; **339**:1957–1963.
- Joint National Committee. The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V). *Arch Intern Med* 1993; **153**:154–183.
- Hansson L, Lindholm LH, Niskanen L, Lanke J, Hedner T, Niklason A, *et al.* Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP) randomised trial. *Lancet* 1999; **353**:611–616.
- Satish S, Stroup-Benham CA, Espino DV, Markides KS, Goodwin JS.



- Undertreatment of hypertension in older Mexican Americans. *J Am Geriatr Soc* 1998; **46**:405–410.
- 13 Stockwell DH, Madhavan S, Cohen H, Gibson G, Alderman MH. The determinants of hypertension awareness, treatment, and control in an insured population. *Am J Public Health* 1994; **84**:1768–1774.
  - 14 Shea S, Misra D, Ehrlich MH, Field L, Francis CK. Predisposing factors for severe, uncontrolled hypertension in an inner-city minority population. *N Engl J Med* 1992; **327**:776–781.
  - 15 WHO/ISH. 1993 guidelines for the management of mild hypertension: memorandum from a WHO/ISH meeting. *Bull World Health Organ* 1993; **71**:503–517.
  - 16 Di Bari M, Marchionni N, Ferrucci L, Pini R, Antonini E, Chiarlone M, *et al.* Heart failure in community-dwelling older persons: aims, design and adherence rate of the ICARE Dicomano Project, an epidemiologic study. *J Am Geriatr Soc* 1999; **47**:664–671.
  - 17 Psaty BM, Lee M, Savage PJ, Ruten GH, German PS, Lyles M. Assessing the use of medications in the elderly: methods and initial experience in the Cardiovascular Health Study. The Cardiovascular Health Study Collaborative Research Group. *J Clin Epidemiol* 1992; **45**:683–692.
  - 18 Pahor M, Chrischilles EA, Guralnik JM, Brown SL, Wallace RB, Carbonin PU. Drug data coding and analysis in epidemiological studies. *Eur J Epidemiol* 1994; **10**:405–411.
  - 19 Applegate WB, Blass JP, Williams TF. Instruments for the functional assessment of older patients. *N Engl J Med* 1990; **322**:1207–1214.
  - 20 McKee PA, Castelli WP, McNamara P, Kannel WB. The natural history of congestive heart failure: the Framingham study. *N Engl J Med* 1971; **285**:1441–1446.
  - 21 Rose G, McCartney P, Reid DD. Self-administration of a questionnaire on chest pain and intermittent claudication. *Br J Prev Soc Med* 1977; **31**:42–48.
  - 22 Buchsbaum DG, Buchanan RG, Welsh J, Centor RM, Schnoll SH. Screening for drinking disorders in the elderly using the CAGE questionnaire. *J Am Geriatr Soc* 1992; **40**:662–665.
  - 23 Chick J, Kreitman N, Plant M. Mean cell volume and gamma-glutamyl-transpeptidase as markers of drinking in working men. *Lancet* 1981; **1**:1249–1251.
  - 24 Heikkinen E, Waters WE, Brzezinski ZJ. WHO Regional Office for Europe (editor): *The elderly in eleven countries. A socio-medical survey* 21st edition. Copenhagen: WHO; 1983.
  - 25 Ferrucci L, Guralnik JM, Bandinelli S, Salani B, Del Lungo I, Antonini E, *et al.* The development of disability in older persons: relationship with mortality and quality of life. In: Ferrucci L, Heikkinen E, Waters WE, Baroni A (editors): *Health and quality of life in older Europeans*. Florence: INCRA–WHO; 1995. pp. 31–66.
  - 26 Folstein MF, Folstein SE, McHugh PR. 'Mini-Mental State': a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; **12**:189–198.
  - 27 Brink TL, Yesavage JA, Lum O, Heersma PH, Adey M, Rose TL. Screening test for geriatric depression. *Clin Gerontol* 1982; **1**:37–44.
  - 28 Derogatis LR, Lipman RS, Rikels K, Uhlenhuth EH, Covi L. The Hopkins Symptom Checklist (HSCL): a self-reported symptom inventory. *Behav Sci* 1974; **19**:1–15.
  - 29 Kasper JD, Simonsick E. Mental health and general well-being. In: Guralnik JM, Fried LP, Simonsick E, Kasper JD, Lafferty ME (editors): *The women's health and aging study: health and social characteristics of older women with disability*. Bethesda, MD: NIH–NIA; 1995. pp. 85–95.
  - 30 Klungel OH, de Boer A, Paes AH, Seidell JC, Nagelkerke NJ, Bakker A. Undertreatment of hypertension in a population-based study in the Netherlands. *J Hypertens* 1998; **16**:1371–1378.
  - 31 Collins R, MacMahon S. Blood pressure, antihypertensive drug treatment and the risks of stroke and of coronary heart disease. *Br Med Bull* 1994; **50**:272–298.
  - 32 Kannel WB, Wolf PA, Verter J, McNamara PM. Epidemiologic assessment of the role of blood pressure in stroke. The Framingham study. *JAMA* 1970; **214**:301–310.
  - 33 Gordon T, Sorlie P, Kannel WB. Problems in the assessment of blood pressure: the Framingham Study. *Int J Epidemiol* 1976; **5**:327–334.
  - 34 Mancia G, Sega R, Milesi C, Cesana G, Zanchetti A. Blood-pressure control in the hypertensive population. *Lancet* 1997; **349**:454–457.
  - 35 Casiglia E, Spolaore P, Mordini P, Maschio O, Colanelli G, Celegon L, *et al.* The CASTEL project (CArdiovascular STudy in the ELderly): protocol, study design, and preliminary results of the initial survey. *Cardiologia* 1991; **36**:569–576.
  - 36 The Italian Longitudinal Study on Aging Working Group. Prevalence of chronic diseases in older Italians: comparing self-reported and clinical diagnoses. *Int J Epidemiol* 1997; **26**:995–1002.
  - 37 Chamontin B, Poggi L, Lang T, Menard J, Chevalier H, Gallois H, *et al.* Prevalence, treatment, and control of hypertension in the French population: data from a survey on high blood pressure in general practice, 1994. *Am J Hypertens* 1998; **11**:759–762.
  - 38 Netea RT, Smits P, Lenders JW, Thien T. Does it matter whether blood pressure measurements are taken with subjects sitting or supine? *J Hypertens* 1998; **16**:263–268.
  - 39 Colhoun HM, Dong W, Poulter NR. Blood pressure screening, management and control in England: results from the health survey for England 1994. *J Hypertens* 1998; **16**:747–752.
  - 40 Bursztyn M, Shpilberg O, Ginsberg GM, Cohen A, Stessman J. Hypertension in the Jerusalem 70 year olds study population: prevalence, awareness, treatment and control. *Isr J Med Sci* 1996; **32**:629–633.
  - 41 Joffres MR, Ghadirian P, Fodor JG, Petrasovits A, Chockalingam A, Hamet P. Awareness, treatment, and control of hypertension in Canada. *Am J Hypertens* 1997; **10**:1097–1102.
  - 42 Istituto Nazionale Di Statistica (ISTAT). *Annuario Statistico Italiano*, 1991. Rome: ISTAT; 1992.
  - 43 Skoog I. Status of risk factors for vascular dementia. *Neuroepidemiology* 1998; **17**:2–9.
  - 44 Psaty BM, Savage PJ, Tell GS, Polak JF, Hirsch CH, Gardin JM, *et al.* Temporal patterns of antihypertensive medication use among elderly patients. The Cardiovascular Health Study. *JAMA* 1993; **270**:1837–1841.
  - 45 Furberg CD, Berglund G, Manolio TA, Psaty BM. Overtreatment and undertreatment of hypertension. *J Intern Med* 1994; **235**:387–397.
  - 46 Messeri FH, Grossman E, Goldbourt U. Are beta-blockers efficacious as first-line therapy for hypertension in the elderly? A systematic review. *JAMA* 1998; **279**:1903–1907.
  - 47 Levin M. The occurrence of lung cancer in man. *Acta Unio Int Contra Cancrum* 1953; **33**:703–712.
  - 48 Lauria G, Gentile M, Fassetta G, Casetta I, Agnoli F, Andreotta G, *et al.* Incidence and prognosis of stroke in the Belluno province, Italy. First-year results of a community-based study. *Stroke* 1995; **26**:1787–1793.
  - 49 Carolei A, Marini C, Di Napoli M, Di Gianfilippo G, Santalucia P, Baldassarre M, *et al.* High stroke incidence in the prospective community-based L'Aquila registry (1994–1998). First year's results. *Stroke* 1997; **28**:2500–2506.

## Appendix

The population attributable risk (PAR) can be calculated from Levin's formula [47]:

$$\text{PAR} = p(r - 1) / [p(r - 1) + 1]$$

where  $p$  is the prevalence of the condition in the population and  $r$  is the relative risk or odds ratio. From the present study, the point estimate for the prevalence of uncontrolled hypertension is 40.6%. Untreated hypertensive subjects are comparable with participants assigned to placebo in randomized clinical trials of antihypertensive treatment. The relative risk of stroke in patients receiving low-dose diuretic, as compared with placebo, is 0.66 [5]. Thus, PAR for stroke in subjects with uncontrolled hypertension is 16.0%.

The annual incidence of first-ever stroke in community-dwelling Italians aged 65 years and over can be calculated from two population-based surveys, which reported 372 of 34 300 [48] and 690 of 55 079 [49] (average, 1.19%) cases of stroke per year in this age range. When referred to the 1991 national population 65 years of age and older (8.4 million) [42], this means 100 295 cases of stroke per year. Thus, the number of strokes which might be prevented each year with better hypertension control in the elderly population is:  $100\,295 \times 16.0\% = 16\,047$ .