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## **ADHERENCA PACIJENATA NA ANTIHIPERTENZIVNOJ TERAPIJI U AMBULANTI IZABRANOG DOKTORA ZA ODRASLE DOMA ZDRAVLJA CETINJE**

**Sažetak:** Adherenca pacijenata na antihipertenzivnoj terapiji se odnosi na mjeru do koje se uzimanje terapije poklapa sa dogovorenim preporukama zdravstvenog radnika. Cilj je bio da se izmjeri adherenca i ispita povezanost sa varijablama socio-demografskog i medikamentnog statusa. Sprovedena je pilot studija presjeka sa 120 ispitanika, starosti  $\geq 18$  godina, koji se liječe od hipertenzije, a koji su aprila i maja 2022. godine posjetili ambulantu izabranog doktora Doma zdravlja Cetinje. Korišćen je upitnik sa socio-demografskim i medikamentnim statusom i Hill-Bone skalom. Adherenca je kategorisana kao dobra ( $\geq 80\%$ ) i lošija ( $< 80\%$ ). Starost ispitanika je bila  $64,6 \pm 9,28$ . Većina je bila ženskog pola, u braku, sa završenom srednjom školom, u penziji i liječenjem hipertenzije  $\geq 11$  godina. Ukupan broj lijekova u redovnoj terapiji je bio  $6,1 \pm 2,85$ , a antihipertenziva  $2,24 \pm 0,85$ . Sumnju na nuspojave antihipertenzivne terapije je imalo 14,2% ispitanika, a većina učestvuje u njenim troškovima. Broj bodova na Hill-Bone skali je bio  $10,04 \pm 1,90$ , a 95% ispitanika je imalo dobru adherencu. Od svih varijabli statistički značajna povezanost je nađena samo za učešće u troškovima antihipertenzivne terapije. Dobijeni rezultati podupiru gledište da su lična uvjerenja pacijenata o neophodnosti uzimanja terapije i opasnostima od neželjenih efekata bolji prediktori adherence nego drugi faktori.

**Ključne riječi:** adherenca, antihipertenzivna terapija, Hill-Bone skala, socio-demografski status, medikamentni status

**Abstract:** Adherence of patients to antihypertensive drugs refers to the extent to which their taking corresponds with agreed recommendations from a health care provider. The goal was to measure adherence and examine the association with socio-demographic and medication status variables. A cross-sectional pilot study was conducted with 120

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respondents, aged  $\geq 18$  years, who are being treated for hypertension and who visited the ambulance of family physician at Primary Health Care Centre Cetinje in April and May 2022. A questionnaire with socio-demographic and medication status and the Hill-Bone scale was used. Adherence was categorized as good ( $\geq 80\%$ ) and worse ( $< 80\%$ ). The age of respondents was  $64,6 \pm 9,28$ . The majority were female, married, with a high school diploma, retired and treated for hypertension for  $\geq 11$  years. The total number of drugs in regular therapy was  $6,1 \pm 2,85$  and antihypertensives  $2,24 \pm 0,85$ . 14,2% of respondents suspected the side effects of antihypertensive drugs and the majority participate in their costs. The number of points on the Hill-Bone scale was  $10,04 \pm 1,90$  and 95% of respondents had good adherence. Of all the variables, a statistically significant association was found only for participation in the costs of antihypertensive drugs. The obtained results support the view that patients' personal beliefs about the necessity of taking therapy and the concerns of side effects are better predictors of adherence than other factors.

**Keywords:** adherence, antihypertensive drugs, Hill-Bone scale, socio-demographic status, medication status

## *Uvod i cilj rada*

Prema preporukama Evropskog udruženja za kardiologiju i Evropskog udruženja za hipertenziju iz 2018. godine, hipertenzija je definisana sa povišenim vrijednostima sistolnog krvnog pritiska  $\geq 140$  mmHg i/ili dijastolnog krvnog pritiska  $\geq 90$  mmHg (1). Nekonrolisani povišeni krvni pritisak značajno povećava ukupni rizik za kardiovaskularne bolesti i komplikacije hipertenzije (2).

Hipertenzija se smatra najčešćim poremećajem u opštoj populaciji (3). Ukupna prevalenca hipertenzije u adultnoj populaciji je procijenjena na oko 30–45%, sa prevalencom od  $> 60\%$  kod ljudi starosti  $> 60$  godina (1). Sa starenjem populacije, sedentarnim načinom života i porastom tjelesne težine prevalenca hipertenzije u svijetu će nastaviti da raste, tako da se procjenjuje da će broj ljudi sa hipertenzijom porasti za 15–20% do 2025. godine, dostižući blizu 1,5 biliona (1).

Uprkos dostupnosti efikasnih antihipertenzivnih lijekova, procenat pacijenata sa kontrolisanim krvnim pritiskom u različitim populacijama ostaje nizak (2). Adherenca pacijenata na antihipertenzivnoj terapiji je pojedinačni najvažniji faktor koji doprinosi ovom neuspjehu da se postigne i održi kontrola krvnoga pritiska (2, 3, 4). Dobra adherenca je povezana sa poboljšanjem kontrole krvnog pritiska i smanjenjem komplikacija hipertenzije (4).

### *Adherenca i faktori koji na nju utiču*

Svjetska zdravstvena organizacija (SZO) je usvojila širu definiciju adherence koja glasi: „Mjera do koje se ponašanje pacijenta – uzimanje lijekova, poštovanje dijete i/ili izvršavanje promjena u životnom stilu poklapa sa dogovorenim preporukama od strane zdravstvenog radnika“ (4). U kontekstu ovog istraživanja adherenca će se odnositi na mjeru do koje se uzimanje antihipertenzivne terapije poklapa sa dogovorenim preporukama od strane zdravstvenog radnika.

Termini adherenca i komplijansa se koriste kao sinonimi (2). Međutim, dok se termin komplijansa odnosi na pasivno praćenje preporuka datih od strane zdravstvenog radnika (2), adherenca podrazumijeva dogovorene preporuke između pacijenta i zdravstvenog radnika (4). Adherenca razvija definiciju komplijanse, isticanjem potrebe za dogovorom pacijenta i ljekara (5).

Adherenca pacijenata se tradicionalno shvata kao dihotomni koncept, tj. Adherentan, odnosno neadherentan pacijent (2). Neadherenca može biti primarna, kada iz nekog razloga pacijent ne uspije da ostvari pravo na lijek, i sekundarna, kada se lijek ne uzima po propisu (5).

Dalje, neadherenca može biti namjerna i nenamjerna. Namjerna neadherenca se odnosi na aktivnu odluku pacijenta o uzimanju ili neuzimanju lijeka zasnovanu na posebnim razlozima kao što su, npr., percepcija terapijskog tretmana kao nepotrebnog, nesklad u komunikaciji između ljekara i pacijenta, trajanje bolesti, neželjeni efekti terapije. Sa druge strane, nenamjerna neadherenca, u čijoj osnovi je zaboravljanje uzimanja lijeka, manje je povezana sa uvjerenjima pojedinačnog pacijenta a više sa demografskim (npr. niže obrazovanje, starije životno doba) i kliničkim karakteristikama (npr. anksioznost, depresija) (2).

U razvijenim zemljama adherenca pacijenata u liječenju hroničnih bolesti u opštoj populaciji je oko 50%, a mnogo je niža u zemljama u razvoju. Procjene u kojoj mjeri se pacijenti pridržavaju farmakoterapije za hipertenziju variraju između 50 i 70% (4).

Adherenca pacijenata na antihipertenzivnoj terapiji je multidimenzionalni fenomen određen međusobnim delovanjem pet grupa faktora nazvanih „dimenzije“ i to: socio-demografski i ekonomski faktori, faktori u vezi sa zdravstvenim timom/sistemom, faktori u vezi sa zdravstvenim stanjem, faktori u vezi sa antihipertenzivnom terapijom i faktori u vezi sa pacijentom. Najvažniji faktori koji pozitivno ili negativno utiču na adherencu pacijenata na antihipertenzivnoj terapiji prikazani su u tabeli br. 1. Dva najvažnija faktora koji doprinose lošoj adherenci su nesumnjivo asimptomatska i doživotna priroda hipertenzije (4).

**Tabela br. 1. Faktori koji utiču na adherencu pacijenata na antihipertenzivnoj terapiji**

Grupe faktora	Pojedinačni faktori
Socio-demografski i ekonomski faktori	(-) Loš socio-ekonomski status; nepismenost; nezaposlenost; ograničena snabdjevenost i visoka cijena lijekova
Faktori u vezi sa zdravstvenim timom/sistemom	(-) Nedostatak znanja i obuke za pružaoce zdravstvene zaštite na upravljanju hroničnim bolestima; neadekvatan odnos između pružaoca zdravstvene zaštite i pacijenta; nedostatak znanja; neadekvatno vrijeme za konsultacije; nedostatak podsticaja i povratne informacije o učinku (+) Dobar odnos između pacijenta i ljekara
Faktori u vezi sa zdravstvenim stanjem	(-) Asimptomatska i doživotna priroda hipertenzije (+) Razumijevanje i percepcija o hipertenziji
Faktori u vezi sa antihipertenzivnom terapijom	(-) Složeni terapijski režimi; trajanje liječenja; slaba podnošljivost lijekova i neželjeni efekti liječenja (+) Monoterapija; rjeđa doza; manje izmjena u terapiji; novije klase lijekova (antagonisti angiotenzina II, inhibitori angiotenzin konvertujućeg enzima, blokatori kalcijumskih kanala)
Faktori u vezi sa pacijentom	(-) Neadekvatno znanje i vještine upravljanja simptomima bolesti i liječenjem; nesvjesnost o troškovima i koristima liječenja; neprihvatanje praćenja bolesti (+) Percepcija zdravstvenog rizika vezanog za bolest; aktivno učešće u praćenju bolesti; učešće u liječenju bolesti
(+) Faktori koji pozitivno utiču na adherencu; (-) Faktori koji negativno utiču na adherencu	

Preuzeto i prilagođeno prema: Sabaté E., Adherence to long-term therapies: Evidence for action. Geneva: World Health Organization, 2003.

### ***Mjerenje adherence***

Metode za mjerenje adherence se mogu podijeliti na direktne i indirektne, subjektivne i objektivne. Svaka od metoda ima svoje prednosti i nedostatke i nijedna se ne može smatrati zlatnim standardom. Direktne metode neposredno dolaze do podataka o adherenci, bilo pomoću direktnog posmatranja pacijenta, mjerenjem koncentracije lijeka ili njegovog metabolita u krvi ili urinu, odnosno mjerenjem biološkoga markera u krvi, koji je dodat formulaciji lijeka. Direktne metode su precizne i objektivne, ali i

skupe, zahtijevaju prisustvo zdravstvenog radnika i podložne su iskrivljenju rezultata od strane pacijenta (6, 7).

U tabeli br. 2 date su direktne metode za mjerenje adherence, kao i njihove prednosti i nedostaci, prema Osterberg i Blaschke (6).

**Tabela br. 2. Direktne metode za mjerenje adherence**

Direktne metode	Prednosti	Nedostaci
Direktno posmatranje pacijenata	Najpreciznije	Pacijenti mogu sakriti tablete u ustima i kasnije ih ispljunuti; nepraktično za rutinsku primjenu
Mjerenje koncentracije lijeka u krvi	Objektivno	Varijacije u metabolizmu i „adherenca bijelog mantila“ mogu dati lažnu sliku adherence; skupo
Mjerenje bioloških markera u krvi	Objektivno, koristi se u kliničkim ispitivanjima, može se koristiti i za mjerenje placeba	Zahtjeva skupe kvantitativne metode i skupljanje bioloških uzoraka

Preuzeto i prilagođeno prema: Osterberg L., Blaschke T., Adherence to Medication. N Engl J Med 2005; 353: 487–97

Indirektne metode posredno dolaze do podataka o adherenci pacijenta. Indirektne metode za mjerenje adherence, kao i njihove prednosti i nedostaci, date su u tabeli br. 3 prema Osterberg i Blaschke. Upitnici za pacijente i procjena kliničkog odgovora su metode koje su relativno lake za korišćenje. Upitnici su najčešća metoda za mjerenje adherence, ali su podložni iskrivljenju rezultata od strane pacijenata i mogu da precijene adherencu pacijenta. Takođe, procjena kliničkoga odgovora kao mjere adherence ima svoje nedostatke, mnogi faktori, osim adherence, mogu uticati na klinički odgovor (6).

**Tabela br. 3. Indirektne metode za mjerenje adherence**

Indirektne metode	Prednosti	Nedostaci
Upitnici za pacijente, samopraćenje pacijenata	Jednostavno, jeftino, najkorisnija metoda u kliničkom okruženju	Podložno greškama koje se povećavaju između posjeta; rezultati podložni iskrivljenju od strane pacijenata

Brojači tableta	Objektivno, kvantitativno, jednostavno za izvođenje	Jednostavna manipulacija podataka od strane pacijenata (npr. bacanje tableta)
Učestalost podizanja lijekova	Objektivno, jednostavno dobijanje podataka	Podizanje lijeka ne znači i uzimanje lijeka; zahtjeva zatvoren farmaceutski sistem
Procjena kliničkog odgovora	Jeftino, načelno jednostavno za izvođenje	Različiti faktori, osim adherence, mogu uticati na klinički odgovor
Elektronski monitori lijekova	Precizni, jednostavno kvantificiranje rezultata, praćenje obrazaca uzimanja lijekova	Skupo, zahtjeva donošenje uređaja radi preuzimanja podataka
Mjerenje fizioloških markera (npr. srčane frekvence kod uzimanja beta blokatora)	Često lako za izvođenje	Marker može biti odsutan iz drugih razloga (npr. povećani metabolizam, slaba apsorpcija, manjak odgovora)
Pacijentovi dnevници	Pomoć pri lošem sjećanju	Jednostavno se mogu izmijeniti od strane pacijenta
Upitnici za njegovatelje ili učitelje ukoliko su pacijenti maloljetni	Jednostavno, objektivno	Podložno iskrivljenju rezultata

Preuzeto i prilagođeno prema: Osterberg L., Blaschke T., Adherence to Medication. N Engl J Med 2005; 353: 487–97

Iako pojedine metode mjerenja adherence imaju prednost u specifičnim kliničkim ili istraživačkim okolnostima, kombinacija metoda povećava preciznost mjerenja, te se preporučuje višemetodni pristup (6, 7).

### ***Cilj rada***

Cilj rada je mjerenje adherence pacijenata na antihipertenzivnoj terapiji u ambulanti izabranog doktora za odrasle Doma zdravlja Cetinje, kao i ispitivanje povezanosti adherence sa socio-demografskim varijablama i varijablama medicamentnog statusa.

## **Metod rada**

### **Ispitanici**

Istraživanje je sprovedeno kao pilot studija presjeka, na uzorku od 120 pacijenata koji se liječe od hipertenzije, a koji su u periodu aprila i maja 2022. godine posjetili ambulantu svog izabranog ljekara u Domu zdravlja Cetinje. U ovoj ambulanti je registrovano 1.550 pacijenata, od čega se 743 pacijenta liječi od hipertenzije.

Kriterijumi za uključenje u studiju su bili: starost ispitanika 18 godina i više, potvrđena dijagnoza hipertenzije unazad godinu dana ili duže, korišćenje makar jednog antihipertenzivnog lijeka u terapiji unazad godinu dana ili duže, dok su iz studije isključeni ispitanici sa kognitivnim oštećenjima, pogoršanjem osnovnog zdravstvenog stanja ili oni koji nisu potpisali informisani pristanak.

### **Upitnik za adherencu pacijenata na antihipertenzivnoj terapiji**

Za ovu svrhu korišćen je autorski upitnik za adherencu pacijenata na antihipertenzivnoj terapiji koji se sastoji iz 3 dijela: socio-demografskog statusa, medikamentnog statusa i standardizovane skale za mjerenje adherence.

Socio-demografski status je obuhvatio pol, starosnu dob, bračni status, obrazovanje i radni status. Medikamentnim statusom je praćeno: dužina liječenja hipertenzije, ukupan broj lijekova, broj antihipertenzivnih lijekova, sumnja na nuspojave antihipertenzivne terapije, učešće u troškovima antihipertenzivne terapije. Socio-demografski i medikamentni status sadrže faktore od potencijalnog uticaja na samu adherencu.

Sastavni dio upitnika je Hill-Bone skala za mjerenje adherence lijekova, za čije korišćenje, prevod i adaptaciju na crnogorskom, srpskom, bošnjačkom i hrvatskom jeziku je dobijeno odobrenje od strane Johns Hopkins University School of Nursing.

Hill-Bone skala za mjerenje adherence lijekova je samostalna skala, ali je ujedno i supskala šire Hill-Bone skale, koja, osim pitanja koja se odnose na uzimanje lijekova, sadrži i pitanja u vezi unosa soli i redovnosti posjećivanja ljekaru. Pripada subjektivnim metodama za mjerenje adherence i ima široku primjenu kod različitih hroničnih bolesti kao što su hipertenzija, dijabetes, moždani udar, HIV infekcija i dr. Sastoji se od 9 pitanja, a svako pitanje ima ponudena 4 odgovora sa odgovarajućim brojem poena prema Likartovoj skali (1 – nikad, 2 – ponekad, 3 – često, 4 – uvijek). Ukupan rezultat se dobija sabiranjem poena pojedinačnih pitanja, pri čemu je minimalan broj poena 9, a maksimalan broj poena 36. Veći broj poena ukazuje na lošiju adherencu i obrnuto. Tzv. perfektna adherenca podrazumijeva ukupan rezultat od 9 poena. Johns Hopkins University School of Nursing ne predlaže granične vrijednosti, na primer za nisku, umjerenu ili visoku adherentnost. Predlaže ispitivanje distribucije rezultata iz datog skupa podataka i određivanje graničnih vrijednosti (na primjer tercila) koje odgovaraju datim podacima (2, 8, 9).

Za izračunavanje procenta adherence pacijenta, na osnovu ostvarenog broja bodova na skali, korišćena je formula: % adherence = 36 - broj bodova pacijenta na skali / 27 x 100, gdje je 36 maksimalan broj bodova, a 27 je raspon bodova na skali (36 – 9). Adherenca je kategorisana kao perfektna (100%), dobra ili prihvatljiva ( $\geq 80\%$ ) i lošija ( $< 80\%$ ), kao u ranijim studijama (10, 11).

### **Procedura prikupljanja podataka i statistička obrada podataka**

Nakon pružene zdravstvene usluge zbog koje su došli u ambulantu svog izabranog doktora, zadovoljenja kriterijuma za uključivanje u ovu studiju i potpisivanja informisanog pristanka ispitanici su zamoljeni da sa istraživačem, u susjednoj slobodnoj ambulanti, odgovore na postavljena pitanja koja čine sastavni dio ranije navedenog upitnika. Pitanja koja su sastavni dio Hill-Bone skale za mjerenje adherence lijekova odnosila su se na posljednjih mjesec dana. Odgovori na pitanja iz medikamentnog statusa provjereni su i naknadnim uvidom u zdravstveni karton pacijenta, kako bismo osigurali pouzdanost podataka.

Prikupljeni podaci su obrađeni uz pomoć programa Microsoft Excel i SPSS (engl. Statistical Package for the Social Sciences) 2022. Urađena je deskriptivna i analitička statistika. Za testiranje normalnosti raspodjele korišćen je Shapiro-Wilk test. Razlika adherence u odnosu na socio-demografske varijable i varijable medikamentnog statusa procijenjena je uz pomoć Mann-Whitney U testa i Kruskal-Wallis testa. Nivo značajnosti  $< 0,05$  smatran je statistički značajnim.

### **Etički aspekt istraživanja**

Za sprovođenje ovog istraživanja dobijena je saglasnost Etičkog komiteta JZU Doma zdravlja Podgorica br. 05/17-4188 od 06.05.2022. godine, a potom i direktora JZU Doma zdravlja Cetinje, gdje je i sprovedeno istraživanje.

## ***Rezultati***

### **Rezultat mjerenja adherence pacijenata na antihipertenzivnoj terapiji**

Prosječan broj bodova koji su ispitanici ostvarili na Hill-Bone skali za mjerenje adherence lijekova je bio  $10,04 \pm 1,90$  (tabela br. 4). Većina pacijenata je na pomenutoj skali imala 9 bodova (57,5%) i 10 bodova (24,2%) (tabela br. 5).

**Tabela br. 4. Ukupan rezultat Hill-Bone skale za mjerenje adherence lijekova**

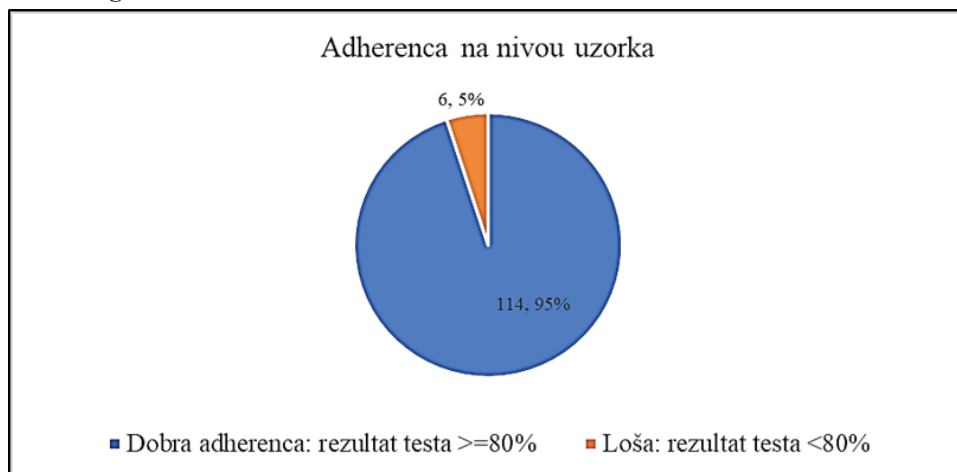
<b>N</b>	<b>Mean <math>\pm</math> SD</b>	<b>Median (IR)</b>	<b>Minimum</b>	<b>Maximum</b>
120	$10,04 \pm 1,90$	9 (9–10)	9	20



**Tabela br. 5. Rezultat Hill-Bone skale za mjerenje adherence lijekova prema broju bodova**

Broj bodova na skali	N	%
9	69	57,5
10	29	24,2
11	6	5,0
12	3	2,5
13	4	3,3
14	3	2,5
15	3	2,5
16	1	0,8
17	1	0,8
20	1	0,8
<b>Ukupno</b>	120	100,0

Izračunavanjem procenta adherence prema ranije objašnjenoj formuli dobijamo da je 95% ispitanika imalo dobru, tj. prihvatljivu adherencu ( $\geq 80\%$ ), što je obuhvatilo sve one ispitanike sa brojem bodova na skali od 9 do 14. Među njima perfektnu adherencu (100%), odnosno 9 bodova na skali, imalo je 57,5% ispitanika. Slabije adherentno ( $< 80\%$ ) je bilo 5% ispitanika, a obuhvatilo je sve one ispitanike sa brojem bodova na skali od 15 do 20 (grafik br. 1).

**Grafik br. 1. Adherenca pacijenata (%) na antihipertenzivnoj terapiji u ambulanti izabranog doktora**

### Socio-demografski i medikamentni status ispitanika

Prosječna starosna dob ispitanika je bila  $64,6 \pm 9,28$ , a većina ispitanika je bila starosti iznad 60 godina (70,8%). Najmlađi pacijent je imao 36 godina, a najstariji 82 godine. Više od dvije trećine ispitanika je ženskog pola (67,5%). Većina ispitanika je bila u braku (63,3%). Što se tiče obrazovanja, većina ispitanika je završila srednju školu (63,3%). U radnom statusu dominiraju penzioneri, sa 69,7%, a nezaposlenost na nivou uzorka je 9,2%.

Većina ispitanika se liječi od hipertenzije  $\geq 11$  godina (63,3%). Prosječan ukupan broj lijekova koje ispitanici uzimaju u redovnoj terapiji je  $6,1 \pm 2,85$ , a raspon od jednoga do čak 15 lijekova. Tri ili više lijekova u redovnoj terapiji uzima 94,2% ispitanika. Prosječan broj antihipertenzivnih lijekova koje ispitanici uzimaju je  $2,24 \pm 0,85$ , a raspon od jednoga do četiri lijeka. Skoro polovina ispitanika (48,3%) uzima po 2 antihipertenzivna lijeka, a skoro četvrtina njih (24,2%) po 3 antihipertenzivna lijeka. Sumnju na nuspojave antihipertenzivne terapije je imalo njih 14,2% ispitanika. Većina ispitanika učestvuje u troškovima antihipertenzivne terapije, bilo da je puna cijena (10,8%) ili kao doplata (53,3%).

Socio-demografski i medikamentni status ispitanika prikazan je u tabeli br. 6 i tabeli br. 7.

**Tabela br. 6. Socio-demografski i medikamentni status ispitanika (1. dio)**

Ispitivana varijabla	N	Mean $\pm$ SD	Median (IR)	Min	Max
Starosna dob	120	$64,6 \pm 9,28$	66,5 (59–71)	36	82
Ukupan broj lijekova	120	$6,1 \pm 2,85$	5,5 (4–8)	1	15
Broj antihipertenziva	120	$2,24 \pm 0,85$	2 (2 – 3)	1	4

**Tabela br. 7. Socio-demografski i medikamentni status ispitanika (2. dio)**

Ispitivana varijabla	Kategorije	N	%
Starosna dob (godine)	36–60	35	29,2%
	> 60	85	70,8%
Pol	Muški	39	32,5%
	Ženski	81	67,5%
Bračni status	Oženjen/udata	76	63,3%
	Neoženjen/neudata	14	11,7%
	Razveden/na	3	2,5%
	Udovac/ica	27	22,5%

Obrazovanje	Bez škole	6	5,0%
	Osnovna škola	27	22,5%
	Srednja škola	76	63,3%
	Viša/visoka škola	5	4,2%
	Fakultet	6	5,0%
Radni status	Zaposlen/na	20	16,8%
	Nezaposlen/na	11	9,2%
	Penzioner/ka	83	69,7%
	Student/kinja/domaćin/ica/ drugo	5	4,2%
Dužina liječenja hipertenzije (u godinama)	1–5	17	14,2%
	6–10	27	22,5%
	11–15	35	29,2%
	> 15	41	34,1%
Ukupan broj lijekova	1	2	1,7%
	2	5	4,2%
	3 ili više	113	94,2%
Broj antihipertenzivnih li- jekova	1	22	18,3%
	2	58	48,3%
	3	29	24,2%
	4	11	9,2%
Sumnja na nuspojave antihi- pertenzivne terapije	Da	17	14,2%
	Ne	103	85,8%
Učešće u troškovima antihi- pertenzivne terapije	Da, puna cijena	13	10,8%
	Da, doplata	64	53,3%
	Ne	43	35,8%
<b>Ukupno</b>		120	100,0%

### Rezultati ispitivanja povezanosti adherence i varijabli socio-demografskog i medikamentnog statusa

Nije nađena statistički značajna povezanost između adherence i sledećih varijabli: pola ( $p = 0,222$ ), starosne dobi ( $p = 0,364$ ), bračnog statusa ( $p = 0,233$ ), obrazovanja ( $p = 0,421$ ), radnog statusa ( $p = 0,195$ ), dužine liječenja hipertenzije ( $p = 0,979$ ), ukupnog broja lijekova ( $p = 0,787$ ), broja antihipertenzivnih lijekova ( $p = 0,187$ ) i sumnje na nuspojave antihipertenzivne terapije ( $p = 0,364$ ). Statistički značajna povezanost je nađena samo između adherence i učešća ispitanika u troškovima antihipertenzivne

terapije ( $p = 0,029$ ). Ispitanici koji su dijelom učestvovali u troškovima (doplata) imali su i najbolju adherencu ( $9,78 \pm 1,84$ ), a adherenca se nije razlikovala između onih koji su plaćali punu cijenu ( $10,2 \pm 2,16$ ) i onih koji nisu učestvovali u troškovima antihipertenzivne terapije ( $10,3 \pm 1,89$ )  $p > 0,05$ . Rezultati ispitivanja povezanosti adherence i varijabli socio-demografskog i medikamentnog statusa prikazani su u tabeli br. 8.

**Tabela br. 8. Rezultati testiranja razlike adherence u odnosu na ispitivane varijable**

Ispitivana varijabla	Kategorija	N	Mean $\pm$ SD	Median (IR)	Vrij. testa	p
Starosna dob (godine)	36–60	35	10,2 $\pm$ 2,52	9 (9–10)	768	0,364
	> 60	85	9,94 $\pm$ 1,58	9 (9–10)		
Pol	Muški	39	10 $\pm$ 2,27	9 (9–10)	1385	0,222
	Ženski	81	10,0 $\pm$ 1,71	9 (9–10)		
Bračni status	Oženjen/udata	76	10,0 $\pm$ 2,07	9 (9–10)	4,273	0,233
	Neoženjen/neudata	14	9,78 $\pm$ 1,62	9 (9–10)		
	Razveden/na	3	11,3 $\pm$ 3,21	10 (9–11)		
	Udovac/ica	27	10,0 $\pm$ 1,32	10 (9–10)		
Obrazovanje	Bez škole	6	10,1 $\pm$ 1,94	9,5 (9–11)	3,892	0,421
	Osnovna škola	27	10,1 $\pm$ 1,89	9 (9–10)		
	Srednja škola	76	9,81 $\pm$ 1,49	9 (9–10)		
	Viša/visoka škola	5	10 $\pm$ 2,23	9 (9–11,5)		
	Fakultet	6	12,3 $\pm$ 4,36	10,5 (9–16,25)		
Radni status	Zaposlen/na	21	10,2 $\pm$ 2,24	9 (9–10,75)	4,697	0,195
	Nezaposlen/na	11	11,1 $\pm$ 3,37	10 (9–11)		
	Penzioner/ka	83	9,81 $\pm$ 1,45	9 (9–10)		
	Student/kinja/domaćin/ica/drugo	5	10,6 $\pm$ 2,50	10 (9–12,5)		
Dužina liječenja hipertenzije (u godinama)	1 – 5	17	11,2 $\pm$ 3,54	9 (9–14,5)	0,189	0,979
	6 – 10	27	9,74 $\pm$ 1,25	9 (9–10)		
	11 – 15	35	9,97 $\pm$ 1,74	9 (9–10)		
	> 15	41	9,80 $\pm$ 1,18	9 (9–10)		
Ukupan broj lijekova	1	2	12 $\pm$ 4,24	12,00	0,478	0,787
	2	5	10,4 $\pm$ 2,6	9 (9,0–12,5)		
	3 ili više	113	9,99 $\pm$ 1,83	9 (9–10)		

Broj antihipertenziva	1	22	10,7 ± 3,08	9 (9–11,5)	4,801	0,187
	2	58	9,72 ± 1,43	9 (9–10)		
	3	29	10,1 ± 1,74	10 (9–10)		
	4	11	10 ± 1	10 (9–11)		
Sumnja na nuspojave antihipertenziva	Da	17	10,7 ± 3,19	10 (9–10)	768	0,364
	Ne	103	9,92 ± 1,58	9 (9–10)		
Učešće u troškovima antihipertenziva	Da, puna cijena	13	10,2 ± 2,16	9 (9–10)	7,057	0,029
	Da, doplata	64	9,78 ± 1,84	9 (9–10)		
	Ne	43	10,3 ± 1,89	10 (9–11)		

## Diskusija

Ovim istraživanjem je utvrđeno da je 95% ispitanika imalo dobru, tj. prihvatljivu adherencu, izmjerenu korišćenjem Hill-Bone skale za mjerenje adherence lijekova ( $\geq 80\%$  rezultata na skali).

Ovaj rezultat odstupa od generalne procjene SZO, prema kojoj je u razvijenim zemljama adherenca pacijenata u liječenju hroničnih bolesti u opštoj populaciji oko 50%, a mnogo je niža u zemljama u razvoju. Takođe, u publikaciji SZO se dodatno navodi da procjene u kojoj mjeri se pacijenti pridržavaju farmakoterapije za hipertenziju variraju između 50 i 70% (4).

Međutim, poređenjem rezultata o stupnju adherentnosti ispitanika na antihipertenzivnoj terapiji sa drugim izražavanjima, gdje je korišćena ista skala za mjerenje adherence lijekova, a stupanj adherentnosti izražen na isti način, dobijaju se različiti podaci. Tako, npr., u istraživanju sprovedenom u Indiji, na 452 ispitanika, više od 80% ispitanika je takođe imalo dobru, tj. prihvatljivu adherencu (10), kao i u istraživanju sprovedenom u Zambiji, na uzorku od 237 ispitanika (70%) (12). U istraživanju sprovedenom u primarnoj zdravstvenoj zaštiti u Namibiji, na uzorku od 120 pacijenata, kolika je i veličina ispitivanog uzorka, manje od 50% ispitanika je imalo dobru, tj. prihvatljivu adherencu (11).

Ovo odstupanje od generalne procjene SZO, a ujedno i ovako dobar rezultat, na početku, možemo objasniti specifičnošću samog uzorka ispitanika za koji je mjerena adherenca. Naime, u pitanju je uzorak ispitanika, tj. pacijenata iz jedne ambulante izabranog doktora za odrasle, koji posjećuju svog izabranog doktora, a ne iz opšte populacije. Druga objašnjenja za ovako dobru adherencu treba tražiti i u potencijalnim faktorima koji je određuju, o čemu će biti diskusije u nastavku.

U vezi sa prethodnim, potrebno je naglasiti da, iako postoji niz različitih skala za mjerenje adherence, među kojima je i Hill-Bone skala, još uvijek ne postoji zlatni standard (13). Takođe, kako ne postoji ni idealna metoda za mjerenje adherence, istovremeno korišćenje više metoda u mjerenju adherence se čini kao najbolje rješenje (6, 7). To daje prostora za novim istraživanjima u kojima će se koristiti i neke druge metode za mjerenje adherence, kao što je npr. učestalost podizanja lijekova u apotekama, procjena kliničkog odgovora na terapiju i dr.

U publikaciji SZO se u grupi socio-demografskih i ekonomskih faktora koji utiču na adherencu ističu nepismenost i nezaposlenost, dok se za starosnu dob navodi da su podaci inkonzistentni, a pol i bračni status se ne pominju kao faktori koji utiču na adherencu pacijenata na antihipertenzivnoj terapiji (4). U radu Hashmi SK i saradnika se navodi da je u njihovoj studiji u Pakistanu, na uzorku prosječne starosti ispitanika od 52 godine, slično kao i u drugim djelovima svijeta, nađeno da se adherence poboljšava u starijem životnom dobu (14). U studiji sprovedenoj u Poljskoj, na uzorku ispitanika prosječne starosti 72,1 godina, nađeno je, pak, da se adherence smanjuje sa godinama života (15). Ovo upućuje na to da je adherence slabija u mlađem životnom dobu, potom se poboljšava, a tek sa većim porastom godina adherence počinje ponovo da pada. U radu AlHadlaq RK i saradnika se navodi da u njihovom istraživanju u Saudijskoj Arabiji nije nađena povezanost adherence i pola, iako postoje studije u kojima je nađena bolja adherentnost ženskog pola (16). Prema publikaciji SZO, neke studije navode da su organizacioni faktori (vrijeme provedeno kod ljekara, kontinuitet njege, stil komunikacije i interpersonalni stil ljekara) mnogo važniji od socio-demografskih varijabli u uticaju na adherencu pacijenata (4).

U ovom istraživanju nije nađena povezanost adherence sa varijablama socio-demografskog statusa (pol, starosna dob, bračni status, obrazovanje, radni status), što je konzistentno i sa rezultatima drugih istraživanja koja su koristila istu skalu za procjenu adherence. Takvo je istraživanje u Sjedinjenim Američkim Državama, na uzorku od 208 koreanskih Amerikanaca (2), već pomenuto istraživanje u Namibiji i Zambiji (11, 12).

Kada su u pitanju socio-demografske varijable, ispitivani uzorak je specifičan u sledećem pogledu: više od dvije trećine ispitanika je ženskog pola, prosječne starosne dobi ispitanika 64,6, većina je bila u braku, sa završenom srednjom školom i u statusu penzionera. Na osnovu ranije pomenutih radova, u prilog dobroj adherenci naših ispitanika može ići ženski pol, prosječna starosna dob ispitanika, dovoljan stepen obrazovanja (srednja škola) i penzionerski status.

Neke od poznatijih odrednica adherentnosti na antihipertenzivnu terapiju, kako se navodi u publikaciji SZO, povezane su sa aspektima samog farmakološkog tretmana i uključuju trajanje liječenja, složenost tretmana, podnošljivost i nuspojave lijekova, snabdjevenost i cijene lijekova. Učestalost doziranja, broj istovremenih lijekova i promjene antihipertenzivnih lijekova su neki od faktora koji doprinose

složenosti tretmana i oni su istraživani u mnogim opservacionim studijama. Kraće trajanje tretmana, njegova jednostavnost (manje pojedinačnih doza antihipertenziva, monoterapija, manje promjena u antihipertenzivnim lijekovima), bolja podnošljivost i manje nuspojava, dobra snabdjevenost i niže cijene lijekova su povezani sa boljom adhirencom (4).

U ovom istraživanju nije nađena povezanost adherence sa dužinom liječenja hipertenzije (trajanjem tretmana), ukupnim brojem lijekova i brojem antihipertenzivnih lijekova, kao ni sa nuspojavama na antihipertenzivnu terapiju. Povezanost adherence i trajanja tretmana nije nađena ni u pomenutim istraživanjima u Indiji i Namibiji (10, 11). Povezanost je nađena u studiji u Palestini, na uzorku od 648 ispitanika, pri čemu je, iznenađujuće, bolja adhirenca zapažena sa dužim trajanjem tretmana hipertenzije (17). Ispitivana povezanost adherence i ukupnog broja lijekova nije nađena u istraživanju u Zambiji, iako se opisuje u literaturi (4, 5), ali je nađena povezanost sa brojem antihipertenzivnih lijekova i pojavom nuspojava antihipertenzivne terapije (12). Pacijenti koji su uzimali tri antihipertenzivna lijeka imali su bolju adhirencu (12). U pomenutoj studiji Hashmi SK i saradnika nađeno je, takođe, da je adhirenca bila bolja sa većim brojem antihipertenzivnih lijekova u terapiji, što je, kako navode, iznenađujuće i u suprotnosti sa onim što je do sada objavljivano u radovima. Za to daju objašnjenje da pacijenti koji uzimaju više antihipertenziva osjećaju da je ozbiljnost njihove bolesti veća i vode više računa oko uzimanja lijekova, kao i to da pacijenti koji uzimaju više lijekova imaju manju vjerovatnoću da ih zaborave, nego kada uzimaju samo jedan lijek (14). U ovom istraživanju, kao i u studiji sprovedenoj u Palestini, nije nađena povezanost adherence i broja antihipertenzivnih lijekova u terapiji (17). Postoje i studije u kojima nije dokazana povezanost adherence i prisustva nuspojava antihipertenzivnih lijekova (10).

Kada je u pitanju medikamentni status, ispitivani uzorak je specifičan u sledećem pogledu: skoro dvije trećine ispitanika se liječi od hipertenzije 11 i više godina, prosječan ukupan broj lijekova koji ispitanici uzimaju u redovnoj terapiji je 6,1, prosječan broj antihipertenzivnih lijekova koji ispitanici uzimaju je 2,24, a sumnju na nuspojave antihipertenzivne terapije je imalo njih 14,2% ispitanika, većinom navodeći hipotenziju. Na osnovu gorepomenutih radova, u prilog dobroj adhirenci naših ispitanika može ići dužina liječenja hipertenzije, s obzirom na to da se radi o pacijentima koji su imali dovoljno vremena da se upoznaju sa karakteristikama svoje bolesti i samim tretmanom, prosječan broj antihipertenziva koji bi mogao uticati da svoju bolest ozbiljnije doživljavaju i manji broj pacijenata sa sumnjom na nuspojave antihipertenzivne terapije.

Većina ispitanika učestvuje u troškovima antihipertenzivne terapije, bilo da je puna cijena ili kao doplata. U ovom istraživanju je nađena povezanost adherence sa učešćem u troškovima antihipertenzivne terapije. Ispitanici koji su dijelom učestvovali u troškovima antihipertenzivne terapije (doplata) imali su i najbolju adhirencu, a

adherenca se nije razlikovala između onih koji su plaćali punu cijenu i onih koji nisu učestvovali u troškovima antihipertenzivne terapije. U studijama u kojima je učešće u troškovima antihipertenzivne terapije izraženo na sličan način kao u ovom istraživanju nije nađena povezanost adherence i učešća u troškovima antihipertenzivne terapije (14, 18). Zdravstveni sistemi, pak, prema literaturi, kreiraju barijere za adherencu visokim cijenama lijekova, doplatama lijekova ili na oba načina (6, 19). Ovakav rezultat, različit od podataka u literaturi, mogli bi objasniti time da doplate za većinu antihipertenzivnih lijekova u našoj zemlji nisu visoke, a kada se već pacijenti odluče da doplate lijek nastoje ga i redovno uzimati.

Ovo je prvo istraživanje o adherenci pacijenata na antihipertenzivnoj terapiji u našoj zemlji, te postoji svijest o ograničenjima koje ono nosi. Istraživanje je sprovedeno na uzorku ispitanika u jednoj ambulanti izabranog doktora za odrasle, koji su došli na pregled tokom istraživačkog perioda, te se dobijeni rezultati na njih odnose i ne mogu se generalizovati na pacijente koji gravitiraju ka Domu zdravlja Cetinje. Iz istraživanja su isključeni pacijenti sa kognitivnim oštećenjima, za koje se zna da su slabije adherentni (5). Korišćena je jedna subjektivna metoda za mjerenje adherence, premda se, prema literature, predlaže višemetodni pristup radi podizanja objektivnosti rezultata. Ispitanicima je istraživač detaljno objašnjavao nejasnoće u vezi sa pitanjima iz upitnika, ali se ne može sa sigurnošću isključiti da pacijenti nisu, makar u najmanjoj mjeri, davali za istraživača prihvatljive odgovore.

## **Zaključak**

U ovom istraživanju adherence pacijenata na antihipertenzivnoj terapiji u ambulanti izabranog doktora za odrasle Doma zdravlja Cetinje utvrđeno je da je 95% ispitanika imalo dobru, tj. prihvatljivu adherencu. Od ispitivanih varijabli socio-demografskog i medikamentnog statusa statistički značajna povezanost je nađena samo između adherence i učešća ispitanika u troškovima antihipertenzivne terapije.

Rezultati ovog istraživanja, a imajući u vidu i nekonzistentnost podataka u literaturi, podupiru gledište istraživača koji su našli da su lična uvjerenja pacijenata o neophodnosti uzimanja terapije i opasnostima od neželjenih efekata bolji prediktori adherence nego socio-demografski i klinički faktori, kao što je broj lijekova u terapiji (20).

Na kraju, treba naglasiti da su potrebna nova istraživanja na uzorku pacijenata iz više ambulanti izabranog doktora za odrasle, korišćenjem i drugih metoda za mjerenje adherence, kao i ispitivanjem ostalih potencijalnih faktora koji mogu uticati na adherencu, a sa ciljem objektivnijeg mjerenja adherence pacijenata na antihipertenzivnoj terapiji i pronalazjenja intervencija koje je poboljšavaju.



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## **Sukob interesa**

Ne postoje sukobi interesa.

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## **ADHERENCE OF PATIENTS TO ANTIHYPERTENSIVE DRUGS IN THE AMBULANCE OF FAMILY PHYSICIAN AT PRIMARY HEALTH CARE CENTRE CETINJE**

**Abstract:** Adherence of patients to antihypertensive drugs refers to the extent to which their taking corresponds with agreed recommendations from a health care provider. The goal was to measure adherence and examine the association with socio-demographic and medication status variables. A cross-sectional pilot study was conducted with 120 respondents, aged  $\geq 18$  years, who are being treated for hypertension and who visited the ambulance of family physician at Primary Health Care Centre Cetinje in April and May 2022. A questionnaire with socio-demographic and medication status and the Hill-Bone scale was used. Adherence was categorized as good ( $\geq 80\%$ ) and worse ( $< 80\%$ ). The age of respondents was  $64,6 \pm 9,28$ . The majority were female, married, with a high school diploma, retired and treated for hypertension for  $\geq 11$  years. The total number of drugs in regular therapy was  $6,1 \pm 2,85$  and antihypertensive  $2,24 \pm 0,85$ . 14,2% of respondents suspected the side effects of antihypertensive drugs and the majority participate in their costs. The number of points on the Hill-Bone scale was  $10,04 \pm 1,90$  and 95% of respondents had good adherence. Of all the variables, a statistically significant association was found only for participation in the costs of antihypertensive drugs. The obtained results support the view that patients' personal beliefs about the necessity of taking therapy and the concerns of side effects are better predictors of adherence than other factors.

**Key words:** adherence, antihypertensive drugs, Hill-Bone scale, socio-demographic status, medication status

### ***Introduction and objective of the paper***

According to the recommendations of the European Society of Cardiology and the European Society of Hypertension from 2018, hypertension is defined as elevated

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values of systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg (1). Uncontrolled elevated blood pressure significantly increases the overall risk for cardiovascular diseases and complications due to hypertension (2).

Hypertension is considered the most common disorder in the general population (3). The overall prevalence of hypertension in the adult population is estimated at around 30-45%, with a prevalence of  $>60\%$  in people aged  $>60$  years (1). As populations age, adopt more sedentary lifestyles, and increase their body weight, the prevalence of hypertension worldwide will continue to rise; therefore it is estimated that the number of people with hypertension will increase by 15-20% by 2025, reaching close to 1.5 billion (1).

Despite the availability of effective antihypertensive drugs, the percentage of patients with controlled blood pressure in different population remains low (2). Adherence of patients to antihypertensive therapy is the single most important factor contributing to this failure to achieve and maintain blood pressure control (2, 3, 4). Good adherence is associated with improved blood pressure control and reduced complications of hypertension (4).

### *Adherence and factors affecting adherence*

World Health Organization (WHO) adopted the following broader definition of adherence: “the extent to which the patient’s behavior– taking medications, following a diet and /or executing lifestyle changes corresponds with the agreed recommendations from a healthcare provider.” In the context of this research, adherence will be related to the extent to which taking of antihypertensive therapy corresponds to the agreed recommendations from a healthcare provider.

The terms adherence and compliance are synonymously used (2). However, while the term compliance refers to the passive monitoring of recommendations given by a health care professional (2), adherence implies agreed recommendations between the patient and the health care professional (4). Adherence develops the definition of compliance, emphasizing the need for agreement between the patient and health care provider (5).

Adherence of patients is traditionally understood as a dichotomous concept, i.e. adherent or non-adherent patient (2). Non-adherence can be primary, when for some reason a patient fails to obtain the medication, and secondary, when the medication is not taken as prescribed (5).

Furthermore, non-adherence can be intentional or unintentional. Intentional non-adherence refers to the patient’s active decision to take or not take the medicine driven by particular reasons such as, for example, perception of therapeutic treatment as unnecessary, miscommunication between physician and patient, duration of illness, side effects of therapy. On the other hand, unintentional non-adherence, which is based on forgetting to take medication, is less related to the beliefs of the individual patient and more to demographic (e.g. lower education, older age) and clinical characteristics (e.g. anxiety, depression) (2).

Adherence to long-term therapy for chronic illnesses in developed countries averages 50%. In developing countries, the rates are even lower. Estimates of the extent to which patients adhere to pharmacotherapy for hypertension vary between 50 and 70% (4).

Adherence of patients to antihypertensive therapy is a multidimensional phenomenon determined by the interaction of five groups of factors called “dimensions”, namely: socio-demographic and economic factors, health team / health system-related factors, health condition-related factors, antihypertensive therapy-related factors and patient-related factors. The most important factors that positively or negatively affect patients’ adherence to antihypertensive therapy are shown in table no. 1. The two most important factors contributing to poor adherence are undoubtedly the asymptomatic and lifelong nature of hypertension (4).

**Table no. 1. Factors affecting patients’ adherence to antihypertensive therapy**

<b>Group of factors</b>	<b>Individual factors</b>
Socio-demographic and economic factors	(-) Low socioeconomic status; illiteracy; unemployment; limited supply and high cost of medication
Health team / health system-related factors	(-) Lack of knowledge and training for health care providers on managing chronic diseases; inadequate relationship between health care provider and patient; lack of knowledge, inadequate time for consultations; lack of incentives and feedback on performance (+) Good relationship between patient and physician
Health condition-related factor	(-) Asymptomatic and lifelong nature of hypertension (+) Understanding and perception about hypertension
Antihypertensive therapy related-factors	(-) Complex treatment regimes; duration of treatment; low drug tolerability, side effects of treatment (+) Monotherapy; less frequent dose; fewer changes in therapy; newer classes of drugs (angiotensin II antagonists, angiotensin-converting enzyme inhibitors, calcium channel blockers)
Patient-related factors	(-) Inadequate knowledge and skills in disease symptoms and treatment management; unawareness of the costs and benefits of treatment; non-acceptance of disease monitoring (+) Perception of health risk related to the disease; active participation in disease monitoring; participation in the treatment of disease
(+) Factors having a positive effect on adherence; (-) factors having a negative effect on adherence.	

Taken and adapted from: Sabaté E. Adherence to long-term therapies: Evidence for action. Geneva: World Health Organization; 2003.

### *Adherence measuring*

Methods for measuring adherence can be broken down into direct and indirect, subjective and objective. Each method has its own advantages and disadvantages, and no method is considered as the gold standard. In direct methods, data on adherence are obtained directly, either by direct observation of the patient, by measuring the concentration of the drug or its metabolite in blood or urine, or by measuring a biological marker in the blood, which is added to the formulation of the drug. Direct methods are precise and objective, but also expensive; they require the presence of a health professional and susceptible to distortion of the results by the patient (6, 7).

In table no. 2, direct methods for measuring adherence are given, as well as their advantages and disadvantages, according to Osterberg and Blaschke (6).

**Table no. 2. Direct methods of measuring adherence**

<b>Direct methods</b>	<b>Advantages</b>	<b>Disadvantages</b>
Directly observed therapy	Most accurate	Patients may hide the tablets in their mouths and discard them later; impractical for routine use
Measurement of concentration of medicine in blood	Objective	Variations in metabolism and “white coat adherence” can give a false impression of adherence; expensive
Measurement of the biological markers in blood	Objective, used in clinical trials, can also be used to measure placebo	It requires expensive quantitative methods and collection of biological samples

Taken and adapted from: Osterberg L, Blaschke T. Adherence to Medication. *N Engl J Med* 2005;353:487-97.

In indirect methods, data on adherence of patients are indirectly obtained. Indirect methods for measuring adherence, as well as their advantages and disadvantages, are given in table no. 3 according to Osterberg and Blaschke. Patient questionnaires and clinical response assessment are relatively easy-to-use methods. Questionnaires are the most common method for measuring adherence, but they are susceptible to misinterpretation and may overestimate patient's adherence. Also, the assessment of clinical response as a measure of adherence has its disadvantages, as many factors other than adherence can affect clinical response (6).

**Table no. 3. Indirect methods of adherence measuring**

Indirect methods	Advantages	Disadvantages
Patient questionnaires, patient self-reports	Simple, inexpensive, the most useful method in the clinical setting	Susceptible to errors with increase between visits; results may be distorted by patient
Pill counts	Objective, quantifiable, simple to perform	Simple alteration of data by patients (e.g. throwing away pills)
Rates of prescription refills	Objective, easy to obtain data	Prescription refill is not equivalent to ingestion of medication; requires a closed pharmaceutical system
Clinical response assessment	Simple, in general easy to perform	Various factors other than adherence may affect clinical response
Electronic medication monitors	Accurate, simple quantification of results, track medication intake patterns	Expensive, device has to be brought to download data
Measurement of physiological markers (e.g. heart rate when taking beta blockers)	Often easy to perform	Marker may be absent for other reasons (e.g. increased metabolism, poor absorption, lack of response)
Patients' diaries	Helpful with poor recall	Can be easily altered by the patient
Questionnaires for caregivers or teachers when patients are minor	Simple, objective	Susceptible to data distortion

Taken and adapted from: Osterberg L, Blaschke T. Adherence to Medication. *N Engl J Med* 2005;353:487-97.

Although certain methods of measuring adherence may have advantages in specific clinical or research settings, the combination of methods increases the accuracy, and a multi-method approach is recommended (6, 7).

### ***Paper objective***

The aim of this paper is to measure the adherence of patients to antihypertensive therapy in the ambulance of family physician at Primary Health Care Centre Cetinje,



as well as to examine the association of adherence with socio-demographic variables and variables of medication status.

## ***Method***

### **Respondents**

The research was conducted as a cross-sectional pilot study using a sample of 120 respondents, who are being treated for hypertension and who visited the ambulance of family physician at Primary Health Care Centre Cetinje in April and May 2022. 1550 patients are registered in this ambulance, of which 743 patients are being treated for hypertension.

The criteria for inclusion in the study were: age of subjects 18 years and older, confirmed diagnosis of hypertension over the past year or longer, use of at least one antihypertensive drug in therapy over the past year or longer, while subjects with cognitive impairments, deterioration of basic health condition or those who did not sign the informed consent were excluded from the study.

### **Questionnaire for adherence of patients to antihypertensive therapy**

For this purpose, an author's questionnaire for adherence of patients to antihypertensive therapy was used, which consists of 3 parts: socio-demographic status, medication status, standardized adherence measuring scale.

Socio-demographic status included gender, age, marital status, education and work status. Medication status was monitoring: length of hypertension treatment, total number of medications, number of antihypertensive medications, suspicion to side effects of antihypertensive therapy, participation in the costs of antihypertensive therapy. Socio-demographic and medication status contain factors that could affect adherence itself.

The Hill-Bone scale for measuring medication adherence is an integral part of the questionnaire. The use of the scale, translation and adaptation in Montenegrin, Serbian, Bosniak and Croatian languages was approved by the Johns Hopkins University School of Nursing.

The Hill-Bone scale for measuring medication adherence is an independent scale, but it is also a subscale of the broader Hill-Bone scale, which, in addition to questions related to taking medication, also contains questions about salt intake and regularity of visits to the doctor. It belongs to subjective methods for measuring adherence and is widely used in various chronic diseases such as hypertension, diabetes, stroke, HIV infection, etc. It consists of 9 questions, and each question has 4 answers with the appropriate number of points according to the Likert scale (1 - never, 2 - some-

times, 3 – often, 4 – always). The total score is obtained by adding up the points of individual questions, with the minimum number of points being 9 and the maximum number of points being 36. The higher number of points indicates worse adherence and vice versa. The so-called perfect adherence implies a total score of 9 points. The Johns Hopkins University School of Nursing does not propose cut-off ranges, such as low, moderate, or high adherence. It suggests examining the distribution of results from a given set of data and determining cut-off values (for example, terciles) that correspond to the given data (2, 8, 9).

To calculate the patient's adherence percentage, based on the achieved number of points on the scale, the following formula was used: % adherence =  $36 - \text{patient's number of points on the scale} / 27 \times 100$ , where 36 is the maximum number of points, and 27 is the range of points on the scale (36- 9). Adherence was categorized as perfect (100%), good or acceptable ( $\geq 80\%$ ) and worse ( $< 80\%$ ), as in line with previous studies (10, 11).

### **Data collection procedure and statistical data processing**

After receiving the health service for which they came to the ambulance of their family physician, meeting the criteria for inclusion in this study and signing the informed consent, the respondents were asked to answer the questions that form an integral part of the aforementioned questionnaire together with the researcher in the free ambulance next door. The questions that are an integral part of the Hill-Bone scale for measuring medication adherence were related to the last month. The answers to the questions from the medication status were verified by subsequent review of the patient's medical record, in order to ensure the reliability of the data.

The collected data were processed in Microsoft Excel and SPSS (Statistical Package for the Social Sciences) 2022. Descriptive and analytical statistics were used. The Shapiro-Wilk test was used to test the normality of the distribution. The difference in adherence in relation to socio-demographic and medication status variables was assessed using the Mann-Whitney U test and the Kruskal-Wallis test. A significance level  $< 0.05$  was considered statistically significant.

### **Ethical aspect of the research**

To conduct this research, the approval of the Ethics Committee of the Primary Health Center Podgorica (No. 05/17-4188 dated 06/05/202 ) was obtained, as well as the approval of the Director of Primary Health Care Center Cetinje, where the research was conducted.

## Results

### Results of patients' adherence to antihypertensive therapy measuring

The average number of points on the Hill-Bone scale for measuring medication adherence obtained by the respondents was  $10.04 \pm 1.90$  (table no. 4). The majority of patients had 9 points (57.5%) and 10 points (24.2%) on the mentioned scale (table no. 5).

**Table no. 4. Total score on the Hill-Bone scale for measuring medication adherence**

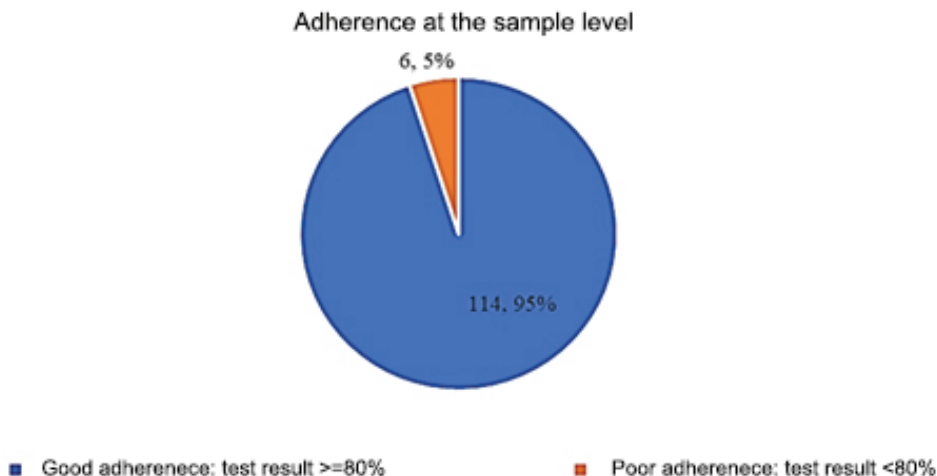
N	Mean $\pm$ SD	Median (IR)	Minimum	Maximum
120	$10,04 \pm 1,90$	9 (9 – 10)	9	20

**Table no. 5. Result of Hill-Bone Scale for measuring medication adherence per number of points**

Number of points on the scale	N	%
9	69	57,5
10	29	24,2
11	6	5,0
12	3	2,5
13	4	3,3
14	3	2,5
15	3	2,5
16	1	0,8
17	1	0,8
20	1	0,8
<b>Total</b>	120	100,0

By calculating the percentage of adherence according to the previously explained formula, the results show that 95% of respondents had good, i.e. acceptable adherence ( $\geq 80\%$ ), which included all those respondents having from 9 to 14 points on the scale. Among them, 57.5% of respondents had perfect adherence (100%), i.e. 9 points on the scale. Less adherent ( $<80\%$ ) was 5% of respondents, and all those respondents having 15 to 20 of points on the scale were included (graph no. 1).

**Graph no. 1. Adherence of patients (%) to antihypertensive therapy in the ambulance of family physician.**



### Socio-demographic and medical status of respondents

The average age of the respondents was  $64.6 \pm 9.28$ , and the majority of respondents were over 60 years old (70.8%). The youngest patient was 36 years old and the oldest 82 years old. More than two thirds of respondents were female (67.5%). Most respondents were married (63.3%). As for education, the majority of respondents graduated from high school (63.3%). The working status is dominated by 69.7% retired people and unemployment at the sample level is 9.2%.

The majority of respondents have been treated for hypertension  $\geq 11$  years (63.3%). The average total number of drugs that the respondents take in regular therapy is  $6.1 \pm 2.85$ , and the range is from one to even 15 drugs. Three or more drugs are taken by 94.2% of respondents in regular therapy. The average number of antihypertensive drugs taken by the respondents is  $2.24 \pm 0.85$ , and the range is from one to four drugs. Almost half of the respondents (48.3%) take 2 antihypertensive drugs, and almost a quarter of them (24.2%) take 3 antihypertensive drugs each. 14.2% of respondents suspected the side effects of antihypertensive therapy. The majority of respondents participate in the costs of antihypertensive therapy, whether it is the full price (10.8%) or a surcharge (53.3%).

The socio-demographic and medical status of the respondents is shown in table no. 6 and table no. 7.

**Table no. 6. Socio-demographic and medical status of respondents (part 1)**

Research variable	N	Mean $\pm$ SD	Median (IR)	Min	Max
Age	120	64,6 $\pm$ 9,28	66,5 (59 – 71)	36	82
Total number of drugs	120	6,1 $\pm$ 2,85	5,5 (4 – 8)	1	15
Number of antihypertensive drugs	120	2,24 $\pm$ 0,85	2 (2 – 3)	1	4

**Table no 7. Socio-demographic and medical status of respondents (part 2)**

Research variable	Categories	N	%
Age (years)	36 – 60	35	29,2%
	> 60	85	70,8%
Gender	Male	39	32,5%
	Female	81	67,5%
Marital status	Married	76	63,3%
	Single	14	11,7%
	Divorced	3	2,5%
	Widower / widow	27	22,5%
Education	No education	6	5,0%
	Primary School	27	22,5%
	Secondary School	76	63,3%
	Higher education	5	4,2%
	High Education	6	5,0%
Employment status	Employed	20	16,8%
	Unemployed	11	9,2%
	Retired	83	69,7%
	Student / housewife /other	5	4,2%
Duration of hypertension treatment (in years)	1 – 5	17	14,2%
	6 – 10	27	22,5%
	11 – 15	35	29,2%
	> 15	41	34,1%
Total number of drugs	1	2	1,7%
	2	5	4,2%
	3 or more	113	94,2%

Number of antihypertensive drugs	1	22	18,3%
	2	58	48,3%
	3	29	24,2%
	4	11	9,2%
Suspected side effects of antihypertensive therapy	Yes	17	14,2%
	No	103	85,8%
Participation in the costs of antihypertensive therapy	Yes, full price	13	10,8%
	Yes, surcharge	64	53,3%
	No	43	35,8%
<b>Total</b>		120	100,0%

### Research results of the association between adherence and variables of socio-demographic and medical status

No statistically significant association was found between adherence and the following variables: gender ( $p = 0.222$ ), age ( $p = 0.364$ ), marital status ( $p = 0.233$ ), education ( $p = 0.421$ ), work status ( $p = 0.195$ ), duration of treatment of hypertension ( $p = 0.979$ ), total number of drugs ( $p = 0.787$ ), number of antihypertensive drugs ( $p = 0.187$ ) and suspected side effects of antihypertensive therapy ( $p = 0.364$ ). Statistically significant association was found only between adherence and respondents' participation in the costs of antihypertensive therapy ( $p = 0.029$ ). Respondents who partially participated in the costs (surcharge) also had the best adherence ( $9.78 \pm 1.84$ ), and adherence did not differ between those who were paying the full price ( $10.2 \pm 2.16$ ) and those who did not participated in the costs of antihypertensive therapy ( $10.3 \pm 1.89$ )  $p > 0.05$ . The results of research of the association between adherence and variables of socio-demographic and medical status are shown in table no. 8.

**Table no. 8. Results of testing the adherence difference in relation to research variables**

Research variable	Category	N	Mean $\pm$ SD	Median (IR)	Test value	P
Age (years)	36 – 60	35	10,2 $\pm$ 2,52	9 (9 – 10)	768	0,364
	> 60	85	9,94 $\pm$ 1,58	9 (9 – 10)		
Gender	Male	39	10 $\pm$ 2,27	9 (9 – 10)	1385	0,222
	Female	81	10,0 $\pm$ 1,71	9 (9 – 10)		

Marital status	Married	76	10,0 ± 2,07	9 (9 – 10)	4,273	0,233
	Single	14	9,78 ± 1,62	9 (9 – 10)		
	Divorced	3	11,3 ± 3,21	10 (9 – 11)		
	Widower / widow	27	10,0 ± 1,32	10 (9 – 10)		
Education	No education	6	10,1 ± 1,94	9,5 (9 – 11)	3,892	0,421
	Primary School	27	10,1 ± 1,89	9 (9 – 10)		
	Secondary School	76	9,81 ± 1,49	9 (9 – 10)		
	Higher education	5	10 ± 2,23	9 (9 – 11,5)		
	High Education	6	12,3 ± 4,36	10,5 (9 – 16,25)		
Employment status	Employed	21	10,2 ± 2,24	9 (9 – 10,75)	4,697	0,195
	Unemployed	11	11,1 ± 3,37	10 (9 – 11)		
	Retired	83	9,81 ± 1,45	9 (9 – 10)		
	Student / housewife / other	5	10,6 ± 2,50	10 (9 – 12,5)		
Duration of hypertension treatment (in years)	1 – 5	17	11,2 ± 3,54	9 (9 – 14,5)	0,189	0,979
	6 – 10	27	9,74 ± 1,25	9 (9 – 10)		
	11 – 15	35	9,97 ± 1,74	9 (9 – 10)		
	> 15	41	9,80 ± 1,18	9 (9 – 10)		
Total number of medicines	1	2	12 ± 4,24	12,00	0,478	0,787
	2	5	10,4 ± 2,6	9 (9,0 – 12,5)		
	3 or more	113	9,99 ± 1,83	9 (9 – 10)		
Number of antihypertensive drugs	1	22	10,7 ± 3,08	9 (9 – 11,5)	4,801	0,187
	2	58	9,72 ± 1,43	9 (9 – 10)		
	3	29	10,1 ± 1,74	10 (9 – 10)		
	4	11	10 ± 1	10 (9 – 11)		
Suspected side effects of antihypertensive therapy	Yes	17	10,7 ± 3,19	10 (9 – 10)	768	0,364
	No	103	9,92 ± 1,58	9 (9 – 10)		

Participation in the costs of antihypertensive therapy	Yes, full price	13	10,2 ± 2,16	9 (9 – 10)	7,057	0,029
	Yes, sur-charge	64	9,78 ± 1,84	9 (9 – 10)		
	No	43	10,3 ± 1,89	10 (9 – 11)		

## Discussion

In this research it was determined that 95% of respondents had a good i.e. acceptable adherence, measured using the Hill-Bone medication adherence scale ( $\geq 80\%$  score on the scale).

This result deviates from the WHO's general assessment, according to which in developed countries patients' adherence to treatment of chronic diseases in the general population is around 50%, and is much lower in developing countries. Also, the WHO publication additionally states that estimates of the extent to which patients adhere to pharmacotherapy for hypertension vary between 50 and 70% (4).

However, by comparing the results on the degree of adherence of subjects to antihypertensive therapy with other research, where the same scale was used to measure medication adherence, and the degree of adherence was researched in the same manner, different data are obtained. For example, in a study conducted in India, on 452 subjects, more than 80% of the subjects also had a good i.e. acceptable adherence (10), as well as in a study conducted in Zambia, on a sample of 237 respondents (70%) (12). In a study conducted in Primary Health Care in Namibia, on a sample of 120 patients, which was also the examined sample, less than 50% of respondents had a good i.e. acceptable adherence (11).

This deviation from the WHO's general assessment, and at the same time such a good result, at the beginning, can be explained by the specificity of the sample of respondents for which adherence was measured. In fact, it is a sample of respondents, i.e. patients from one family physician's ambulance, who pay visits to their chosen physician, and not from the general population. Other explanations for such good adherence should be sought in the potential factors that determine it, which will be discussed below.

In connection with the above, it should be emphasized that although there are a number of different scales for measuring adherence, including the Hill-Bone scale, there is still no gold standard (13). Also, since there is no ideal method for measuring adherence, the simultaneous use of several methods in measuring adherence seems to be the best solution (6, 7). This allows for new researches in which some other methods will be used to measure adherence, such as, for example, frequency of picking up drugs in pharmacies, assessment of clinical response to therapy, etc.



In the WHO publication, in the group of socio-demographic and economic factors that influence adherence, illiteracy and unemployment are highlighted, while data on age are inconsistent, and gender and marital status are not mentioned as factors that influence adherence of patients to antihypertensive therapy. (4). In the paper by Hashmi SK et al., it is stated that in their study in Pakistan, on a sample of subjects with an average age of 52 years, it was found that adherence improves in older age, similar to other parts of the world (14). In a study conducted in Poland, on a sample of respondents with an average age of 72.1 years, it was found that adherence decreases with age (15). This indicates that adherence is lower at younger ages, then it improves, and only in much older age does adherence begin to decrease again. In the paper by AlHadlaq RK et al., it is stated that in their research in Saudi Arabia, no association between adherence and gender was found, although there are studies in which better adherence was found in women (16). According to the WHO publication, some studies state that organizational factors (time spent with doctors, continuity of health care, communication style and interpersonal style of doctors) are much more important than socio-demographic variables in influencing patients' adherence (4).

In this study, no association of adherence with socio-demographic status variables (gender, age, marital status, education, work status) was found, which is consistent with the results of other studies that used the same scale to assess adherence. Such research was conducted in the United States of America, on a sample of 208 Korean Americans (2), and the already mentioned research in Namibia and Zambia (11, 12).

When it comes to socio-demographic variables, the examined sample is specific in the following respect: more than two-thirds of the respondents are female, the average age of the respondents is 64.6, and the majority were married and retired with a high school diploma. Based on the previously mentioned papers, the female gender, average age of the respondents, sufficient level of education (high school) and retired status can contribute to good adherence of our respondents.

Some of the more familiar definitions of adherence to antihypertensive therapy, as stated in the WHO publication, are related to aspects of pharmacological treatment itself and include duration of treatment, complexity of treatment, tolerability and side effects of drugs, supply and price of drugs. Frequency of dosing, number of concurrent drugs taken and changes in antihypertensive drugs are some of the factors that contribute to the complexity of treatment and they have been researched in many observational studies. Shorter duration of treatment, its simplicity (fewer individual antihypertensive doses, monotherapy, fewer changes in antihypertensive drugs), better tolerability and fewer side effects, good supply and lower prices of drugs are associated with better adherence (4).

In this research, no association of adherence was found with the duration of hypertension treatment (treatment duration), the total number of drugs and the number of antihypertensive drugs, as well as with side effects of antihypertensive therapy. The association between adherence and duration of treatment was not found in the aforementioned studies in India and Namibia (10, 11). An association was found in a study conducted in Palestine, on a sample of 648 subjects, where, surprisingly, better adherence was observed with a longer duration of hypertension treatment (17). The examined relationship between adherence and the total number of medications was not found in the research in Zambia, although it is described in the literature (4, 5); however, a relationship was found with the number of antihypertensive medications and the occurrence of side effects of antihypertensive therapy (12). Patients taking three antihypertensive drugs had better adherence (12). In the aforementioned study by Hashmi SK and associates, it was also found that adherence was better with more antihypertensive drugs used in therapy, which, as they state, is surprising and contrary to what has been published so far. They explain this as that patients who take more antihypertensive drugs feel that their disease is more severe and they are more careful about taking the drugs, as well as that patients who take more drugs are less likely to forget taking them than when they only have to take one drug (14). In this research, as well as in the study conducted in Palestine, no correlation was found between adherence and the number of antihypertensive drugs in therapy (17). There are also studies in which no correlation between adherence and the presence of side effects of antihypertensive drugs has been proven (10).

When it comes to medication status, the examined sample is specific in the following respect: almost two-thirds of the respondents have been treated for hypertension for 11 years and more, the average total number of drugs that the respondents take in regular therapy is 6.1, the average number of antihypertensive drugs that the respondents take is 2,24, and 14.2% of the respondents suspected side effects of antihypertensive therapy, most citing hypotension. Based on the above-mentioned papers, the length of treatment for hypertension can be in favor of the good adherence of our subjects, given that these are patients who had enough time to familiarize themselves with the characteristics of their disease and the treatment itself, the average number of antihypertensive that could affect them experience their disease more seriously as well as smaller number of patients with suspected side effects of antihypertensive therapy.

The majority of respondents participate in the costs of antihypertensive therapy, whether it is the full price or a surcharge. In this research, adherence was found to be related to participation in the costs of antihypertensive therapy. Respondents who partially participated in the costs of antihypertensive therapy (surcharge) had the best adherence, and adherence was not distinguished between those who were paying the full price and those who did not participate in the costs of antihyper-

tensive therapy. In studies in which participation in the costs of antihypertensive therapy was expressed in a similar way as in this research, no association between adherence and participation in the costs of antihypertensive therapy was found (14, 18). Health systems, on the other hand, according to the literature, create barriers to adherence with high prices of drugs, surcharges for drugs, or both (6, 19). This result, which is different from the data in the literature, could be explained by the fact that the surcharges for most antihypertensive drugs in our country are not high, and once patients decide to pay extra for the drug, they tend to take it regularly.

This is the first study on adherence of patients to antihypertensive therapy in our country, and there is awareness of its limitations. The research was conducted on a sample of respondents in one ambulance of one family physician for adults, who came for an examination during the research period, and the results obtained apply to them and cannot be generalized to patients who gravitate towards the Cetinje Health Center. Patients with cognitive impairments, who are known to be less adherent, were excluded from the study (5). One subjective method was used to measure adherence, although according to the literature, in order to increase the objectivity of the results a multi-method approach is suggested. The researcher explained in detail the ambiguities related to the questions from the questionnaire to the respondents, but it cannot be ruled out with certainty that the patients did not, at least to the smallest extent, give answers that were acceptable to the researcher.

## ***Conclusion***

In this study of patients' adherence to antihypertensive therapy in the ambulance of family physician for adults at the Cetinje Health Center, it was determined that 95% of respondents had a good, i.e. acceptable adherence. Of the examined variables of socio-demographic and medication status, a statistically significant correlation was found only between adherence and the respondents' participation in the costs of antihypertensive therapy.

The results of this research, bearing in mind the inconsistency of the data in the literature, support the view of the researchers who found that patients' personal beliefs about the necessity of taking therapy and the dangers of side effects are better predictors of adherence than socio-demographic and clinical factors such as the number of drugs in therapy (20).

In the end, it should be emphasized that new research are needed to be conducted on a sample of patients from several ambulances of family physicians for adults, using also other methods for measuring adherence, as well as examining other potential factors that can affect adherence, with the aim of more objective measurement of patients' adherence to antihypertensive therapy and finding interventions to improve it.

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### *Conflict of interest*

There are no conflicts of interest.

### *Literature*

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