# Negative predictors of treatment success in outpatient therapy of arterial hypertension in Poland. Results of the CONTROL NT observational registry 

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#### Abstract

Background: Identification of factors interfering with adequate control of arterial hypertension $(\mathrm{HT})$ in the course of antihypertensive therapy is necessary to reduce the incidence of cardiovascular disorders and optimise clinical practice guidelines. Aim: The study objective was to conduct a screening assessment of the rate of uncontrolled hypertension among hypertensive patients coming to a routine follow-up visit, and to characterise patients with inadequate control of HT in the aspect of their cardiovascular risk profile and therapeutic strategies used. Methods: The CONTROL NT registry was a nationwide observational study performed by physicians in the outpatient setting in Poland. Patient data were collected twice: between April and September 2011 and between January and August 2012. During screening, the physician completed a questionnaire with patient basic clinical information. The impact of the selected demographic and clinical parameters on treatment success defined as blood pressure (BP) lowering to $<140 / 90 \mathrm{mmHg}$ when measured in the office at the second visit was investigated with univariate and multivariate logistic regression models. Results: In total 1288 outpatient physicians participated in the CONTROL NT registry. In the screened group of 34,919 patients with a history of HT, $66.9 \%$ had abnormal BP readings in the office. In 15,262 patients with inadequate control of hypertension included in further analysis, the mean age was $59.3 \pm 11.9$ years, $47.9 \%$ were women, the disease duration was $8.2 \pm 6.5$ years and antihypertensive therapy was used for $7.4 \pm 6.0$ years. At least three cardiovascular risk factors were found in $46 \%$ of patients, with the most common dyslipidaemia ( $77.4 \%$ ) and abdominal obesity ( $74.8 \%$ ). In $56.6 \%$ of patients at least one concomitant disease was diagnosed, the most common being diabetes (29.8\%). At the time of enrolment $21.5 \%$ of patients received no antihypertensive drugs, one, two, three (or more) drug combinations and fixed-dose combinations were received by $16.8 \%, 28.5 \%, 31.5 \%$ and $4.0 \%$ of patients, respectively. The most commonly used drug class was angiotensin-converting enzyme inhibitors ( $50 \%$ ), followed by beta-blockers ( $42 \%$ ) and diuretics (39\%). Significant negative predictors of BP control included: body mass index $\geq 30 \mathrm{~kg} / \mathrm{m}^{2}$, heart rate $\geq 70 \mathrm{bpm}$, history of hypertension $\geq 7$ years, and kidney disease (the odds ratios adjusted by age and gender - $0.61 ; 0.76 ; 0.79$; and 0.76 , respectively). Conclusions: The percentage of Polish outpatients with adequate HT control is unsatisfactory. Patients with diabetes, chronic kidney disease, dyslipidaemia, overweight or obesity, longer disease and treatment duration and poor treatment compliance require a particularly careful assessment of risk factors and comorbidities, appropriate therapy intensification, and more frequent use of antihypertensive fixed-dose combinations.


Key words: arterial hypertension, hypertension control, antihypertensive therapy, cardiovascular risk, public health
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## INTRODUCTION

Adequate control of blood pressure (BP) is essential for reducing the risk of cardiovascular (CV) disorders, the leading cause of death [1, 2]. Arterial hypertension is estimated to cause over seven million deaths in the world per year [1-4]. This disease is also an important issue in Poland, where a steady increase in its prevalence has been observed [5, 6]. Although CV mortality in Poland has decreased in the last decades, it still remains markedly higher than in Western European countries [7].

Numerous research studies conducted so far have unequivocally confirmed a lower risk of CV complications in patients with achieved target BP values. Meta-analyses including data of over 160,000 patients showed that lowering systolic BP (SBP) values by 20 mmHg reduces cardiovascular disease (CVD) incidence by $40-45 \%$ [8]. Unfortunately, despite the increasing number of available antihypertensive drugs, the percentage of patients achieving the treatment targets defined in the European Society of Cardiology guidelines still remains unsatisfactory [5, 6, 9-12], which emphasises the need for higher efficacy in the treatment of arterial hypertension.

Effective comprehensive treatment of arterial hypertension should be based on the most recent knowledge, which is why the guidelines for the diagnosis and treatment of this disease are regularly updated. However, cross-sectional studies conducted in large patient populations, investigating the current status of treatment of this disease, are also of significant importance. They are necessary to optimise disease management strategies. For this purpose, in many countries, including Poland, population programmes evaluating the prevalence and control of CV risk factors have been and are being conducted.

Proper conduct of extensive epidemiological studies is a challenging task, requiring, for example, representative selection of the population sample, uniform and rigorously applied methodology of BP measurement and hypertension diagnosis, and also standardised devices used for measurements [12]. Therefore, the number of reliable studies on epidemiology of arterial hypertension is limited. In the last two decades, studies on a representative group of Poles were conducted in 1994-2004 (NATPOL I-III programmes) [5], 2003-2005 (WOBASZ study) [12], and 2011 (NATPOL 2011 study) [6]. Knowledge obtained from such initiatives is not only valuable for physicians but is also of significant importance for planning a health policy of the state. It makes it possible to modify population strategies with regard to CVD prevention and to predict future mortality trends. So far, there has been no study in the Polish population that has included a large representative group of patients with previously diagnosed hypertension and aimed to identify patients with uncontrolled arterial hypertension and to describe their clinical characteristics.

The objectives of the CONTROL NT observational registry were to assess the frequency of abnormal BP values at
routine follow-up visits in Polish outpatients diagnosed with arterial hypertension, and also to determine the coexisting CV risk factors and treatment strategies used in patients with inadequately controlled BP. The study was performed in an outpatient setting because it is primary care physicians who give the most advice about the treatment of arterial hypertension [13].

## METHODS

The CONTROL NT registry was designed as a nationwide non-interventional observational study for physicians in an outpatient setting in Poland, aimed at conducting a screening assessment of the rate of uncontrolled hypertension among patients with a history of arterial hypertension coming for a routine follow-up visit, and to characterise patients with inadequately controlled arterial hypertension with regards to their CV risk profile and therapeutic strategies used in the treatment of arterial hypertension.

The study was conducted in accordance with art. 37a-37al of Polish Pharmaceutical Law.

Patient data were collected twice: between April and September 2011 and between January and August 2012. Each physician participating in the study conducted screening of consecutive patients with a history of arterial hypertension (or undergoing diagnosis of arterial hypertension) coming for a routine follow-up visit to the physician's office. Patient screening was conducted until the selection of 10 patients with uncontrolled hypertension or inclusion of max. 50 patients into the screening. In the course of screening, the physician completed a form with basic information on the patient (gender, age, BP measurement, primary risk factors, treatments used). In 10 patients with arterial hypertension selected in the screening phase, who met the criterion of inadequate control of arterial hypertension (defined as SBP $\geq 140 \mathrm{mmHg}$ and/or diastolic BP [DBP] $\geq 90 \mathrm{mmHg}$ measured in the office on the visit day), physicians collected additional data on medical history, physical examination (BP measured in the office, resting heart rate [HR]), results of laboratory tests and other data from medical records. Moreover, the physician collected data on the currently used antihypertensive treatment (products and their doses) and its modifications. The observation was supplemented by office BP readings and details of treatment at the subsequent routine visit.

Each patient enrolled to the program was identified with an individual number and his/her initials (the first letter of the forename and surname). Before inclusion into the programme, the physician had to inform the patient about the objectives and methods of the observational programme as well as about the scope of data that would be disclosed for its purpose, and to obtain the patient's consent for disclosure of medical data.

The data were collected and processed with a support of an educational grant from Servier Polska Sp. z o.o. Microsoft Access was used for data collection and processing.

## Statistical analysis

Statistical analysis was performed with the use of SAS v. 9.3 (SAS Institute, Cary, North Carolina, USA). The study group was characterised with standard methods of descriptive statistics. Mean value and standard deviation were provided for approximately normally distributed continuous variables, and median value and interquartile range were provided for variables with strongly asymmetric distributions. Absolute and relative frequencies by classes were provided for categorical variables. The impact of the selected (demographic and clinical) parameters on treatment success was investigated with univariate and multivariate logistic regression models. The results are presented as odds ratios (OR) with $95 \%$ confidence intervals (CI). The logistic regression model took into account factors that had a statistically significant impact on treatment success defined as BP lowering to $<140 / 90 \mathrm{mmHg}$ when measured in the office at the second visit.

## RESULTS

In total 1288 outpatient physicians participated in the CONTROL NT registry, representing both primary healthcare and specialist consultation clinics and private practices. The percentage shares of the individual sites are presented in Figure 1. The list of all sites participating in the CONTROL NT registry is provided in supplemental materials (Appendix 1 - see journal website).

Screening involved in total 34,919 patients with a history of arterial hypertension. From this group, physicians selected 15,262 patients with abnormal BP pressure readings in the office, for whom additional medical data were collected.

## Screening results

In the group of screened Polish outpatients with arterial hypertension, the mean age was $58.4 \pm 13.0$ years and $51.7 \%$ were women. Two-thirds of patients (66.9\%) had abnormal BP readings in the office. Primary CV risk factors (cigarette smoking, dyslipidaemia, abdominal obesity) were noted in $74.4 \%$ of patients, and coexisting diseases (diabetes, coronary artery disease [CAD], chronic kidney disease, cerebrovascular disease) were noted in $50.4 \%$ of patients. Hypotensive agents were used by $76.4 \%$ of patients.

## Clinical characteristics of patients with uncontrolled hypertension

In the group of 15,262 patients with inadequate control of hypertension included in further analysis (persons in whom all data modules for multivariate logistic regression analysis were available), the disease duration was $8.2 \pm 6.5$ years (median 7.0 ) and antihypertensive therapy was used for $7.4 \pm 6.0$ years (median 6.0). The clinical characteristics of the study subjects are presented in Table 1.

Patients were aged $59.3 \pm 11.9$ years, and $47.9 \%$ of them were women. The mean values of SBP and DBP measured in


Figure 1. Outpatient clinics participating in the Polish CONRTOL NT registry

Table 1. Baseline clinical characteristics of 15,262 Polish outpatients with uncontrolled arterial hypertension observed in the CONTROL NT registry

| Women | $47.9 \%$ |
| :--- | :---: |
| Age [years] | $59.3 \pm 11.9$ |
| Height [cm] | $169.7 \pm 8.4$ |
| Body weight [kg] | $84.4 \pm 14.2$ |
| Body mass index [kg/m] | $29.3 \pm 4.5$ |
| Waist circumference [cm] | $94.5 \pm 12.3$ |
| Systolic blood pressure [mmHg] | $159.8 \pm 14.2$ |
| Diastolic blood pressure [mmHg] | $95.4 \pm 9.1$ |
| Heart rate [bpm] | $78.2 \pm 10.2$ |

Data are presented as mean $\pm$ standard deviation or percentage.
the office on the visit day were 160 mmHg and 95 mmHg , respectively, and the mean HR was 78 bpm.

At least three CV risk factors (out of the following: current cigarette smoking, dyslipidaemia, abdominal obesity, carbohydrate disorders, and premature CVD in the family) were found in $46 \%$ of patients. The most common were dyslipidaemia ( $77.4 \%$ ) and abdominal obesity (defined as waist circumference in men $\geq 94 \mathrm{~cm}$, in women $\geq 80 \mathrm{~cm} ; 74.8 \%$ ). During the study, $24.4 \%$ of patients smoked cigarettes and $39.4 \%$ of patients reported smoking cessation in the past. Elevated body mass index (BMI) $\geq 25 \mathrm{~kg} / \mathrm{m}^{2}$ and $\geq 30 \mathrm{~kg} / \mathrm{m}^{2}$ was calculated for $84.2 \%$ and $40 \%$ of study subjects, respectively, and $H R \geq 70$ bpm on the visit day was found in $83.4 \%$ of study subjects. The prevalence of primary CV risk factors is illustrated in Figure 2.

In more than half ( $56.6 \%$ ) of the patients at least one concomitant disease was diagnosed, mainly diabetes (29.8\%)


Figure 2. Prevalence of primary cardiovascular risk factors in 15,262 Polish outpatients with uncontrolled arterial hypertension. Risk factors in medical history (definitions on the basis of the 2011 guidelines of the Polish Society of Hypertension): Abdominal obesity — waist circumference: male (M) 294 cm , female (F) $\geq 80 \mathrm{~cm}$; Positive family history - premature cardiovascular diseases in the family ( $\mathrm{M}<55$ years and/or $\mathrm{F}<65$ years); Dyslipidaemia - hypercholesterolaemia or hypertriglyceridaemia; Carbohydrate metabolism disorders - fasting plasma glucose $\geq 5.6 \mathrm{mmol} / \mathrm{L}(100 \mathrm{mg} / \mathrm{dL})$ or impaired glucose tolerance in oral glucose tolerance test


Figure 3. Prevalence of comorbidities in the observed group of 15,262 Polish outpatients with uncontrolled arterial hypertension; TIA - transient ischaemic attack
and CAD (28.5\%). The rates of arterial hypertension comorbidities are presented in Figure 3.

## Treatment regimens for arterial hypertension

One-fifth of patients with arterial hypertension (21.5\%) were not taking an antihypertensive drug at the time of enrollment. They included persons classified by physicians as having the "recently diagnosed" hypertension (19.9\%) and persons with hypertension in their history, but untreated at that time. 16.8\% of patients received one antihypertensive drug, $28.5 \%$ two drugs in combination therapy, and $31.5 \%$ received three or more drugs before inclusion into the study.

In the analysis of the drugs used by therapeutic class, the most commonly used drug class, in both monotherapy and polytherapy, was angiotensin-converting enzyme inhibitors (ACEI; noted in 50\% of study subjects), followed by beta-blockers (42\%) and diuretics (39\%). Fixed-combination
products (qualified as polytherapy in the analysis) were received by only $4 \%$ of study subjects.

The most commonly used ACEI was ramipril ( $21 \%$ of study subjects), the most commonly used beta-blocker was bisoprolol ( $18 \%$ of study subjects), the most commonly used diuretic was indapamide ( $24 \%$ of study subjects), and the most commonly used calcium channel blocker was amlodipine (23\% of study subjects). Combinations of perindopril with amlodipine predominated in the small group of fixed-combination products. The frequency of use of the individual classes of antihypertensive drugs is presented in Figure 4.

The mean doses of the most commonly used drugs of the classes of ACEI, beta-blockers, diuretics, calcium channel blockers, and sartans are noted in Table 2.

The modification of antihypertensive treatment prescribed after the first visit enabled BP control (BP $<140 / 90 \mathrm{mmHg}$ measured in the office at the second visit) in $60 \%$ of study


Figure 4. Prevalence of use of the individual classes of antihypertensive drugs in 15,262 outpatients with uncontrolled arterial hypertension in the Polish CONTROL NT registry; ACEI - angiotensin converting enzyme inhibitors

Table 2. Mean daily and median doses of the most commonly used drugs from the classes of angiotensin-converting enzyme inhibitors, beta-blockers, diuretics, calcium channel blockers and sartans

| International non-proprietary name | Mean daily dose [mg] | Median dose [mg] |
| :--- | :---: | :---: |
| ramipril | $7.2 \pm 2.9$ | 5.0 |
| perindopril (arginine) | $6.1 \pm 2.2$ | 5.0 |
| enalapril | $16.7 \pm 9.1$ | 20.0 |
| bisoprolol | $5.0 \pm 3.2$ | 5.0 |
| metoprolol | $54.6 \pm 25.9$ | 50.0 |
| carvedilol | $18.0 \pm 11.0$ | 12.5 |
| indapamide | $1.6 \pm 0.8$ | 1.5 |
| furosemide | $42.4 \pm 16.9$ | 40.0 |
| hydrochlorothiazide | $17.6 \pm 6.4$ | 12.5 |
| amlodipine | $6.3 \pm 2.4$ | 5.0 |
| lacidipine | $3.8 \pm 1.1$ | 4.0 |
| nitrendipine | $20.1 \pm 9.8$ | 20.0 |
| losartan | $51.2 \pm 12.6$ | 50.0 |
| valsartan | $122.2 \pm 42.1$ | 160.0 |
| telmisartan | $72.0 \pm 16.4$ | 80.0 |

Data are presented as mean $\pm$ standard deviation and medians.
Note: The listed representatives of the individual classes of antihypertensive drugs were the ones used most frequently five years ago in Poland (at the time of the study).
subjects. A reduction in SBP of at least 10 mmHg could be obtained in most patients ( $93.5 \%$ ). The mean interval between the follow-up visits at which BP was measured was $30.7 \pm 13.0$ days.

Multivariate analysis was performed to identify variables contributing to treatment success, defined as BP lowering below $140 / 90 \mathrm{mmHg}$ as measured in the office at the subsequent follow-up visit (Table 3). Significant negative predictors
of BP control included elevated $\mathrm{BMI} \geq 30 \mathrm{~kg} / \mathrm{m}^{2}$, increased $H R \geq 70 \mathrm{bpm}$, longer duration of hypertension $\geq 7$ years, and coexisting kidney disease (the OR for those factors adjusted by age and gender were $0.61,0.76,0.79$, and 0.76 , respectively, $\mathrm{p}<0.001$ ). Patients who did not receive fixed-dose combinations had a significantly lower chance of BP lowering to target values in comparison with individuals who were receiving this treatment at the first visit ( $\mathrm{OR} 0.62, \mathrm{p}<0.001$ ). On the

Table 3. Negative predictors of blood pressure lowering below $140 / 90 \mathrm{mmHg}$ as measured in the office at the subsequent follow-up visit V2

| Parameter | N | OR* | (95\% CI) | p ( $\chi^{2}$ Wald test) |
| :---: | :---: | :---: | :---: | :---: |
| Elevated $\mathrm{BMI}\left[\mathrm{kg} / \mathrm{m}^{2}\right]$ | 14,860 |  |  | $<0.001$ |
| $\mathrm{BMI} \geq 25$ and $<30$ vs. $\mathrm{BMI}<25$ | 14,860 | 0.81 | (0.74-0.90) |  |
| $\mathrm{BMI} \geq 30$ vs. $\mathrm{BMI}<25$ | 14,860 | 0.61 | (0.55-0.68) |  |
| $\mathrm{BMI} \geq 30$ vs. $\mathrm{BMI} \geq 25$ and $<30$ | 14,860 | 0.75 | (0.70-0.81) |  |
| Abdominal obesity (waist circumference: male $\geq 94 \mathrm{~cm}$, female $\geq 80 \mathrm{~cm}$ ) | 14,026 | 0.81 | (0.75-0.88) | < 0.001 |
| $\mathrm{HR} \geq 70$ bpm vs. $\mathrm{HR}<70 \mathrm{bpm}$ | 14,910 | 0.76 | (0.69-0.83) | < 0.001 |
| Longer duration of HT ( $\mathrm{HT} \geq 7$ years vs. $\mathrm{HT}<7$ years) | 11,874 | 0.79 | (0.73-0.85) | < 0.001 |
| Longer duration of HT treatment (HT 2 years vs. $\mathrm{HT}<6$ years) | 11,360 | 0.82 | (0.76-0.89) | < 0.001 |
| Not receiving antihypertensive treatment | 15,001 | 0.81 | (0.74-0.88) | $<0.001$ |
| Current smoking | 15,001 | 0.82 | (0.76-0.89) | < 0.001 |
| Dyslipidaemia | 15,001 | 0.83 | (0.76-0.89) | $<0.001$ |
| Family history of premature cardiovascular diseases | 15,001 | 0.97 | (0.90-1.03) | 0.318 |
| Carbohydrate metabolism disorders | 15,001 | 0.85 | (0.79-0.91) | < 0.001 |
| Diabetes | 15,001 | 0.82 | (0.77-0.88) | < 0.001 |
| Renal function impairment | 15,001 | 0.81 | (0.73-0.91) | < 0.001 |
| Kidney diseases | 15,001 | 0.76 | (0.66-0.87) | < 0.001 |
| Coronary artery disease | 15,001 | 0.97 | (0.90-1.05) | 0.501 |
| Cerebrovascular disease | 15,001 | 0.81 | (0.72-0.92) | 0.001 |
| Peripheral artery disease | 15,001 | 0.82 | (0.74-0.92) | $<0.001$ |

*OR — odds ratio adjusted by the patient's age and gender; Cl — confidence interval; BMI — body mass index; HR — heart rate; HT — arterial hypertension
other hand, no significant relationship was noted between the diagnosis of CAD or positive familial history of premature CVD and probability of therapeutic success in the treatment of arterial hypertension.

## DISCUSSION

Periodic assessment of hypertension treatment at the population level constitutes an essential component of planning the strategy, reducing the incidence of CV disorders, and optimising daily clinical practice guidelines. For this purpose, the CONTROL NT registry was created, as a wide snapshot of the treatment status, a cross-sectional study describing the status of outpatient antihypertensive treatment in Poland on the basis of data from almost 35,000 patients with arterial hypertension, which was conducted five years ago.

In contrast to numerous epidemiological studies based on a single BP measurement [14-16], in the CONTROL NT registry medical data collected at two subsequent follow-up visits along with office readings of BP were analysed, which was of significant importance for reliable assessment of the hypertension control.

A worrying finding was the fact that $2 / 3$ of patients with arterial hypertension, who attended a routine treatment monitoring visit required treatment intensification. The ob-
served percentage of patients with proper control of arterial hypertension was unsatisfactory, but it represented significant progress in comparison with the NATPOL PLUS study where the level of BP control in the whole study population was $12 \%$, and in the population receiving antihypertensive treatment it was $22 \%$ [5]. In the WOBASZ study the percentage of patients with adequately controlled hypertension was $10 \%$ in men and $16 \%$ in women [12]. However, the results obtained were less optimistic than the observations of the NATPOL 2011 study, where an increase in the efficacy of BP control in patients with diagnosed and treated arterial hypertension was up to $42 \%$ in comparison with previous studies [6].

The efficacy of hypertension treatment in Poland is considered to be comparable to Western Europe countries [16], and slightly higher than other Central and Eastern Europe countries where adequate BP control was found in $27.1 \%$ of study subjects [17]. Nevertheless, the percentage of patients with effectively treated arterial hypertension is lower than, for example, in the United States (an increase from $27.3 \%$ to $53 \%$ in the last two decades [14, 18]), Canada (64.6\%) [19], or in Australia (50\%) [20].

Particularly alarming is the fact that, similar to observations in the study by Abu-Saad et al. [21], the diagnosis of CAD was not associated with better control of coexisting arterial
hypertension, although high benefits from BP lowering have been proven in this patient group [22].

Numerous studies have reported worse BP control in patients with diabetes, elevated BMI, dyslipidaemia, or poor compliance with antihypertensive treatment, $[15,16,18,19]$, which was confirmed in the CONTROL NT study. On the other hand, in contrast to the results of some clinical trials [15], the presented registry indicates a significant effect of other modifiable CV risk factors, such as smoking, on the level of BP control. Furthermore, based on the available data, poor control of hypertension was markedly more common in men than women [17, 18]. In the CONTROL NT study, the predominance of men with uncontrolled hypertension was observed, which may suggest that this issue is becoming more and more common in women.

The most commonly used drugs were ACEI, which are the mainstay of treatment of arterial hypertension in patients with diabetes and/or CAD, which were diagnosed in about one-third of the study population. Most patients needed therapy with more than one antihypertensive agent. Nevertheless, as in the BP-CARE study, an international clinical trial including 7860 patients treated for arterial hypertension, extensive use of combination antihypertensive treatment did not translate into adequate BP control at the population level [17]. Therefore, the use of fixed-dose combinations may play a particular role in this population, including the combinations of most popular drugs (ACEI and beta-blockers), including those that were not available on the pharmaceutical market at the time of the CONTROL NT study, but that are now available in Poland in 2017. The use of a fixed-dose combination of an ACEI and a beta-blocker may prove particularly important, especially in the context of the present study with respect to the contribution of increased HR to failure to achieve the hypertension treatment target of $\mathrm{BP}<140 / 90 \mathrm{mmHg}$.

The level of hypertension control in the group of patients who came to follow-up visits to undergo efficacy assessment and modification of the drug therapy they received is definitely unsatisfactory. In as many as $40 \%$ of the patients with inadequate control of hypertension, the antihypertensive treatment prescribed at screening did not result in normal values of BP as measured in the office at the subsequent follow-up visit, which indicates the continued need for improving the efficacy of treatment of this disease. The numerous postulated causes of the lack of general success of antihypertensive treatment include patient-dependent factors, such as poor compliance with drug treatment and absence of lifestyle changes, and causes related to the physician's approach, the most important of which are the lack of adequate reaction to unsatisfactory treatment effects, the so-called therapeutic inertia [23]. As indicated by some reports, in over $80 \%$ of ineffectively treated patients, physicians do not modify treatment [24]. What is more, the delay in making therapeutic decisions by the physician much more commonly involves patients with a high risk of CVD [24].

Just increasing dose or adding another antihypertensive drug if BP control is not achieved may, however, be insufficient if the frequency of use of fixed-dose combinations is not increased in clinical practice. In view of the need for long-term treatment and common unawareness of the treated patients of the chronic nature of the disease, compliance with use of the prescribed antihypertensive agents is poor [25]. Hence the current approach to hypertension treatment attributes a growing role to fixed-combination products, the use of which significantly improves treatment compliance and also increases the frequency of adequate BP control, as shown in the available meta-analyses [25]. Moreover, the available data suggest that when starting drug therapy of recently diagnosed arterial hypertension from initial-dose combination products, a higher treatment efficacy may be achieved compared with monotherapy or standard combination treatment in the form of separate tablets [26]. At the time of conducting the CONTROL NT study, the use of antihypertensive fixed-dose combinations in Poland was infrequent (only a few per cent), while currently it stands at more than ten per cent, which remains highly unsatisfactory.

Although the benefits arising from the use of fixed-dose combinations are emphasised in the published guidelines and consensus statements of the Polish Society of Cardiology (recommendation class Ilb, level of evidence B) [22, 27-29] they were prescribed, as mentioned above, in as few as $4 \%$ of the study population. Today, practically all drug combinations that have been well studied in randomised prospective clinical trials are available on the Polish pharmaceutical market in a wide range of doses, which allows appropriate personalisation of treatment [29]. Therefore, to improve the results of hypertension treatment on a countrywide scale, it is important to increase the awareness of the potential hidden in fixed-dose antihypertensive combinations still underused by physicians.

## Limitations of the study

As suggested by the results of some studies, the first BP measurement at a medical visit is usually higher than subsequent measurements, and thus it may lower the rates of adequate BP control in the population [30]. The studies in which the average BP value from the second and third measurements at the same visit was calculated demonstrate much higher levels of hypertension control [14, 30]. Therefore, inclusion of the first BP measurement in the calculations in the CONTROL NT study could lead to an overestimation of the percentage of patients with uncontrolled arterial hypertension. Furthermore, the presence of white coat hypertension could have had a similar impact on the results, but it is a limitation of all registry studies based on office measurements of BP.

On the other hand, the fact that the same values of BP were adopted as the target values in the whole study population, including diabetes patients, may be a cause of underestimation of the percentage of patients with inadequate
control of arterial hypertension. The use of stricter criteria of adequate control of arterial hypertension, assuming lowering of DBP to $<85 \mathrm{mmHg}$ in this patient group [22], would probably have led to a demonstration of even lower BP control in outpatients.

Conducting the CONTROL NT study at medical visits enabled the recognition of inadequate control of BP on the basis of BP measurements performed by healthcare professionals and not only on the basis of interviews and presented results of home measurements, as in some observational registries [16]. On the other hand, this approach to the selection of study subjects prefers patients with a potentially higher prevalence of clinical evident comorbidities, who, having observed disturbing BP values measured at home, seek medical advice. Therefore, the percentage of patients with inadequate control of hypertension in the CONTROL NT study may be lower than in the whole population of patients diagnosed with arterial hypertension.

Furthermore, the screening assumption, according to which, after attaining a number of 10 patients with inadequate BP control, the physician finishes her or his part of recruitment, could also have affected the representativeness of the study population. Moreover, the study does not take into account non-pharmacological therapy, important in antihypertensive treatment, the effect of which on achieving target BP values is emphasised in guidelines published by cardiac societies [22].

Finally, the results of the CONTROL NT study are being published five years after it was conducted. However we believe that the data are still valuable because they indicate the necessary directions for modification of antihypertensive treatment in the Polish population.

## CONCLUSIONS

The percentage of Polish outpatients receiving antihypertensive treatment, who achieve adequate control of arterial hypertension is still unsatisfactory in clinical practice. Observations from the CONTROL NT study define profiles of patients who are expected to present a particular challenge in antihypertensive treatment. These are patients with comorbidities such as diabetes or chronic kidney disease, patients with dyslipidaemia, and those with excess weight (overweight or obese), longer disease and/or treatment duration, or poor treatment compliance. These patients require particular attention when making therapeutic decisions, including meticulous assessment of coexisting risk factors and comorbidities (more frequent follow-up visits), stronger motivation to adhere to treatment, and more frequent use of antihypertensive fixed-dose combinations.

Conflict of interest: CONTROL NT study — collection of data with the support of an educational grant from Servier Polska sp. z o.o.; no other conflicts declared.

## References

1. Lewington S, Clarke R, Qizilbash N, et al. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002; 360(9349): 1903-1913, indexed in Pubmed: 12493255.
2. Danaei G, Finucane MM, Lin JK, et al. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and $5 \cdot 4$ million participants. Lancet. 2011; 377(9765): 568-577, doi: 10.1016/S0140-6736(10)62036-3, indexed in Pubmed: 21295844.
3. Ezzati M, Hoorn SV, Rodgers A, et al. Comparative Risk Assessment Collaborating Group, Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. Lancet. 2002; 360(9343): 1347-1360, doi: 10.1016/S0140-6736(02)11403-6, indexed in Pubmed: 12423980.
4. WHO. Global health risks: mortality and burden of disease attributable to selected major risks. Geneva: World Health Organization. 2009.
5. Zdrojewski T, Bandosz P, Szpakowski P, et al. Ocena wybranych problemów dotyczących rozpowszechnienia i terapii nadciśnienia tętniczego w Polsce na podstawie badania NATPOL PLUS. W: Postępy w nefrologii i nadciśnieniu tętniczym. [The evaluation of selected problems concerning the prevalence and therapy of arterial hypertension in Poland based on the NATPOL PLUS Study] T. 2. 2002. Więcek A, Kokot F (red.). Medycyna Praktyczna, Kraków. 2003.
6. Wyniki badania NATPOL; doniesienia konferencyjne i relacje z konferencji prasowych - dane nieopublikowane w jednej podstawowej publikacji, [The results of the NATPOL Study, conference presentations and press conferences materials available at_www.natpol.pl]
7. Müller-Nordhorn J, Binting S, Roll S, et al. An update on regional variation in cardiovascular mortality within Europe. Eur Heart J. 2008; 29(10): 1316-1326, doi: 10.1093/eurheartj/ehm604, indexed in Pubmed: 18256043.
8. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009; 338: b1665, doi: 10.1136/bmj.b1665, indexed in Pubmed: 19454737.
9. MacMahon S, Alderman M, Lindholm L, et al. Blood-pressure-related disease is a global health priority. J Hypertens. 2008; 26(10): 2071-2072, doi: 10.1097/hjh.0b013e32830f45d9.
10. Gaziano TA. Accurate hypertension diagnosis is key in efficient control. Lancet. 2011; 378(9798): 1199-1200, doi: 10.1016/S0140-6736(11)61299-3, indexed in Pubmed: 21868084.
11. Hajjar I, Kotchen JM, Kotchen TA. Hypertension: trends in prevalence, incidence, and control. Annu Rev Public Health. 2006; 27: 465-490, doi: 10.1146/annurev.publhealth.27.021405.102132, indexed in Pubmed: 16533126.
12. Tykarski A, Posadzy-Małaczyńska A, Wyrzykowski B, et al. Rozpowszechnienie nadciśnienia tętniczego oraz skuteczność jego leczenia u dorosłych mieszkańców naszego kraju. Wyniki programu WOBASZ. [The prevalence of arterial hypertension and treatment efficacy of among the adult residents of our country. The results of the WOBASZ Programme] Kardiol Pol. 2005; 63(supl. 4).
13. Pittrow D, Kirch W, Bramlage P, et al. Patterns of antihypertensive drug utilization in primary care. Eur J Clin Pharmacol. 2004; 60(2): 135-142, doi: 10.1007/s00228-004-0731-6, indexed in Pubmed: 15042351.
14. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. JAMA. 2010; 303(20): 2043-2050, doi: 10.1001/jama.2010.650, indexed in Pubmed: 20501926.
15. Labeit AM, Klotsche J, Pieper L, et al. Changes in the prevalence, treatment and control of hypertension in Germany? A clinical-epidemiological study of 50.000 primary care patients. PLoS One. 2012; 7(12): e52229, doi: 10.1371/journal.pone.0052229, indexed in Pubmed: 23284945.
16. Wolf-Maier K, Cooper RS, Banegas JR, et al. Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. JAMA. 2003; 289(18): 2363-2369, doi: 10.1001/jama.289.18.2363, indexed in Pubmed: 12746359.
17. Brambilla G, Bombelli M, Seravalle G, et al. Blood pressure control and cardiovascular risk profile in hypertensive patients from central and eastern European countries: results of the BP-CARE study. Eur Heart J. 2011; 32(2): 218-225, doi: 10.1093/eurheartj/ehq394, indexed in Pubmed: 21047877.
18. Bromfield SG, Bowling CB, Tanner RM, et al. Trends in hypertension prevalence, awareness, treatment, and control among US adults 80 years and older, 1988-2010. J Clin Hypertens (Greenwich). 2014; 16(4): 270-276, doi: 10.1111/jch.12281, indexed in Pubmed: 24621268.
19. McAlister FA, Wilkins K, Joffres M, et al. Changes in the rates of awareness, treatment and control of hypertension in Canada over the past two decades. CMAJ. 2011; 183(9): 1007-1013, doi: 10.1503/cmaj.101767, indexed in Pubmed: 21576297.
20. Carrington MJ, Jennings GL, Stewart S. Pattern of blood pressure in Australian adults: results from a national blood pressure screening day of 13,825 adults. Int J Cardiol. 2010; 145(3): 461-467, doi: 10.1016/j.ijcard.2009.06.003, indexed in Pubmed: 19573941.
21. Abu-Saad K, Chetrit A, Eilat-Adar S, et al. Blood pressure level and hypertension awareness and control differ by marital status, sex, and ethnicity: a population-based study. Am J Hypertens. 2014; 27(12): 1511-1520, doi: 10.1093/ajh/hpu081, indexed in Pubmed: 24795402.
22. Grupa Robocza Europejskiego Towarzystwa Nadciśnienia Tętniczego (ESH) i Europejskiego Towarzystwa Kardiologicznego (ESC) do spraw postępowania w nadciśnieniu tętniczym. Wytyczne ESH/ESC dotyczące postępowania w nadciśnieniu tętniczym w 2013 roku. [2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European

Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)]. Kardiol Pol. 2013; 71(supl. III): 27-118.
23. Fine LJ, Cutler JA. Hypertension and the treating physician: understanding and reducing therapeutic inertia. Hypertension. 2006; 47(3): 319-320, doi: 10.1161/01.HYP.0000200692.23410. c9, indexed in Pubmed: 16432049.
24. Redon J, Erdine S, Böhm M, et al. SHARE Steering Committee. Physician attitudes to blood pressure control: findings from the Supporting Hypertension Awareness and Research Europe-wide survey.J Hypertens. 2011; 29(8): 1633-1640, doi: 10.1097/HJH.0b013e328348c934, indexed in Pubmed: 21720274.
25. Gupta AK, Arshad S, Poulter NR. Compliance, safety, and effectiveness of fixed-dose combinations of antihypertensive agents: a meta-analysis. Hypertension. 2010; 55(2): 399-407, doi: 10.1161/HYPERTENSIONAHA.109.139816, indexed in Pubmed: 20026768.
26. Feldman RD, Zou GY, Vandervoort MK, et al. A simplified approach to the treatment of uncomplicated hypertension: a cluster randomized, controlled trial. Hypertension. 2009; 53(4): 646-653, doi: 10.1161/HYPERTENSIONAHA.108.123455, indexed in Pubmed: 19237683.
27. Widecka K, Grodzicki T, Narkiewicz K, et al. Zalecenia dotyczące postępowania w nadciśnieniu tętniczym 2011. Wytyczne Polskiego Towarzystwa Nadciśnienia Tętniczego. [Polish Society of Hypertension Guidelines on the management of arterial hypertension 2011] Nadciśnienie Tętnicze. 2011; 4: 211-235.
28. Gaciong Z, Narkiewicz K, Tykarski A, et al. Miejsce gotowych połączeń lekowych w terapii nadciśnienia tętniczego - stanowisko ekspertów. [The role of fixed dose combinations in the treatment of arterial hypertension - expert consensus.] Nadciśnienie Tętnicze. 2009; 13: 363-370.
29. Wożakowska-Kapłon B, Filipiak K, Czarnecka D, et al. Miejsce leków złożonych w terapii nadciśnienia tętniczego - aktualne problemy w Polsce Stanowisko Ekspertów Polskiego Towarzystwa Nadciśnienia Tętniczego i Sekcji Farmakoterapii Sercowo-Naczyniowej Polskiego Towarzystwa Kardiologicznego. [Combination therapy in the management of hypertension - current problem in Poland. Expert consensus statement of the Polish Society of Hypertension and Polish Cardiac Society Working Group on Cardiovascular Pharmacotherapy]. Nadciśnienie Tętnicze. 2013; 71(4): 3-9.
30. Handler J, Zhao Y, Egan BM. Impact of the number of blood pressure measurements on blood pressure classification in US adults: NHANES 1999-2008. J Clin Hypertens (Greenwich). 2012; 14(11): 751-759, doi: 10.1111/jch.12009, indexed in Pubmed: 23126346.

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