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ANALYSIS OF 17 FACTORS POTENTIALLY RELATED TO HYPERTENSION CONTROL IN THE SIBERIAN URBAN SAMPLE

<i>Aim</i>	To identify non-pharmacological factors associated with ineffective blood pressure (BP) control among individuals with arterial hypertension (AH) in a Siberian urban population sample.
<i>Material and methods</i>	A considerable proportion of individuals with AH does not achieve BP goals. BP control is influenced by a number of non-drug determinants, including non-modifiable and multiple modifiable factors. In a population sample (men/women, 55–84 years old, n=3,898, 2015–2018, HAPIEE project, Novosibirsk), a category of individuals with AH receiving antihypertensive therapy (AHT) (n=2,449) was selected and two groups with adequate and inadequate BP control (ABPC and IABPC, respectively) were identified. We evaluated associations of IABPC and a series of potentially related factors, including gender, age, AH duration, type 2 diabetes mellitus, cardiovascular diseases (CVD), anthropometric and biochemical parameters, behavioral (smoking, alcohol consumption, physical activity (PA)) and socioeconomic factors (education, marital status, economic activity, material deprivation).
<i>Results</i>	In a sample of 55–84-year-old individuals with AH taking AHT, ABPC was 30.7%. In the multivariate logistic model, IABPC was directly associated with male gender (odds ratio (OR) 1.72; 95% confidence interval (CI) 1.28–2.31), AH duration longer than 10 years (OR 2.55; 95% CI 2.07–3.14), alcohol consumption 1–3 times a month (OR 1.36; 95% CI 1.02–1.81) and 1–4 times a week (OR 1.91; 95% CI 1.26–2.89) and was inversely associated with moderate PA (OR 0.78; 95% CI 0.62–0.98). In men, IABPC was additionally inversely associated with history of CVD (OR 0.62; 95% CI 0.42–0.92). In women, IABPC was additionally associated with economically inactive status (OR 1.39; 95% CI 1.03–1.86) and inversely associated with smoking (OR 0.51; 95% CI 0.29–0.87).
<i>Conclusion</i>	In a Siberian population sample of 55–84-year-olds, one third of individuals with AH receiving AHT adequately controlled their BP. Inadequate BP control was directly associated with male gender, long history of AH, frequent alcohol consumption, and economically inactive status (in women), and was inversely associated with moderate PA, CVD (in men), and smoking (in women). Attention to non-pharmacological determinants may help optimize BP control.
<i>Keywords</i>	Arterial hypertension; antihypertensive therapy; inadequate blood pressure control; non-pharmacological determinants of inadequate blood pressure control.
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Introduction

Arterial hypertension (AH) is the most common risk factor (RF) for the development of cardiovascular diseases (CVDs) and the most common cause of death worldwide [1–3]. Current multicenter studies demonstrate a stable global prevalence of AH [4], but the aging of the population is associated with an increase in the number of people with AH, that increased by 41% in Europe and America and by 141% in Southeast Asia and the Pacific region from 1999 to 2019 [5]. Epidemiological studies have shown a continuous relationship between blood pressure (BP) and the risk of CVD and cardiovascular death [1, 2]; randomized clinical trials (RCTs) have demonstrated the effect of antihyperten-

sive therapy (AHT) on reducing the risk of cardiovascular complications [6].

Despite current guidelines (ESC 2024 [2], ACC/AHA 2017 [7], RSC, 2024 [8]) and a wide choice of AHT, a large number of patients with AH do not achieve target BP values [4, 9–11]. According to current estimates by the World Health Organization, 54% of adults with AH worldwide have a confirmed diagnosis, 42% take AHT, and only 21% control their BP [5]; insufficient BP control represents a *locus minoris resistentiae* in the fight against AH.

Beyond the effects of specialized therapy (with appropriate regimen and dosage), a number of non-pharmacological factors influence BP control, including non-modi-

fiable factors (genetics, gender, age, disease duration) and modifiable factors (obesity, nutrition, behavioral and socioeconomic factors).

Given the high prevalence of AH in the Russian Federation [12–14] and the interpopulation and interregional heterogeneity of BP control, analysis of a wide range of potential non-pharmacological determinants of BP control in various population samples is relevant.

Aim

To identify non-pharmacological factors associated with inadequate BP control among patients with AH in a Siberian urban population sample.

Material and methods

The study was performed in participants of the 3rd screening of a population-based cohort (Novosibirsk, HAPIEE project, 2015–2018) in a sample of AH patients receiving AHT (n=2476, age 55–84 years). This study was approved by the Ethics Committee of the Research Institute of Internal and Preventive Medicine (Protocol #33 dated June 20, 2024). All participants signed informed consent to participate in the study.

The study had a cross-sectional design. The protocol included an epidemiological assessment of CVD and their RFs using standardized questionnaires and measurements [15], including AH history, use of AHT, AH duration, information about family history of AH, history of diabetes mellitus (DM), CVDs and other chronic diseases, menopausal status, self-rated health, behavioral RFs for CVD development (smoking, alcohol consumption, physical activity (PA) level), sociodemographic characteristics, and objective measurements (BP, anthropometry, electrocardiography, blood lipid and glucose levels).

Blood pressure (BP) was measured three times (Omron M-5) and mean values were calculated. Using the 2024 European Society of Cardiology guidelines [2], the presence of AH was defined by epidemiological criteria of systolic BP (SBP) or diastolic BP (DBP) $\geq 140/90$ mm Hg and/or use of AHT during the recent 2 weeks. Regular use of AHT was assessed for 12 months without regard to the dosage of the medicine coded according to the Anatomical Therapeutic Chemical Classification System (ATC) [16]. Previously we have described the AHT profile in an AH population [17].

This analysis included AH patients receiving AHT.

Inclusion criteria: the 3rd screening respondents, men and women aged 55–84 years; presence of AH according to epidemiological criteria; use of AHT during the recent 2 weeks; and signed informed consent for the study.

Exclusion criteria: age under 55 or over 85 years; absence of AH according to epidemiological criteria; no AHT

for established AH; incomplete data on BP measurements and/or AHT use; and absence of signed informed consent for the study.

The analysis group was divided into two categories:

- 1) adequate AH control (AHC), SBP <140 mm Hg and DBP <90 mm Hg on AHT during the previous 2 weeks;
- 2) inadequate AH control (IAHC), SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg on AHT during the previous 2 weeks.

In the study sample, 3,138 (80.9%) patients had AH. The analysis included 2,476 AH patients receiving AHT. Later, we excluded 27 patients with technically incomplete BP measurements, which resulted in a total of 2,449 participants with AHC or IAHC.

Two categories of AH duration were identified: ≥ 10 years and <10 years, based on three screenings. Family history of AH was assessed based on AH in first-degree relatives. Women in menopause and with preserved menstrual cycles were grouped for analysis.

Current smoking status was defined as smoking at least one cigarette per day. Alcohol consumption was assessed with a graded frequency questionnaire [18], and five groups were formed: abstainers, those who drank less than once a month, 1–3 times a month, 1–4 times a week, and 5 or more times a week. Leisure time PA was assessed using a standard questionnaire. The mean number of hours per week (h/wk) spent performing physical work or sports was determined. Three groups were identified based on the tertiles of the distribution of h/wk of leisure time PA for men and women [19].

Marital status was categorized as “married” (living together) or “single.” Educational attainment was categorized as higher, secondary, vocational, and primary. Economic activity was dichotomized as “economically active” (EA), including working pensioners, and “economically inactive” (EIA) participants.

The level of material deprivation was assessed by responses to three questions: how often does the respondent experience financial difficulties when purchasing food, buying clothing, and paying rent and utility bills? Responses were coded from 0 to 4 points, a summary material deprivation scale was calculated, and classified into four groups: 0 points (no material deprivation), 1–3 points, 4–8 points, and 9–12 points, according to the categorization in the HAPIEE project [20].

Height, waist circumference (WC), and hip circumference (HC) were measured to the nearest 0.1 cm; body weight was measured to the nearest 0.1 kg. The WC/HC index and body mass index (BMI, kg/m²) were calculated. Obesity was defined as a BMI ≥ 30 kg/m² [21], and abdominal obesity (AO) was defined as a WC ≥ 94 cm (men) and ≥ 80 cm (women) [22].

Table 1 (Beginning). Characteristics of study groups receiving AHT, with adequate and inadequate BP control

Factor	n	Adequate BP control	Inadequate BP control	p
Evaluated AH patients receiving AHT, n	2476	761	1715	–
Patients included in analysis, n (%)	2449	753 (30.7)	1696 (69.3)	–
Sex: male/female, n (%)	2449	174 (23.7)/560 (76.3)	579 (33.8) / 1136 (66.2)	<0.001
Age, years	2449	69.5±6.8	70.3±6.8	0.012
SBP, mm Hg	2448	127.3±9.0	159.2±16.3	<0.001
DBP, mm Hg	2448	75.4±7.4	88.4±10.7	<0.001
HR, beats/min	2443	70.1±10.1	72.3±11.9	<0.001
BMI, kg/m ²	2439	30.4±5.57	30.7±5.59	0.227
Obesity, BMI >30 kg/m ² , n (%)	1222	369 (50.6)	853 (49.9)	0.740
WC /HC, conv. units	2434	0.89±0.08	0.91±0.08	<0.001
AO (WC ≥94 cm for men; ≥80 cm for women), n (%)	2078	621 (85.5)	1457 (85.3)	0.857
TC, mmol/l	2442	5.4±1.2	5.5±1.2	0.203
LDL C, mmol/l	2442	3.4±1.1	3.5±1.1	0.372
HDL C, mmol/l	2442	1.3±0.4	1.3±0.4	0.630
TG, mmol/l	2442	1.5±0.98	1.6±0.9	0.350
FPG, mmol/l	2442	6.4±1.8	6.6±1.99	0.029
GGTP, mmol/l	2442	33.2±31.9	35.9±34.1	0.064
IHD, n (%)	2449	150 (20.4)	320 (18.7)	0.306
Type 2 DM, n (%)	2448	178 (24.3)	434 (25.3)	0.575
Treatment for type 2 DM (among patients with type 2 DM), n (%)	2447	133 (18.1)	270 (15.8)	0.144
CVD, n (%)	2449	200 (27.2)	427 (24.9)	0.222
AH duration, n (%)	2448			
≥10 years	1890	476 (64.9)	1414 (82.5)	<0.001
<10 years	558	258 (35.1)	300 (17.5)	
Family history of AH, n (%)	1474	432 (59.0)	1042 (60.8)	0.402
Menopause, n (%)	1695	557 (99.5)	1120 (98.7)	0.241
Menopause age, years	1663	49.1±4.7	49.3±4.6	0.389
Menopause duration, years	1663	20.3±8.6	21.1±8.2	0.070
HRT, n (%)	1695	3 (0.5)	11 (1.0)	0.241

Serum total cholesterol (TC), triglycerides, high-density lipoprotein cholesterol, and glucose concentrations were measured fasting (KoneLab 300i, USA; enzymatic method); low-density lipoprotein cholesterol was calculated according to Friedwald. Fasting serum glucose levels were converted to fasting plasma glucose (FPG) (EASD, 2007).

The composite category of CVD was established for ischemic heart disease (IHD) (Rose exertion angina [23], ischemic changes on the electrocardiogram or myocardial infarction, acute coronary syndrome, history of coronary revascularization) or stroke/transient ischemic attack, confirmed by hospitalization data. The presence of DM was established if there was an indication of DM in history with treatment and/or an FPG level ≥7 mmol/l [24].

Statistical analysis was performed using SPSS v.13.0; v.23.0. The results are presented as mean ± standard deviation (SD) or as absolute numbers (frequency of variable), n (%). Comparison of frequencies was performed using the Pearson *chi-square* test. Quantitative comparisons of two groups were performed using the Student's *t*-test for

normal distribution. ANOVA with Bonferroni correction was used for comparison of more than two groups. For non-normal distributions, data transformed by natural logarithms were compared. Associations of the studied factors with IAHC were analyzed in single- and multivariate logistic regression models.

Factors were tested as dichotomous or categorical variables (3 or more categories). Model 1 was standardized for gender and age. Model 2 included gender, age, smoking, obesity, AO, presence of CVD, type 2 DM, AH duration, family history of AH, TC concentration, PA, frequency of alcohol consumption (FAC), and self-rated health. Model 3 included the listed covariates, as well as educational attainment, marital status, EA, and material deprivation. Differences were considered statistically significant at *p*<0.05.

Results

In the sample of AH patients aged 55–84 years taking AHT, 30.7% achieved target BP values. The main characteristics of the AHC and IAHC groups are presented in Table 1.

Table 1 (Ending). Characteristics of study groups receiving AHT, with adequate and inadequate BP control

Factor	n	Adequate BP control	Inadequate BP control	p
Smoking, n (%)	2442			
• Smokers	229	72 (9.8)	157 (9.2)	0.194
• Ex-smokers	411	108 (14.8)	303 (17.7)	
• Non-smokers	1802	552 (75.4)	1250 (73.1)	
FAC, n (%)	2442			
• >5 times per week	22	3 (0.4)	19 (1.1)	<0.001
• 1–4 times per week	221	40 (5.5)	181 (10.6)	
• 1–3 times per month	486	127 (17.3)	359 (21.0)	
• < 1 time per month	1059	348 (47.5)	711 (41.6)	
• alcohol abstainers	654	214 (29.2)	440 (25.7)	
PA (leisure time), h/week	2439	11.7±6.5	12.2±6.5	0.138
PA (terciles), n (%)	2439			
• low (T1)	904	300 (41.2)	604 (35.3)	0.023
• moderate (T2)	795	220 (30.2)	575 (33.6)	
• high (T3)	740	209 (28.7)	531 (31.1)	
Education, n (%)	2449			
• primary	167	53 (7.2)	114 (6.6)	0.476
• vocational	702	223 (30.4)	479 (27.9)	
• secondary	804	227 (30.9)	577 (33.6)	
• higher	776	231 (31.5)	545 (31.8)	
Marital status, n (%)	2448			
• Single	1073	357 (48.7)	716 (41.7)	0.001
• Married	1375	376 (51.3)	999 (58.3)	
Economic activity, n (%)	2436			
• EA (including employed pensioners)	557	182 (25)	375 (22)	0.107
• EIA	1879	547 (75)	1332 (78)	
Material deprivation (0–12 score scale), n (%)	2436			
Score 0	1322	376 (51.6)	946 (55.4)	0.021
Score 1–2	627	182 (25)	445 (26.1)	
Score 3–5	464	160 (21.9)	304 (17.8)	
Score 6–12	23	11 (1.5)	12 (0.7)	
Self-rated health, n (%)	2449			
• Very good / good / fair	2034	602 (82)	1432 (83.5)	0.370
• Very poor / poor	415	132 (18)	283 (16.5)	

In Table 1 and Table 2: the results are presented as mean ± standard deviation (SD), unless otherwise stated. AH, arterial hypertension; AHT, antihypertensive therapy; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; BMI, body mass index; WC/HC, waist circumference-to-hip ratio; AO, abdominal obesity; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; FPG, fasting plasma glucose; GGT, gamma-glutamyl transferase; IHD, ischemic heart disease; DM, diabetes mellitus; CVDs, cardiovascular diseases; HRT, hormone replacement therapy; FAC, frequency of alcohol consumption; PA, physical activity; EA, economically active; EIA, economically inactive. Bold indicates p-values for statistically significant differences.

The proportion of women in the IAHC group was less than in the AHC group (66.2% vs. 76.3%). SBP and DBP, heart rate (HR), WC/HC, AH duration, and FPG were higher in the IAHC group than in the AHC group. The FAC was significantly higher in the IAHC group, and conversely, the AHC group contained more individuals who did not consume alcohol. There were fewer patients with low PA in the IAHC group than in the AHC group (35% vs. 41%). Married individuals had poorer BP control compared to single individuals. The IAHC group had fewer people who frequently experienced financial difficulties.

The groups with IAHC and AHC did not differ significantly in age, BMI, incidence of obesity, AO, blood lipid composition, presence of IHD, CVDs and type 2 DM, menopausal status in women, smoking, family history of AH, self-rated health, level of education, and EA.

At the second stage, we assessed the associations of IAHC with potential determinants (Table 2). In Model 1 controlling for age and gender in the pooled analysis, we found direct associations of IAHC with age, male gender, family history of AH, AH duration of more than 10 years, and FAC. An inverse association was found

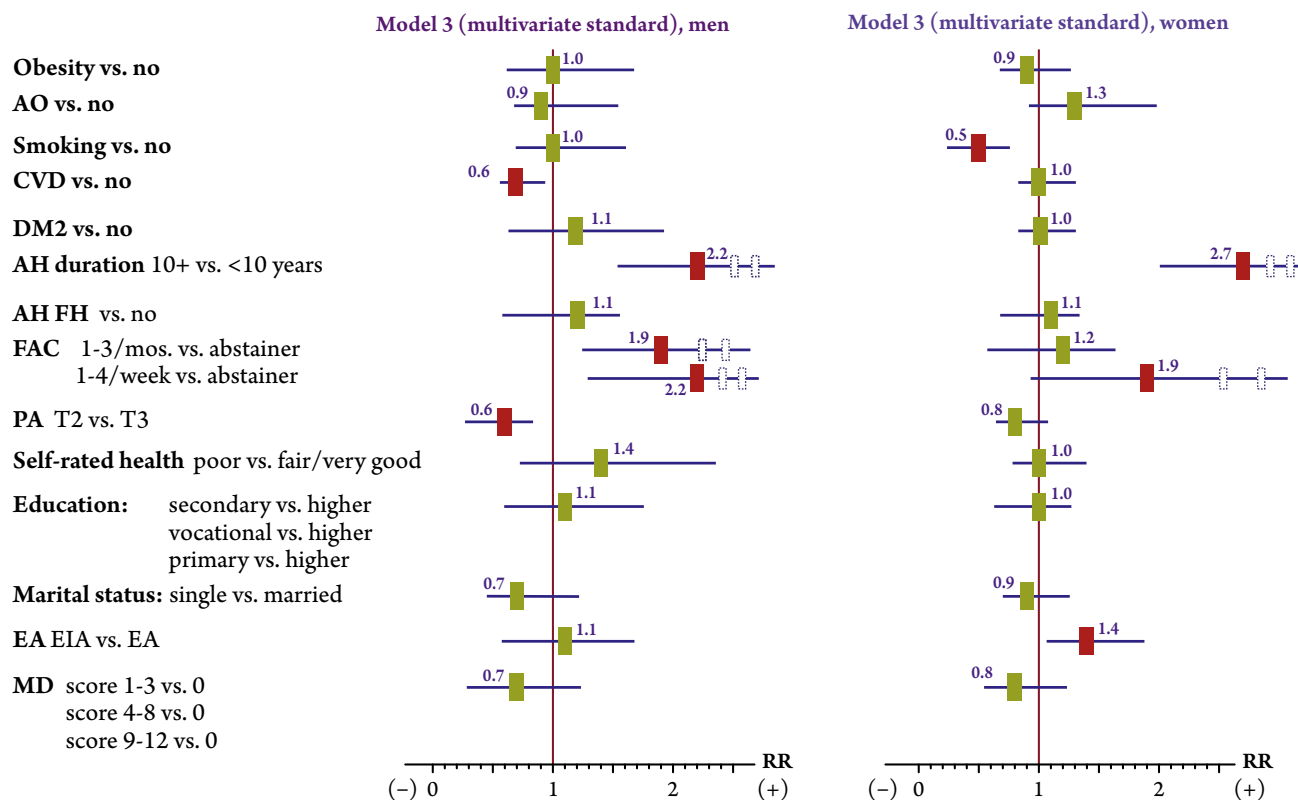
Table 2. Evaluation of associations of non-pharmacological factors with inadequate hypertension control in a population-based sample combined by sex (logistic regression)

Factor	n	Model 1, OR (95% CI); p	Model 2, OR (95% CI); p	Model 3, OR (95% CI); p
Age, for one year	2449	1.018 (1.005–1.031); 0.008	1.013 (0.999–1.028); 0.077	1.010 (0.994–1.027); 0.221
Women	1696	1.0	1.0	1.0
Men	753	1.656 (1.359–2.018); <0.001	1.752 (1.331–2.306); <0.001	1.721 (1.283–2.308); <0.001
Obesity (BMI ≥ 30 kg/m ²): no	1217	1.0	1.0	1.0
Obesity (BMI ≥ 30 kg/m ²): yes	1222	1.086 (0.908–1.298); 0.367	0.942 (0.770–1.152); 0.560	0.942 (0.768–1.154); 0.564
AO (WC ≥ 94 cm for men; >80 cm for women): no	357	1.0	1.0	1.0
AO (WC ≥ 94 cm for men; >80 cm for women): yes	2078	1.246 (0.959–1.619); 0.100	1.151 (0.859–1.542); 0.348	1.136 (0.846–1.526); 0.398
CVD: no	1822	1.0	1.0	1.0
CVD: yes	627	0.803 (0.656–0.981); 0.032	0.822 (0.664–1.017); 0.071	0.815 (0.658–1.010); 0.061
Type 2 DM: no	1836	1.0	1.0	1.0
Type 2 DM: yes	612	1.052 (0.859–1.288); 0.623	0.992 (0.799–1.232); 0.944	0.984 (0.791–1.224); 0.883
Smoking: non-smokers	1802	1.0	1.0	1.0
Smoking: ex-smokers	411	0.860 (0.644–1.148); 0.305	0.858 (0.633–1.161); 0.321	0.856 (0.631–1.161); 0.317
Smoking: smokers	229	0.729 (0.521–1.020); 0.065	0.716 (0.503–1.018); 0.063	0.705 (0.494–1.007); 0.054
AH duration: <10 years	558	1.0	1.0	1.0
AH duration: ≥ 10 years	1890	2.538 (2.077–3.100); <0.001	2.576 (2.093–3.171); <0.001	2.550 (2.069–3.144); <0.001
Family history of AH: no	971	1.0	1.0	1.0
Family history of AH: yes	1474	1.212 (1.010–1.454); 0.039	1.098 (0.907–1.328); 0.338	1.095 (0.903–1.329); 0.355
FAC: alcohol abstainer	654	1.0	1.0	1.0
FAC: less than 1 time per month	1059	1.053 (0.852–1.301); 0.634	1.011 (0.811–1.261) 0.921	1.004 (0.803–1.255); 0.971
FAC: 1–3 times per month	486	1.368 (1.044–1.792); 0.023	1.335 (1.005–1.774); 0.046	1.358 (1.018–1.812); 0.038
FAC: 1–4 times per week	221	2.017 (1.354–3.004); 0.001	1.911 (1.267–2.883); 0.002	1.912 (1.264–2.893); 0.002
FAC: >5 times per week	22	2.634 (0.762–9.106); 0.126	2.487 (0.693–8.921); 0.162	2.430 (0.675–8.748); 0.174
PA (h/week: T3)	740	1.0	1.0	1.0
PA (h/week: T2)	795	0.755 (0.608–0.936); 0.010	0.755 (0.602–0.946); 0.015	0.776 (0.617–0.975); 0.030
PA (h/week: T1)	904	1.016 (0.811–1.273); 0.891	0.996 (0.788–1.259); 0.974	1.005 (0.794–1.272); 0.970
Self-rated health				
• fair/good/very good	2034	1.0	1.0	1.0
• poor/very poor	415	0.889 (0.705–1.122); 0.322	1.019 (0.795–1.306); 0.879	1.026 (0.798–1.317); 0.844
Education: higher	776	1.0	(–)	1.0
Education: secondary	804	0.900 (0.622–1.301); 0.574	(–)	0.943 (0.637–1.396); 0.770
Education: vocational	702	0.994 (0.794–1.245); 0.959	(–)	1.009 (0.797–1.278); 0.937
Education: primary	167	1.148 (0.921–1.430); 0.219	(–)	1.185 (0.938–1.498); 0.154
Marital status: married	1375	1.0	(–)	1.0
Marital status: single	1073	0.877 (0.727–1.057); 0.169	(–)	0.887 (0.724–1.087); 0.248
EA	557	1.0	(–)	1.0
EIA	1879	1.189 (0.947–1.494); 0.136	(–)	1.250 (0.983–1.591); 0.069
Material deprivation: score 0	1322	1.0	(–)	1.0
Material deprivation: score 1–3	627	1.052 (0.850–1.302); 0.641	(–)	1.043 (0.837–1.302); 0.706
Material deprivation: score 4–8	464	0.819 (0.652–1.030); 0.088	(–)	0.833 (0.653–1.062); 0.140
Material deprivation: score 9–12	23	0.432 (0.188–0.995); 0.049	(–)	0.601 (0.253–1.428); 0.248

OR, odds ratio; CI, confidence interval.

Model 1, controlling for gender and age; Model 2 – Model 1 (+) controlling for smoking, obesity, AO, CVD, type 2 DM, AH duration, family history of AH, TC, PA, FAC, and self-rated health; Model 3 – Model 2 (+) controlling for education, marital status, EA, and material deprivation; ORs for significant differences are shown in bold.

Figure 1. Associations of non-pharmacological factors with inadequate BP control in AH patients receiving antihypertensive therapy (forest plot of logistic regression results)



Model 3: controlling for age, smoking, obesity, AO, CVD, type 2 DM, AH duration, family history of AH, TC, PA, FAC, self-rated health, education, marital status, EA, and material deprivation.

AH, arterial hypertension; AHT, antihypertensive therapy; AO, abdominal obesity; AH FH, family history of AH; CVD, cardiovascular disease; T2DM, type 2 diabetes mellitus; FAC, frequency of alcohol consumption; PA, physical activity; EA, economically active; ENA, economically inactive; MD, material deprivation.

with the presence of CVD, and moderate *vs.* low or high PA levels. The level of material deprivation was marginally associated with IAHC ($p=0.049$). In Model 3 (controlling for all factors), direct associations of IAHC with AH duration of more than 10 years and frequent alcohol consumption, and a U-shaped association with PA level persisted.

In grouping by gender (Fig. 1), the odds of IAHC in men doubled with an AH duration of more than 10 years ($p<0.001$), consistently increased 1.9 times with FAC 1–3 times a month ($p=0.021$), and 2.2 times with FAC 1–4 times a week ($p=0.011$). The odds of IAHC decreased by 40% in men with CVD ($p=0.016$) and moderate *vs.* low PA ($p=0.034$), regardless of other factors. Women had a direct association of IAHC with age ($p=0.003$), presence of AO ($p=0.044$), and single marital status ($p=0.046$), but the significance of the contribution of these variables was leveled after adjusting for other factors. In women, long-term AH increased the odds of IAHC by 2.7 times ($p<0.001$), a FAC of several times a week by 2 times ($p=0.048$), and the EIA status by almost 1.5 times ($p=0.031$), while IAHC was inversely associated with smoking ($p=0.014$), regardless of other factors.

Discussion

In a Siberian population sample of 55–84-year-olds examined from 2015 to 2018, 30% of individuals with AH receiving AHT adequately controlled their BP. IAHC was positively associated with male gender, long-term AH, FAC, and EIA status (in women) and inversely associated with moderate PA, presence of CVD (in men), and smoking (in women).

In the ESSE-RF study ($n=5,563/9,737$; 25–64 years; 2012–2013), high HR, general obesity, and high TG and FPG levels were positively associated with ineffective AH treatment in men, and only with HR and obesity in women [13]. In ESSE-RF2 ($n=3,000/3,714$; 2017), the odds of IAHC in men increased with AO (by 1.6 times), IHD (by 2.3 times), and in women with older age, rural residence (by 2 times), and general obesity or AO (by 1.5 times) [14].

Our results partially differ from the data of the ESSE-RF2 and ESSE-RF3 studies, but are comparable in a number of factors. Thus, the direct association of IAHC with male gender and increasing age (without control for other factors) is similar to the data obtained in the ESSE-RF2 and ESSE-RF3 studies [12, 14]. Most studies reveal a neg-

ative contribution of male gender to AH control, but conflicting data also available. For example, in a Swedish study ($n=229,864$), women younger than 60 years had better BP control than men; after 60 years of age, the situation reversed [25].

Our inverse association of IAHC with the presence of CVD in men differs from that in the ESSE-RF2 study, which demonstrated a direct association between ineffective AH treatment and IHD in men. Our result is comparable with the results of the Tromsø Study, in which BP control in men after myocardial infarction was better due to regular RF monitoring [26]. Our data on the association of IAHC with obesity are partially consistent with the results of the ESSE-RF and ESSE-RF2 studies, since we found an association of AO with IAHC only in women, taking into account gender and age; this association decreased to non-significant in the multivariate analysis. This may be explained by the older age of our sample, while the association of AH with obesity is more pronounced in young people [27].

In the MUCH study (2016; $n=2514$; 60.2 ± 10 years; Sarajevo) [28], the predictors of IAHC were male gender, long-term AH, obesity, smoking, and DM, which is partly consistent with our data. The effect of long-term AH on IAHC may be associated with the pronounced initial degree of AH, comorbidity [27], target organ damage, and the development of complications [29].

In our sample, IAHC was inversely associated with a moderate level of PA, and the relationship was U-shaped. Many population-based studies and RCTs have confirmed the beneficial effect of regular physical exercise on BP. A meta-analysis by L. Pescatello et al. (2019) [30] (15 RCTs, almost 500 thousand participants) showed that regular aerobic exercise resulted in a decrease in SBP (by 5–17 mm Hg) and DBP (by 2–10 mm Hg), and that an inverse dose-response relationship existed between PA and the development of AH in adults with normal BP [30]. Similar data were obtained in a meta-analysis of 37 RCTs [31] and for the elderly [32]. Another review showed that physical exercise reduced ambulatory BP [33]. Early epidemiological studies (INTERSALT, Framingham Study, CARDIA, Nurses' Health Study) found lower BP values and risk of AH in individuals with regular free-time PA, which reduced the risk of AH by 20–30% in a time- and dose-dependent manner [34].

The mechanisms of the relationship between PA and BP control are multifactorial, including improvement of endothelial function, vasodilation, and regulation of the autonomic nervous system [30]. Contrastingly, physical inactivity is associated with insulin resistance, sympathicotonia, and decreased nitric oxide production [34]. In a systematic review (26 studies, $n=11,600$, Africa), old-

er age, AH duration, lack of adherence to PA, chewing tea leaves, and coffee consumption were independent predictors of IAHC [35].

We did not find a direct association between smoking and AH control, which is consistent with the ESSE-RF data [13]. The association between smoking and AH is assessed controversially: a number of studies have shown similar or lower BP values and the risk of developing AH in smokers compared to non-smokers [36–39], while other studies have found associations between smoking and the risk of developing AH [40]. A Mendelian randomization study (CARTA Consortium; $n=141,317$) revealed an association between smoking intensity and HR, but did not find an association with SBP, DBP, or AH [39]. The acute effect of nicotine can cause sympathicotonia and endothelial dysfunction; smoking AH patients are susceptible to the development of severe forms of AH, while the chronic effect of tobacco on BP is less clear or small [40–42]. The heterogeneity of the results is related with the interaction of smoking, alcohol consumption, and body weight in the complex effect on BP [38, 40, 41]. In China, the 10-year risk of developing AH was 1.5 times higher in heavy smokers than in non-smokers, but when smoking and alcohol consumption interacted, the risk of developing AH was 2.5 higher [40]. A study from the China Kadoorie Biobank ($n=512,891$; 30–79 years) revealed a negative association between smoking and BP, but interaction with alcohol consumption significantly increased BP in regular smokers who consumed alcohol [38]. The effect of smoking cessation on reducing BP has been described. That effect was associated with restoration of endothelial function and a decrease in HR, including due to a simultaneous reduction in alcohol consumption [42].

The association of alcohol consumption with IAHC in our sample was consistent with the summarized data on the relationship between alcohol consumption and AH/BP [43, 44]. A meta-analysis by Briasoulis et al. (2012) [43] (16 studies; $n>200,000$; 4–20 years of follow-up) found an association between moderate alcohol consumption (>30 g/day, ethanol) and the risk of AH in men and a J-shaped relationship in women. A later meta-analysis (20 studies; $n=361,254$) revealed a consistent increase in the risk of AH with an increase in alcohol consumption from 1 (12 g) to 5 alcohol servings per day in men and an increase in the risk of AH starting from 2 servings per day in women [44]. Alcohol has a short-term vasodilatory effect, followed by vasoconstriction. The effects of chronic heavy alcohol consumption include activation of the sympathetic and renin-angiotensin-aldosterone systems, increased HR, peripheral resistance, arterial stiffness, endothelial dysfunction, and an association with metabolic syndrome [45].

With regard to BP control, a meta-analysis (n=2,865) showed a dose-dependent effect: among those consuming >2 alcohol servings per day, a 50% reduction in alcohol consumption was associated with a decrease in SBP/DBP by 5.50/3.97 mm Hg [44]. The interaction between alcohol consumption and AHT is also important, resulting in a decrease in the effectiveness of beta-blockers, angiotensin-converting enzyme inhibitors, and diuretics [44, 46].

We found an association between the EIA status and IAHC in women and found no statistically significant associations for the contribution of education, marital status, and material deprivation. In the EIA group of women, the likelihood of IAHC was 40% higher than among employed women, which was confirmed in several studies [47–49], but contrary evidence is also available [50, 51].

The EIA status is heterogeneous. In the unemployed, stress due to job loss and decreased access to healthcare resources can contribute to the AH aggravation [47, 48]. Upon retirement, patients may experience a decline in health indicators, including BP control related with a decrease in income, social capital, PA (previously associated with the job), unhealthy diet, as well as a decrease in cognitive potential and the risk of depression [48, 49]. At the same time, several studies have shown an improvement in healthy behavior due to a decrease in work stress, an increase in sleep duration, and PA in leisure time [48, 50, 51].

The Chinese CHS (n=84,696; 2012–2015) study showed an increase in SBP and pulse BP after retirement in men, while in women there was a tendency for BP to decrease [48], and a greater increase in BP with low education. Men are more susceptible to the effects of changes in social status and income upon retirement than women, and in women, the effect of the “double” work and household load decreases in retirement; low education is accompanied by an unhealthy lifestyle and accumulation of RFs [48, 51].

In our sample, the odds index of IAHC increased slightly with decreasing education level, but not statistically significantly, which differs somewhat from the associations with control or BP level in the ESSE-RF study and a multipopulation analysis of 8 databases [13, 52]. For example, according to the ESSE-RF study, low education was associated with ineffective treatment of AH in men taking AHT, but this association did not reach statistical significance in women [13]. Apparently, the lack of a reliable association with education is due to the older age of the sample (55–84 years in Novosibirsk), with a greater contribution of education to AH control in young and middle-aged individuals (25–64 years in the ESSE-RF study).

Apparently, a complex of social factors (income, education, occupation, economic status) [52], united by the concept of socioeconomic status [53], contributes to the BP control. An inverse relationship between socioeconomic status and the incidence of AH has been reliably demonstrated; however, a recent review indicated that socioeconomic status does not play a key role in BP control in high-income countries, in contrast to low- and middle-income countries [54].

Study limitations and strengths

In the population sample, we were unable to account for medication regimens and dosages, which precludes assessing the adequacy of therapy in the AHC and IAHC groups. However, this approach is typical for epidemiological studies. In both groups, approximately the same proportion of patients (90%) used AHTs that had undergone blinded validation by ATC, and this limitation could not be the source of differences in treatment adequacy between the groups. We studied a sample of 55–84-year-old individuals, which limits the extrapolation of the results to younger groups. At the same time, given the increasing incidence of AH in older age, our data reflect barriers to AHC in the most susceptible population.

The study has several strengths. There are population-based studies of IAHC factors in Russia and abroad. Studies in the Russian Federation have generally included patients in the 35–74-year age range [12, 55], but there are also moderate-sized studies in elderly patients [56]. In our study, we obtained new data for older patients in a large sample. These data support the contribution of certain IAHC determinants in old age; they do not confirm the contribution of a number of known factors, but identify new associations with aging. As for studies in populations of Europe, the USA, China, and other countries, they have logical heterogeneity, and the results of the Siberian study add to the understanding of the spectrum of IAHC determinants, taking into account population specificity in the context of climate and geographic, ethnic, and other sources of variability.

Conclusion

Despite extensive research into the causes of insufficient treatment of patients with AH, the availability of effective AHTs and guidelines for the AH treatment, BP control remains inadequate worldwide.

In the Siberian population-based sample of individuals aged 55–84 years, examined from 2015 through 2018, only 30% of patients with AH receiving AHT had adequate BP control. Ineffective BP was positively associated with male gender, long-standing AH, frequent alco-

hol consumption, and economic inactivity (in women), and was inversely associated with PA, presence of CVD (in men), and smoking (in women). Focusing on non-pharmacological determinants may help optimize AH control.

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Conflict of interest

The authors declare no obvious or potential conflicts of interest related to this publication.

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