Patterns of persistence with antihypertensive medications in newly diagnosed hypertensive patients in Italy: a retrospective cohort study in primary care

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Objective To describe patterns of persistence and related primary care costs associated with first antihypertensive treatment.

Design and setting Retrospective cohort study during 2000–2001, using information from 320 Italian general practitioners.

Participants We studied 13 303 patients with newly diagnosed hypertension, who received a first single antihypertensive prescription within 3 months after diagnosis.

Main outcome measures Persistence with first-line single treatment, categorized as follows: continuers: patients continuing the first-line medication for at least 1 year; combiners: patients receiving an additional antihypertensive drug and continuing the initial medication; switchers: patients changing from the first-line to another class of antihypertensive drug and discontinuing the initial treatment; discontinuers: patients stopping the first-line treatment without having another prescription until the end of the follow-up. Primary care costs were expressed as the cost of hypertension management per person-year of follow-up.

Results In the study cohort, 19.8% were continuers, 22.1% were combiners, 15.4% were switchers, and 42.6% were discontinuers. Continuation was greatest with angiotensin II type 1 receptor blocking agents (25.2%), calcium channel blockers (23.9%) and angiotensin-converting enzyme inhibitors (23.3%). Severe hypertension [hazards ratio 1.30; 95% confidence interval (CI) 1.18 to 1.43] and severe health status (hazards ratio 1.22; 95% CI 1.15 to 1.30) increased the risk of discontinuation. The likelihood of needing an additional antihypertensive drug was associated with mild-to-severe baseline blood pressure, diabetes (hazards ratio 1.20; 95% CI 1.06 to 1.36), and familial history of cardiovascular disease (hazards ratio 1.24; 95% CI 1.10 to 1.39). Discontinuers accounted for 22.4% of the total primary care cost. Initial treatment with angiotensin II type 1 receptor blocking agents and β-blockers resulted in incremental primary care costs of €145.2 and €144.2, respectively, compared with diuretics. Combiners and switchers increased the primary care cost by €140.1 and €11.7, compared with continuers.

Conclusion Persistence with first-line single antihypertensive drugs is extremely low during the first year of treatment. Potential cost saving should be possible by reducing the high frequency of discontinuation. Diuretics represent the least expensive therapeutic option, although further investigations in the long-term are needed to analyse the effects of persistence on therapeutic effectiveness and related costs. *J Hypertens* 23:2093–2100 © 2005 Lippincott Williams & Wilkins.

Introduction

Hypertension is one of the most important preventable causes of cardiovascular disease mortality worldwide [1]. In the USA, around 30% of individuals aged 35 years and over are hypertensive, whereas in Europe more than 40% suffer high blood pressure (BP) [2]. In view of its high prevalence, hypertension represents a burden for the national health systems in terms of morbidity/mortality and use of resources, accounting for more than 50% of deaths from stroke and 25% of those from coronary heart

diseases (CHD) [1]; 37.2 billion dollars were spent in the USA in the year 2003 [3].

A meta-analysis of clinical trials and cohort studies has shown that decreasing diastolic BP by 5 mmHg reduces the risk of stroke and CHD from any pretreatment value by an estimated 34 and 21%, respectively [4]. Recent trials [5] have reaffirmed previous recommendations that older antihypertensive agents are probably as effective in preventing cardiovascular disease and stroke as the newer and more expensive drugs such as angiotensin-converting enzyme (ACE) inhibitors or calcium channel blockers (CCBs). Thiazide-type diuretics should in general be considered as first-line BP-decreasing agents, as they are the least expensive.

However, findings in clinical practice have raised concern about the extremely high extent of under-treatment and non-persistence with antihypertensive treatment, which hampers the effectiveness of these medications [6]. The differences in persistence between clinical trials and clinical practice and, potentially, between drugs should be considered when the costs of antihypertensive treatment are being ranked. Non-persistence with treatment might affect the costs of therapy as a result of switching [7], and failure to attain targets may result in reduced cardiovascular benefits [8].

In the light of the above considerations, we assessed the patterns of persistence with antihypertensive medications in newly treated hypertensive patients in primary care in Italy, by estimating the 1-year risk and the determinants for stopping initial treatment, requiring additional therapy, or switching to other classes of antihypertensive drug. We also measured the direct primary care costs of the management of hypertension according to type of first-line treatment, and the costs attributable to various patterns of persistence with medication.

Methods
Data source
The Health Search Database is an Italian general practice research database that comprises the complete electronic medical records of all patients registered in the lists of participating physicians. Physicians have received formal training for data entry and use standard software to record data. A unique patient code links demographic and prescription information, clinical events and diagnoses, hospital admissions, and cause of death.

Data are subject to a range of quality checks. Any variations within agreed ranges are investigated and submitted to each participating physician. General practitioners (GPs) who fail to meet standard quality criteria are not considered for participation in epidemiological studies [9]. The validity of the data has been demonstrated in previous studies, which consistently reported

that the prevalence of hypertension was comparable to that derived from other sources of information [10,11]. At the time when this study was initiated, 320 GPs, covering a patient population of 409 724, were considered suitable to participate.

Identification of the study cohort
The study cohort included all newly diagnosed hypertensive patients (ICD-9: 401–404, 437.2) aged 35 years and over during the years 2000–2001, who were registered with one of the participating GPs for at least 1 year before entry into the study, and receiving at least one antihypertensive medication (anatomical therapeutic chemical classification codes) within 3 months after diagnosis. To ensure the selection of individuals with incident hypertension, patients who had received prescriptions for antihypertensive drugs in the previous 6 months were excluded. To assess the 1-year patterns of persistence with the antihypertensive drugs, patients with fewer than 365 days of valid follow-up after entry to the cohort were also excluded.

On the basis of the first prescription (index date), patients were assigned to one of six cohorts: diuretics (C03); α-blockers (C02CA); β-blockers (C07); ACE inhibitors (C09A); CCBs (C08); angiotensin receptor blockers (ARBs) (C09C). Individuals were excluded if they received as first-line treatment one-pill combination therapy such as ACE-inhibitors + diuretics or multiple-pill medications such as ACE-inhibitors + CCBs because they are more likely to ensure better compliance [12], and to be selectively prescribed for high-risk patients.

Analysis of the pattern of persistence with medication
For each of the six drug cohorts, the duration of exposure was calculated in terms of person-time. The theoretical duration was calculated by dividing the total amount of active drug in each prescription by the recommended defined daily dose. Consecutive prescriptions of drugs belonging to the same cohort were combined as one treatment period if they were less than 2 months apart. The accumulation of person-time in a given cohort ended at the earliest of the following occasions: prescription of any antihypertensive drug belonging to another cohort; failure to obtain a repeat prescription within a period of 2 months from the end of the previous one; death; end of the follow-up.

On the basis of the first and potential subsequent classes of drugs, patients were further classified into one of the following groups: *continuers*: patients continuing the first-line medication for at least 1 year; *combiners*: patients receiving an additional type of antihypertensive drug and continuing the initial medication; *switchers*: patients changing from the first-line to another antihypertensive class and discontinuing the initial treatment; *discontinuers*:

patients stopping the first-line therapy without having another antihypertensive prescription during follow-up.

Covariates

For each patient, the following determinants were assessed at baseline: age, sex, comorbidity (CHD, heart failure, diabetes, stroke, dyslipidaemia, chronic obstructive pulmonary disease, prostatic diseases), BP values calculated as the average between the last two separate measurements made by physicians within 3 months before the index date, and familial history for cardiovascular diseases, diabetes, and dyslipidaemia. The chronic disease score was calculated as an overall measure for severity of health status [13].

Cost analysis

For each drug class, primary care costs were expressed as the cost of the management of hypertension per person-year of follow-up. They included specialists' visits, diagnostic procedures, laboratory costs, and pharmacological treatments linked to the diagnostic code, quantified according to the Italian National Health System (NHS) by means of charges pertaining in 2000–2001.

Statistical analysis

Standard statistical methods were used to describe patients' demographics, clinical status, and patterns of persistence with medication for each cohort. A univariate Cox regression analysis was performed to identify all

potential confounders for the persistence measures of discontinuing, combining, or switching. Those found to be significant at the 5% level were then fitted together into the final multivariate models at different stages [14].

The association between primary care cost and type of first-line treatment was assessed using multivariate linear regression, with diuretics as reference group and with adjustment for potential confounding factors. All analyses were performed with STATA 7.0 (STATA Corporation, College Station, Texas, USA).

Results

Characteristics of the study cohorts

Among 24 540 newly diagnosed hypertensive patients, 4967 (20.2%) were excluded from the study because they did not receive any antihypertensive treatment within 90 days after diagnosis, and 6270 (25.5%) because their first-line treatment was a one-pill combination therapy (3369) or multiple-pill medications (2901). The final study cohort comprised 13 303 patients, the majority treated with ACE inhibitors (34.6%), CCBs (20.3%), and diuretics (16.4%) (Table 1).

Diuretics were preferentially prescribed to women (70.4% of diuretics users) and older patients (mean age 68.2 ± 13.1 years). Generally, individuals receiving diuretics had the greatest pulse BP (65.4 mmHg) and systolic blood pressure (155.8 mmHg). Patients treated

Table 1 Clinical and demographic characteristics of the study population by drug class

	Antihypertensive drug						
	α-blockers (n = 662)	Diuretics (n = 2177)	β-blockers (n = 1780)	CCBs (n = 2700)	ACE-inhibitors (n = 4602)	ARBs (n = 1382)	P
Sex[b]	345 (52.1)	1533 (70.4)	1087 (61.1)	1385 (51.3)	2484 (54.0)	770 (55.7)	<0.0001
Age (years)[c]	65.1 ± 13.3	68.2 ± 13.1	58.5 ± 11.8	68.6 ± 12.3	66.0 ± 12.8	64.0 ± 12.6	<0.0001
BP values at initial treatment[c]							
Systolic	152.9 ± 18.7	155.8 ± 19.8	151.7 ± 18.9	154.1 ± 20.3	153.1 ± 19.1	153.2 ± 18.6	<0.05
Diastolic	91.9 ± 10.3	90.4 ± 10.1	92.1 ± 10.9	89.4 ± 11.7	90.1 ± 10.6	90.6 ± 10.2	<0.0001
BP categories at initial treatment[a,d]							<0.0001
High normal	34 (9.6)	138 (9.6)	141 (13.4)	156 (13.1)	324 (12.6)	94 (11.5)	
Mild hypertension	120 (33.7)	430 (30.0)	339 (32.2)	373 (31.2)	833 (32.4)	262 (32.0)	
Moderate hypertension	149 (41.9)	618 (43.1)	406 (38.5)	430 (36.0)	1019 (39.6)	329 (40.1)	
Severe hypertension	53 (14.9)	248 (17.3)	168 (15.9)	236 (19.7)	398 (15.5)	139 (16.5)	
Patients with concurrent diseases[e]							
Coronary heart disease	17 (2.6)	81 (3.7)	54 (3.0)	146 (5.4)	179 (3.9)	54 (4.0)	<0.0001
Heart failure	7 (1.06)	22 (1.01)	6 (0.34)	26 (0.96)	45 (0.98)	14 (1.01)	=0.191
Diabetes	76 (11.5)	133 (6.1)	66 (3.7)	252 (9.3)	564 (12.3)	101 (7.3)	<0.0001
Stroke	17 (2.6)	54 (2.5)	14 (0.8)	118 (4.4)	141 (3.1)	43 (3.1)	<0.0001
Dyslipidemia	59 (8.9)	167 (7.7)	115 (6.5)	200 (7.4)	415 (9.0)	220 (8.7)	<0.05
COPD	42 (6.3)	155 (7.1)	45 (2.5)	153 (5.7)	244 (5.3)	85 (6.2)	<0.0001
Prostatic disease	45 (6.8)	85 (3.9)	41 (2.3)	140 (5.2)	218 (4.7)	53 (3.8)	<0.0001
Patients with two or more comorbidities[e]	64 (9.7)	188 (8.6)	91 (5.1)	316 (11.7)	479 (10.4)	129 (9.3)	<0.0001
Chronic disease score[e]							
0	73 (11.0)	217 (10.0)	287 (16.1)	323 (12.0)	538 (11.7)	150 (10.9)	<0.0001
1–2	270 (40.8)	786 (36.1)	837 (47.0)	1129 (41.8)	122 (2.7)	49 (3.5)	
≥3	319 (48.2)	1174 (53.9)	656 (36.9)	1248 (46.2)	3942 (85.7)	1183 (85.6)	

CCBs, calcium channel blockers; ACE, angiotensin-converting enzyme; ARBs, angiotensin II type 1 receptor blocking agents; BP, blood pressure; COPD, chronic obstructive pulmonary disease. [a]High normal: 130–139/85–99 mmHg; Mild hypertension: 140–159/90–99 mmHg; Moderate hypertension: 160–179/100–109 mmHg; Severe hypertension: ≥180/≥110 mmHg (European Society of Hypertension–European Society of Cardiology guidelines [12]). General practitioners did not record BP values in 5869 patients. Values are [b]number (% female), [c]mean ± SD, [d]number (prevalence among patients with BP values recorded), [e]number (prevalence among patients).

Fig. 1
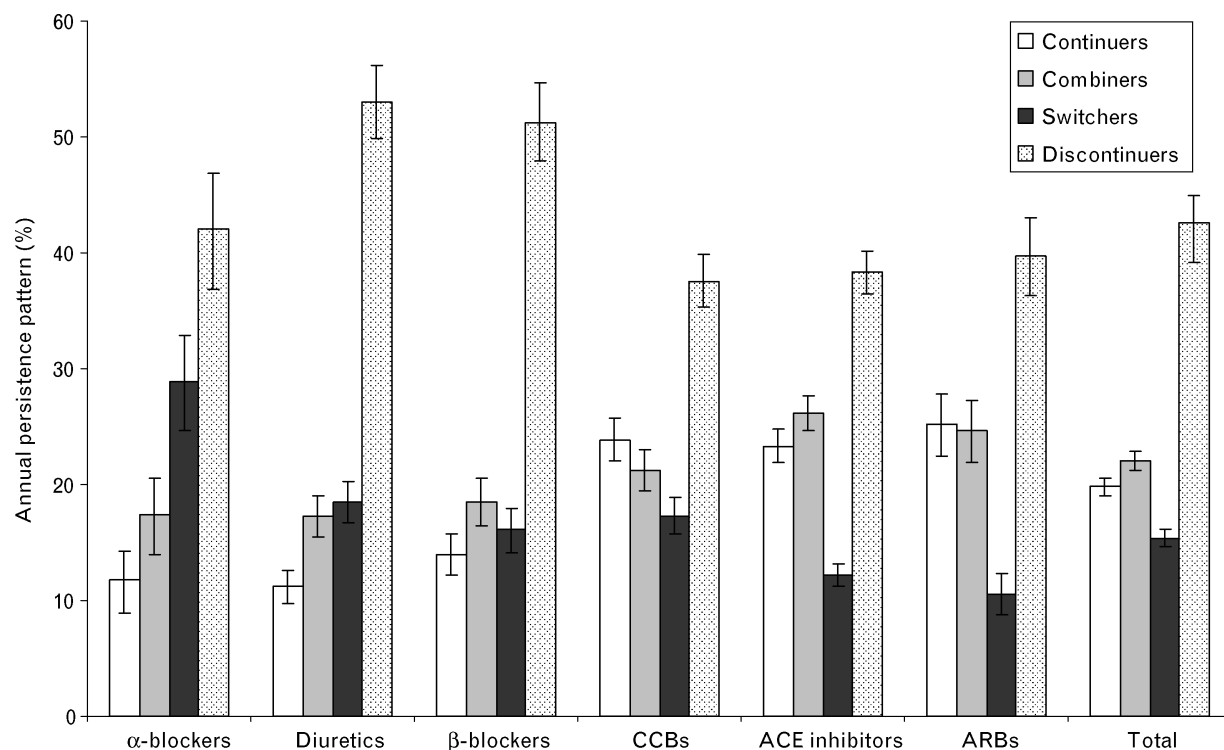
Patterns of persistence with medication (prevalance and 95% confidence intervals) for class of drugs at enrolment. to the study. CCBs, calcium channel blockers; ACE, angiotensin-converting enzyme; ARBs, angiotensin II type 1 receptor blocking agents.

initially with ACE inhibitors or CCBs more often had comorbid conditions.

A relatively large proportion of patients (11.9%) was diagnosed with hypertension while having high-normal BP values recorded at baseline; the majority of them (60%) had no associated clinical condition.

Persistence with medication

In the overall study cohort, 19.8% were continuers, 22.1% combiners, 15.4% switchers, and 42.6% discontinuers. Continuation rates were greatest for those taking ARBs (25.2%), CCBs (23.9%), and ACE inhibitors (23.3%); they were low with diuretics (11.2%) and α-blockers (11.8%) (Fig. 1). The need for additional antihypertensive agents was greatest in those starting on ARBs, CCBs, and ACE inhibitors, whereas switching of treatment was most frequent in those starting on α-blockers (28.9%), diuretics (18.5%), and CCBs (17.3%). These findings were confirmed in the multivariate models.

The risk of discontinuation of medication decreased with increasing age, familial history of cardiovascular diseases, and diabetes, whereas severe hypertension and a chronic disease score of at least 3 were independent predictors of an increased risk (Table 2).

Table 2 Association between baseline characteristics and discontinuation of first-line treatment

Variable[a]	Adjusted hazard ratio[b]	95% CI	P
Sex (female)	1.06	1.02–1.10	0.002
Age (1-year increase)	0.997	0.995–0.998	<0.001
BP values at baseline (high normal)			
Mild hypertension	1.00	0.92–1.09	0.861
Moderate hypertension	1.11	1.02–1.21	0.013
Severe hypertension	1.30	1.18–1.43	<0.001
Patients with concurrent diseases (absent)			
Diabetes	0.96	0.90–1.03	0.369
COPD	1.09	1.00–1.19	0.032
Chronic disease score (0)			
1–2	1.08	1.01–1.16	0.019
≥3	1.22	1.15–1.30	<0.001
Familial history (absent)			
Cardiovascular diseases	0.90	0.84–0.96	0.002
Diabetes	0.85	0.76–0.96	0.014
Dyslipidaemia	1.15	1.01–1.30	0.032
Antihypertensive drug class (diuretics)			
α-Blockers	0.91	0.83–1.00	0.070
β-Blockers	0.70	0.65–0.75	<0.001
Calcium channel blockers	0.56	0.52–0.60	<0.001
ACE inhibitors	0.50	0.47–0.54	<0.001
ARBs	0.44	0.41–0.48	<0.001

CI, confidence interval; BP, blood pressure; COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme; ARBs, angiotensin II type 1 receptor blocking agents. [a]Reference categories for the categorical variables in parentheses. [b]Each variable in the model was adjusted for other factors in the Table.

Table 3 Association of baseline characteristics and likelihood of adding on a antihypertensive drug of a class different from first-line treatment

Variable[a]	Adjusted hazard ratio[b]	95% CI	P
BP values at baseline (high normal)			
Mild hypertension	1.21	1.00–1.47	0.043
Moderate hypertension	1.53	1.27–1.84	<0.001
Severe hypertension	2.50	2.07–3.04	<0.001
Patients with two or more comorbidities (no)	1.03	0.90–1.19	0.605
Patients with diabetes (absent)	1.20	1.06–1.36	0.003
Chronic disease score (0)			
1–2	0.72	0.63–0.82	<0.001
≥3	0.84	0.75–0.94	0.002
Familial history (absent)			
Cardiovascular diseases	1.24	1.10–1.39	<0.001
Diabetes	1.10	0.89–1.35	0.343
Dyslipidaemia	0.99	0.79–1.23	0.951
Antihypertensive drug class (diuretics)			
α-Blockers	1.00	0.81–1.23	0.978
β-Blockers	1.07	0.92–1.24	0.364
Calcium channel blockers	1.24	1.09–1.42	0.001
ACE inhibitors	1.45	1.29–1.64	<0.001
ARBs	1.35	1.16–1.57	<0.001

CI, confidence interval; BP, blood pressure; ACE, angiotensin-converting enzyme; ARBs, angiotensin II type 1 receptor blocking agents. [a]Reference categories for the categorical variables in parentheses. [b]Each variable in the model was adjusted for other factors in the Table.

Patients with mild to severe BP values at baseline, diabetes [hazards ratio 1.20; 95% confidence interval (CI) 1.06 to 1.36], and familial history of cardiovascular disease (hazards ratio 1.24; 95% CI 1.10 to 1.39) were more likely to receive an additional drug, whereas a risk reduction was reported for a high chronic disease score (Table 3). None of the investigated covariates was significantly associated with the risk of switching first-line therapy.

We conducted two sensitivity analyses. First, we changed the criterion of continuous use from a permitted gap of 2 months to one of 3 months. Secondly, we selected a subgroup of patients older than 65 years without any comorbidity, thus assessing the effects of differential residual confounders among the drug cohorts. The findings did not significantly affect the patterns of persistence in taking medication.

Estimation of cost
Overall, the primary care costs attributable to one person-year of hypertension management were estimated at €238.6, 76.1% associated with the cost of drug acquisition, 16.3% with diagnostic procedures, and 7.6% with specialists' visits. First-line treatment with diuretics had the lowest 1-year primary care cost per patient (€140.4), whereas treatment with ARBs (€324.4), and α-blockers (€304.5) resulted in the highest costs (Fig. 2). In each drug cohort, the cost of those who required treatment with an additional drug was greatest, whereas those who discontinued medication had the lowest direct costs. Switching and continuation of medication were comparable in terms of costs per drug class.

The level of the annual primary care cost was associated with sex (€10.5 less in women), and presence of diabetes,

CHD, and dyslipidaemia (increased by €44.1, €40.4, and €13.5, respectively). After adjustment, first-line treatment with ARBs and α-blockers was associated with an increase in cost of €145.2 and 144.2 per person-year, respectively, compared with diuretics, whereas the incremental cost of other first-line medications was less than €100 (Table 4).

Discussion
This study has revealed several important findings. First, a high proportion of patients stopped any antihypertensive treatment within the first year and 19.2% continued with the first-line monotherapy. Secondly, almost 10% of patients had only high-normal BP, without comorbidity, yet were treated with antihypertensive drugs, which is not in line with recommendations [12]. The observed findings are consistent with those reported in a large body of the literature, which shows an overall high rate of discontinuation, particularly with diuretics and α-blockers, and a low rate of individualized treatments associated with comorbidities [6,15–17].

Patients' health status, the severity of their hypertension, socioeconomic factors, and tolerability profiles might explain the differences in discontinuation rates observed with the antihypertensive drugs [18,19]. According to the study findings, severe BP at baseline, high chronic disease scores, and younger age were the most relevant predictors. However, controlling for these variables did not significantly change the reported differences.

Fretheim and Oxman [20] examined the patterns of prescription of antihypertensive drugs in 10 countries and the possible socio-economic reasons for variations between countries. Suggested factors included reimbursement policies, traditions, opinion leaders having conflicts of

Fig. 2
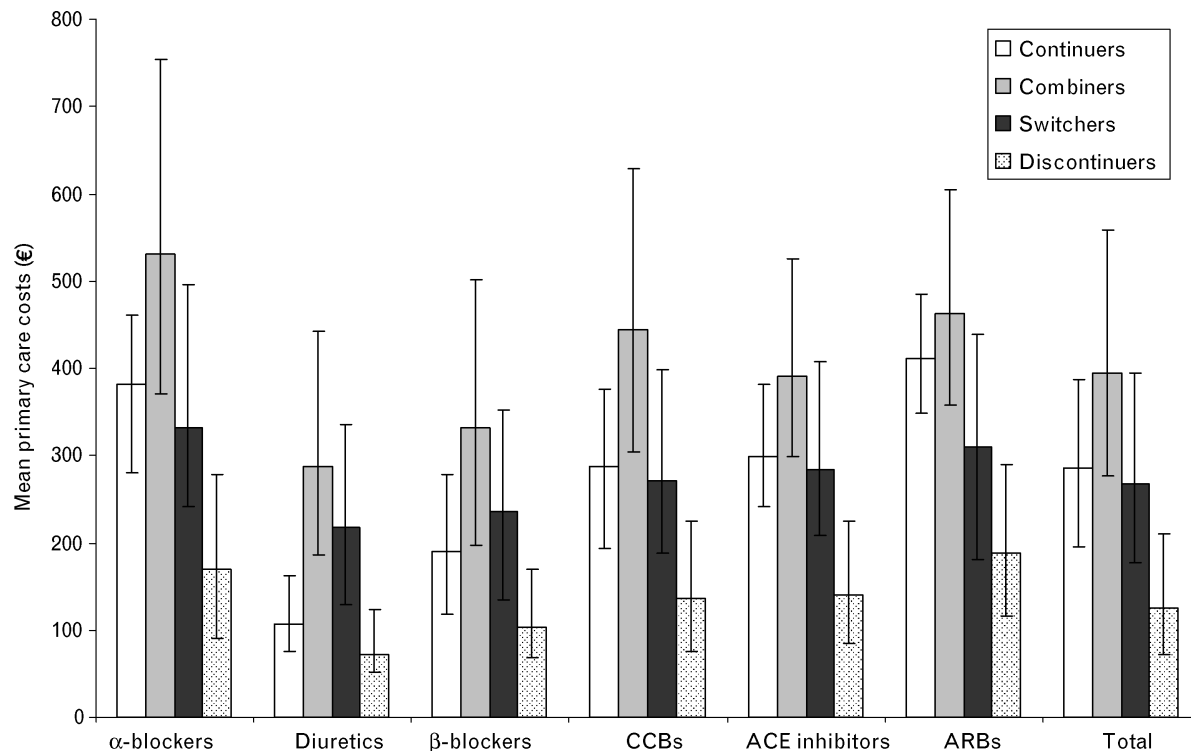
Annual primary care costs (mean and interquartile range) by drug cohort and persistence category. CCBs, calcium channel blockers; ACE, angiotensin-converting enzyme; ARBs, angiotensin II type 1 receptor blocking agents.

interests, domestic pharmaceutical production, and clinical practice guidelines. Another study conducted in Canada [21] reported a 25% decreased risk of discontinuation among individuals with medication insurance coverage, compared with other methods of payments. Such factors might therefore have an impact on the selection of the initial drug to be prescribed, but they can only partially explain the different rates of persistence with medication in Italy, because the NHS provides full reimbursement for all classes of antihypertensive drug.

The most common reasons for poor persistence are the patient's perception of a risk of side effects and their idea that they have no need to take medication if they are symptom-free [21]. This might be particularly relevant to newly hypertensive patients whose initial medication is diuretics and α-blockers, as those drugs are perceived to have a worse tolerability profile [7].

Among patients continuing with the first-line medication, 38.5% required the additional of another drug to the initial treatment. This is in line with the findings of the Antihypertensive and Lipid Lowering to Prevent Heart Attack Trial [22], which estimated that 40% of patients require two or more drugs to control their hypertension, after 1 year of follow-up. In our study, patients with severe BP at

Table 4   Multiple linear regression of annual primary care costs

Variable[a]	Regression coefficient[b]	95% CI	P
Sex (female)	−10.5	−16.3 to −4.6	<0.001
BP values at baseline (high normal)			
Mild hypertension	−13.7	−26.5 to −0.88	0.036
Moderate hypertension	−12.4	−24.9 to −0.07	0.051
Severe hypertension	2.79	−11.6 to 17.2	0.865
Patients with concurrent diseases (absent)			
Diabetes	44.1	33.3 to 54.9	<0.001
Coronary heart diseases	40.7	25.1 to 56.4	<0.001
Dyslipidaemia	13.5	2.45 to 24.6	<0.001
Chronic disease score (0)			
1–2	−30.0	−40.3 to −19.2	<0.001
≥3	−22.0	−31.1 to −12.9	<0.001
Familial history (absent)			
Cardiovascular diseases	14.5	4.61 to 24.4	0.004
Diabetes	24.0	6.79 to 41.3	0.006
Persistence pattern (continuers)			
Combiners	140.1	127.0 to 153.3	<0.001
Switchers	11.7	−1.29 to 24.7	0.078
Discontinuers	−116.3	−128.8 to −103.8	<0.001
Antihypertensive drug class (diuretics)			
α-Blockers	144.2	129.7 to 158.8	<0.001
β-Blockers	30.6	19.8 to 41.3	<0.001
Calcium channel blockers	84.8	75.1 to 94.4	<0.001
ACE inhibitors	74.8	65.8 to 83.9	<0.001
ARBs	145.2	133.5 to 156.9	<0.001

CI, confidence interval; BP, blood pressure; ACE, angiotensin-converting enzyme; ARB, angiotensin II type 1 receptor blocking agent. [a]Reference categories for the categorical variables in parentheses. [b]Each variable in the model was adjusted for other factors in the Table, age, and the presence of stroke, chronic obstructive pulmonary disease, and familial history of dyslipidaemia. Increased cost in euros compared with reference group.

baseline exhibited a 2.5-fold increased likelihood of requiring an additional drug. Other associated factors were the familial history of cardiovascular diseases and the presence of diabetes; this is in agreement with the most recent guidelines [12,23], which highlight the need for two or more drugs to achieve BP control in patients at high risk of cardiovascular events.

The level of persistence with antihypertensive treatment has short-term and long-term economic implications. Our findings showed that hypertensive patients who newly start a monotherapy with an antihypertensive drug cost on average €238.6 per person-year. Discontinuers were found to be the least costly group during the first 12 months after initiation of monotherapy. However, these patients accounted for 22.4% of the total expenditure of the cohort, without foreseeable clinical benefit. The long-term costs to the NHS as a result of a lack of beneficial cardiovascular effects may be high in this group. A study from the UK [7] has estimated that 39% of the direct costs of hypertension could be attributed to patients who discontinue or switch treatment.

Among continuers, the primary care cost was least for those who started on diuretics, compared with those given the newer antihypertensive drugs. Add-on medication (€140.1 per person-year) had a strong impact on costs across the different classes of drug. Despite this, when adjusted for patterns of persistence and clinical variables, diuretics were associated with significantly lower costs, and incremental primary care costs ranged from €30.1 for β-blockers to €145.1 for ARBs.

The annual average primary care cost was significantly affected by the presence of diabetes, cardiovascular diseases, and dyslipidaemia. The resulting incremental primary care costs can be explained by the need of physicians to use additional resources (increased frequency of diagnostic procedure tests and specialists' visits) for the management of patients with these comorbidities, because the need to control the BP is matched to the need to reduce their cardiovascular risk [24,25].

The findings of this study should be interpreted in the light of certain limitations. First, our analysis was limited to 1 year of follow-up, therefore it is difficult to assess the long-term effectiveness and related costs of the various antihypertensive treatments. Secondly, we could not assess the cost of hospital admissions and the indirect costs associated with the use of the drugs – that is, the impact on individual productivity and quality of life, which are generally related to the tolerability profile. Such measures comprise the largest portion of health expenditure [26]. However, in studies with 1 year of follow-up conducted among newly diagnosed hypertensive patients the impact of admission to hospital is unlikely to affect the costs.

In conclusion, in considering potential strategies for reducing the costs of hypertension, health managers and GPs should make special efforts to reduce the remarkably high proportion of patients who discontinue their medication and those who do not benefit from any antihypertensive treatment. Among patients who continue treatment, the need to use two or more antihypertensive drugs that has been reported in clinical trials has now been confirmed in everyday clinical practice. From an NHS perspective, diuretics remain the least expensive first-line treatment option; the lower persistence with this medication, however, might translate into greater long-term costs as a result of more cardiovascular events. Further long-term investigations are needed to assess the effects of the pattern of persistence with medication on therapeutic effectiveness and related costs.

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