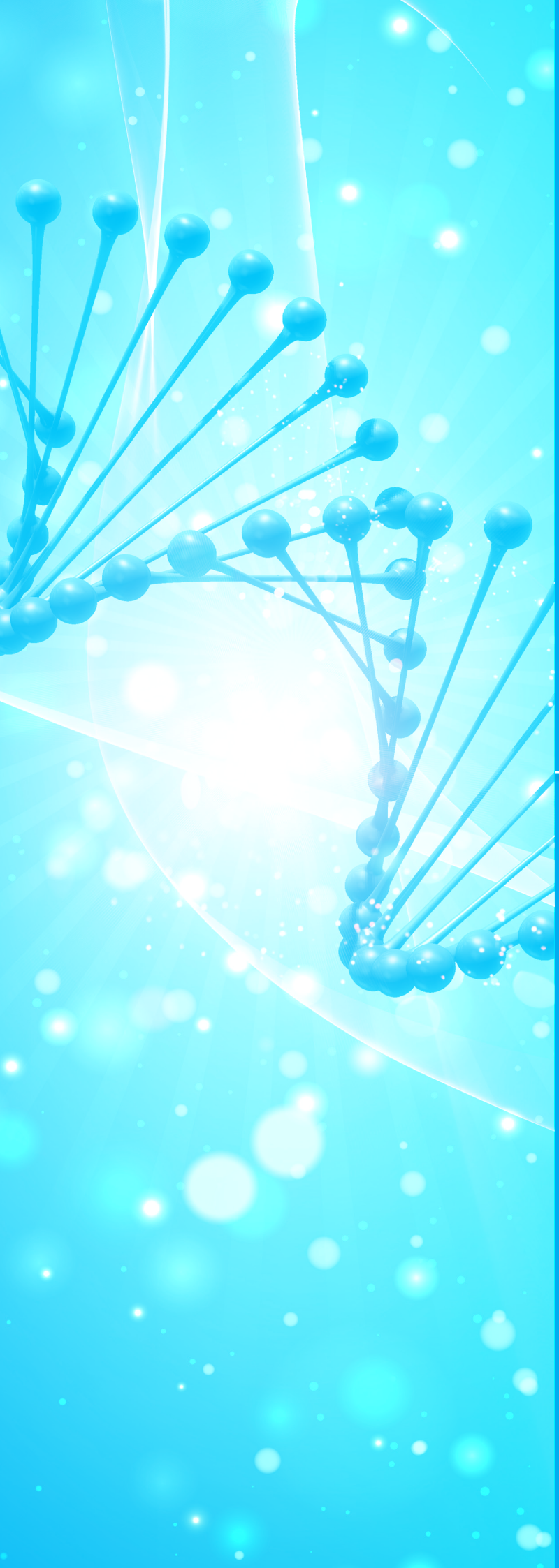

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# POVEZANOST HEMSEKSA SA SEKSUALNIM PONAŠANJEM I POLNO PRENOSIVIM INFEKCIJAMA KOD MUŠKARACA KOJI IMAJU SEKSUALNE ODNOSE SA MUŠKARCIMA U BEOGRADU

**Milan Bjekić[1], Dubravka Salemović[2], Hristina Vlajinac[3], Jelena Marinković[4]**

[1] Gradski zavod za kožne i venerične bolesti, Beograd, Republika Srbija
[2] Klinika za infektivne i tropske bolesti, Klinički centar Srbije, Beograd, Republika Srbija
[3] Institut za epidemiologiju, Medicinski fakultet, Beograd, Republika Srbija
[4] Institut za statistiku i informatiku, Medicinski fakultet, Beograd, Republika Srbija

[*] Korespondencija: prim. dr Milan Bjekić, Gradski zavod za kožne i venerične bolesti, Džordža Vašingtona 17, 11000 Beograd, Srbija; e-mai: milinkovski@gmail.com

**SAŽETAK**

**Uvod/Cilj:** Hemseks je česta praksa među muškarcima koji imaju seksualne odnose sa muškarcima (MSM). Cilj ovog istraživanja bio je da se proceni prevalencija hemseksa među MSM populacijom u Beogradu i njegova povezanost sa njihovim ponašanjem i polno prenosivim infekcijama.
**Metode:** Studija preseka sprovedena je u dve zdravstvene ustanove u Beogradu i obuhvatila je 469 MSM osoba. Anonimnom anketom od svih ispitanika su prikupljeni podaci o demografskim karakteristikama, razlogu dolaska lekaru, seksualnoj anamnezi i upotrebi seksualizovanih droga u prethodnih šest meseci.
**Rezultati:** Od 469 ispitanika 123 (26,2%) je praktikovalo hemseks, a gama-hidroksibutirat (GHB) i gama-butirolakton (GBL) su bile najčešće korišćene seksualizovane droge (84,6%). Prema rezultatima multivarijantne logističke regresione analize učesnici koji su praktikovali hemseks značajno su se razlikovali od ostalih ispitanika u sledećim karakteristikama: češće su bili zaposleni (Unakrsni odnos – UO=2,50; 95% interval poverenja - 95%IP=1,19-5,26; p=0,015), imali su veći broj seksualnih partnera u poslednjih šest meseci (UO=1,39; 95%IP=1,14-1,72; p=0,002) i analne seksualne odnose bez upotrebe kondoma (UO=3,23; 95%IP=1,64-6,25; p=0,001), češće su praktikovali grupni seks tokom poslednjih šest meseci (UO=4,35; 95%CI=2,38-7,69; p<0,001), konzumirali su veće količine alkohola (UO=2,50; 95%CI=1,54-4,00; p<0,001) i češće su imali bakterijsku polno prenosivu infekciju u poslednjih godinu dana (UO=2,70; 95%CI=1,61-4,54; p<0,001). Učestalost upotrebe rekreativnih droga bila je ređa kod ispitanika koji su praktikovali hemseks (UO=0,59; 95%CI = 0,41-0,88; p=0,009).
**Zaključak:** MSM osobe koje su imale hemseks češće su praktikovale visoko rizično seksualno ponašanje i češće su obolevale od bakterijskih polno prenosivih infekcija. Rastući fenomen hemseksa među MSM populacijom zahteva podizanje svesti o problemima hemseksa kako među pripadnicima ove vulnerabilne populacije, tako i među zdravstvenim radnicima.

**Ključne reči:** hemseks, MSM, seksualno ponašanje, polno prenosive infekcije

## Uvod

Rekreativne droge predstavljaju (i)legalne hemijske supstance koje zbog svog psihoaktivnog dejstva izazivaju osećaj zadovoljstva i uživanja, umanjuju inhibicije ali sa druge strane uzrokuju i različite zdravstvene probleme i nastanak zavisnosti kod korisnika. Najčešće korišćeni su amfetamini, nitrati, kokain, marihuana, ekstazi i lekovi za lečenje erektilne disfunkcije (1), kao i takozvane seksualizovane droge – hemseks (engl. *chemsex*), naročito korišćene u populaciji muškaraca koji imaju seksualne odnose sa muškarcima (MSM), pre ili u toku seksualnog odnosa, da bi pojačale seksualni učinak i zadovoljstvo (2). Hemseks u užem smislu obuhvata gama-hidroksibutirat (GHB- *gamma-hydroxybutyrate*) i gama-butirolakton (GBL- *gamma-butyrolactone*), kristalni metamfetamin i mefedron (2,3). Upotreba ovih droga povezana je sa visokorizičnim seksualnim ponašanjem i češćim prenošenjem polno prenosivih infekcija (PPI) (4). Sve veća upotreba novih psihoaktivnih supstanci u Evropi zahte-

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# CHEMSEX RELATED SEXUAL BEHAVIOURS AND SEXUALLY TRANSMITTED INFECTIONS AMONG MEN WHO HAVE SEX WITH MEN IN BELGRADE

**Milan Bjekić[1], Dubravka Salemović[2], Hristina Vlainac[3], Jelena Marinković[4]**

[1] City Institute for Skin and Venereal Diseases, Belgrade, Republic of Serbia
[2] Institute of Infectious and Tropical Diseases, Clinical Centre of Serbia, Belgrade, Republic of Serbia
[3] Institute of Epidemiology, Faculty of Medicine, University of Belgrade, Republic of Serbia
[4] Institute of Statistics and Informatics, Faculty of Medicine, University of Belgrade, Republic of Serbia

[*] Correspondence: dr Milan Bjekić, MD, PhD, City Institute for Skin and Venereal Diseases, George Washington 17, 11000 Belgrade, Republic of Serbia, e-mail: milinkovski@gmail.com

**SUMMARY**

**Background/Aim:** Chemsex is a common practice among men who have sex with men (MSM). The aim of this study was to assess the prevalence of chemsex in the MSM population in Belgrade and its association with their behaviour and sexually transmitted infections.
**Methods:** A cross-sectional study was conducted at two institutes in Belgrade over a six-month period and it covered 469 MSM. Data on demographic characteristics, reasons of attendance, sexual history, sexual behaviour and sexualized drugs use in the previous six months were collected from all participants by the use of a questionnaire.
**Results:** Chemsex was practiced by 123 (26.2%) participants and GHB/GBL was most commonly used (84.6%). According to the results of multivariate logistic regression analysis those practicing chemsex differed from other participants significantly, independently of other factors, in the following characteristics: they were more frequently employed (Odds Ratio – OR=2.50, 95% confidence interval – 95%CI=1.19-5.26, p=0.015), had a greater number of sex partners in the last six months (OR=1.39, 95%CI =1.14-1.72, p=0.002), had condomless anal sex (OR=3.23, 95%CI=1.64-6.25, p=0.001) and group sex more frequently in the last six months (OR=4.35, 95%CI= 2.38-7.69, p<0.001), used a greater quantity of alcohol (OR=2.50, 95%CI 1.54-4.00, p<0.001), and had bacterial STIs more frequently in the last year (OR=2.70, 95%CI=1.61-4.54, p<0.001). The frequency of recreational drugs use was lower in those engaged in chemsex (OR=0.59, 95%CI=0.41-0.88, p=0.009).
**Conclusion:** MSM engaged in chemsex practiced high risk sexual behaviour and suffered from bacterial sexually transmitted infections more frequently. The growing phenomenon of chemsex among MSM requires raising awareness about issues regarding chemsex both among the members of this vulnerable population and healthcare workers.

**Key words:** chemsex, men who have sex with men (MSM), sexual behaviour, sexually transmitted infections

## Introduction

Recreational drugs are (il)legal chemical substances that, due to their psychoactive effect, cause the feeling of pleasure and enjoyment, reduce inhibitions, but on the other hand, they also cause various health problems and addiction in users. The most commonly used are amphetamines, nitrates, cocaine, marijuana, ecstasy and drugs used for the treatment of erectile dysfunction (1), as well as the so-called sexualized drugs – chemsex, which are mostly used by the population of men who have sex with men (MSM), before or during sexual intercourse in order to enhance sexual performance and satisfaction (2). Chemsex in the narrower sense includes gamma-hydroxybutyrate (GHB) and gamma-butyrolactone (GBL), crystal methamphetamine and mephedrone (2,3). The use of these drugs is associated with high-risk sexual behavior and more frequent transmission

va proširenje liste seksualizovanih droga da se ne bi previdео njihov uticaj na seksualno ponašanje i udruženost sa PPI (6). Neke rekreativne droge koje imaju povoljan uticaj na seksualno zadovoljstvo, poput popersa, marihuane i lekova koji se koriste za erektilnu disfunkciju ne ubrajaju se u hemseks zbog njihove česte upotrebe u različite svrhe (7).

Istraživanje sprovedeno u Republici Srbiji u toku 2014. godine je pokazalo da je 8% odrasle populacije uzrasta od 18 do 64 godine koristilo tokom života neku psihoaktivnu supstancu, a najčešće su je koristili muškarci (12,8%) starosne dobi od 18 do 34 godine (8). Marihuana je bila najčešće korišćena psihoaktivna supstanca, dok su se amfetamin, kokain i ekstazi veoma retko koristili u opštoj populaciji, a novije psihoaktivne supstance (NPS) poput ketamina i GHB je koristilo manje od 0,1% mlađih odraslih osoba (8). Upotreba NPS u Srbiji se registruje kod MSM osoba koje obično koriste GHB tokom seksualnih aktivnosti i kod mladih koji ih konzumiraju na žurkama i muzičkim festivalima (9).

S obzirom na to da nemamo podatke o učestalosti i vrstama rekreativnih droga koje se koriste među MSM populacijom u našoj zemlji, a posebno podatke o upotrebi seksualizovanih droga, cilj ovog istraživanja je bio da se utvrdi prevalencija hemseksa i njegova povezanost sa seksualnim ponašanjem i PPI među MSM populacijom u Beograd.

## Metod

U studiju preseka u toku šestomesečnog perioda (1.08.2022–31.01.2023. godine) uključeni su pripadnici MSM populacije koji su došli na pregled u Gradski zavod za kožne i venerične bolesti u Beogradu i u ambulantu za HIV infekciju Infektivne klinike Kliničkog centra Srbije. Od svih ispitanika podaci su prikupljeni upitnikom. Upitnik je sadržao pitanja koja su se odnosila na njihove osnovne demografske karakteristike, HIV-status i eventualnu upotrebu preekspozicione profilakse za HIV (engl. *pre-exposure prophylaxis*, PrEP), seksualno ponašanje u poslednjih šest meseci, na podatke o lečenim bakterijskim PPI u poslednjih godinu dana, kao i o upotrebi rekreativnih droga tokom seksa u poslednjih šest meseci. Takođe su prikupljeni podaci o korišćenju ilegalnih droga u poslednjih šest meseci [(hemseks: GHB, GBL, ekstazi – 3,4-metilendioksimetamfetamine (engl. *Methylenedioxymethamphetamine* – MDMA), ketamin, mefedron, kristalni metamfetamin i amfetamin), ili druge rekreativne droge (oralni inhibitori fosfodiesteraze 5 za erektilnu disfunkciju, popers i marihuanu)] i o upotrebi intravenskih droga. Procena upotrebe alkohola u poslednjih godinu dana vršena je na osnovu skraćene verzije upitnika Svetske Zdravstvene Organizacije – AUDIT testa (engl. *Alcohol Use Disorders Identification Test*) (10) prema kojoj su ispitanici klasifikovani u tri grupe (manje rizično pijenje, rizično pijenje i visoko rizično pijenje).

Pacijentima sa simptomima polnih bolesti rađeni su testovi na gonoreju, hlamidijazu i sifilis. Ovi testovi su rađeni i kod pacijenata koji su bili izloženi PPI. Ispitanici koji nisu imali simptome PPI nego su došli zbog nekog drugog razloga (dermatološki problemi u anogenitalnoj regiji poput gljivične infekcije - *tinea cruris*, *lichen sclerosus*-a ili su došli na savetovanje) nisu bili testirani na polne bolesti. Gonoreja je dijagnostikovana identifikacijom intracelularnih diplokoka u leukocitima iz uretralnog sekreta obolelih, dok je uretralna hlamidijaza potvrđena pozitivnim PCR (engl. *Polymerase chain reaction*; polimeraza lančana reakcija) testom. Pozitivnim specifičnim treponemskim serološkim testom (engl. *Treponema Pallidum Haemagglutination Assay* – TPHA; Treponema Pallidum hemaglutinacioni test) i nespecifičnim treponemskim testom (engl. *Venereal Disease Research Laboratory* - VDRL; laboratorijski test za istraživanje venеričnih bolesti) postavljene su dijagnoze primarnog sifilisa, sekundarnog sifilisa i ranog latentnog sifilisa. Testovi za HIV i hepatitis nisu bili rađeni, ali svi naši ispitanici su znali svoj HIV status. Dozvolu za istraživanje odobrio je Etički odbor Gradskog zavoda za kožne i venerične bolesti u Beogradu (br. 1861/3).

U statističkoj analizi korišćene su univarijantna i multivarijantna logistička regresiona analiza. Sve varijable koje su prema rezultatima univarijantne logističke regresione analize bile povezane sa hemseksom na nivou statističke značajnosti $p \leq 0,1$ bile su uključene u multivarijantnu analizu, dok su varijable koje su bile ograničene samo na deo ispitivane populacije (upotreba PrEP-a, broj i učestalost upotrebe rekreativnih droga) jedna po jedna dodavane u nove modele multivarijantne analize. Metod selekcije bio je unazadni (engl. *backward*) *Wald* test, dok su sve *p* vrednosti bile bazirane na dvosmernom (engl. *two-tailed*) testu, a statistički značajnim smatrane su vrednosti $p < 0,05$. Softverski paket programa *IBM SPSS Statis-*

of sexually transmitted infections (STIs) (4). The increasing use of new psychoactive substances in Europe requires the expansion of the list of sexualized drugs so that their influence on sexual behavior and association with STIs would not be overlooked (6). Some recreational drugs that have a beneficial effect on sexual pleasure, such as poppers, marijuana, and drugs used for erectile dysfunction are not included in chemsex because of their frequent use for different purposes (7).

The research, which was conducted in the Republic of Serbia in 2014, showed that 8% of the adult population aged 18 to 64 used a psychoactive substance during their lifetime, while it was most frequently used by men (12.8%) aged 18 to 34 (8). Marijuana was the most frequently used psychoactive substance, while amphetamine, cocaine and ecstasy were very rarely used in the general population, and newer psychoactive substances (NPSs) such as ketamine and GHB were used by less than 0.1% of young adults (8). The use of NPSs in Serbia was registered among MSM who frequently used GHB during sexual activities and among young people who used it at parties and music festivals (9).

Given that we do not have data on the frequency and types of recreational drugs used in the population of MSM in our country, and especially data on the use of sexualized drugs, the aim of this study was to determine the prevalence of chemsex and its association with sexual behavior and STIs among MSM in Belgrade.

## Methods

The members of the MSM population who came for an examination or to the counseling center for sexually transmitted diseases of the City Institute for Skin and Venereal Diseases in Belgrade and for the regular check-up in the outpatient clinic for HIV at the Clinic for Infectious Diseases of the Clinical Center of Serbia were included in a cross-sectional study during a six-month period (August 1, 2022–January 31, 2023). Data were collected from all respondents using a questionnaire. The anonymous questionnaire contained questions related to their basic demographic characteristics, HIV-status and eventual use of pre-exposure prophylaxis for HIV (English: pre-exposure prophylaxis, PrEP), sexual behavior in the last six months, data on treated bacterial PPIs in the last year, as well as the use of recreational drugs during sex in the last six months. Also, data were collected on the use of illegal drugs in the last six months [(hemsex: GHB, GBL, ecstasy - 3,4-methylenedioxymethamphetamine (MDMA), ketamine, mephedrone, crystal methamphetamine and amphetamine), or other recreational drugs (oral phosphodiesterase 5 inhibitors for erectile dysfunction, poppers, and marijuana)] and on intravenous drug use. The assessment of alcohol use in the last year was carried out on the basis of a shortened version of the World Health Organization's AUDIT test (Alcohol Use Disorders Identification Test) (10), according to which the respondents were classified into three groups (low-risk drinking, risky drinking and high-risk drinking).

All patients who had symptoms of STIs were tested for gonorrhea, chlamydia and syphilis. These tests were also performed for patients who were exposed to PPIs. Those participants who did not have the symptoms of STIs but came due to some other reasons (dermatological problems in the anogenital region such as fungal infections – *tinea cruris*, *lichen sclerosus* or came for counseling) were not tested for STDs. Gonorrhea was diagnosed by identifying intracellular diplococci in leukocytes from the urethral secretions of patients, while urethral chlamydia was confirmed by a positive PCR (Polymerase chain reaction) test. A positive specific treponema serological test (Treponema Pallidum Hemagglutination Assay - TPHA) and a non-specific treponema test (Venereal Disease Research Laboratory - VDRL) were used for diagnosing primary, secondary and early latent syphilis. Tests for HIV and hepatitis were not performed, but all our subjects knew their HIV status. The permit for the research was approved by the Ethics Committee of the City Institute for Skin and Venereal Diseases in Belgrade (No. 1861/3).

Univariate and multivariate logistic regression analysis were used in the statistical analysis of differences between participants who practiced chemsex and those who did not. All variables, which were associated with chemsex at the level of statistical significance $p<0.1$ according to the results of univariate analysis, were included in the multivariate analysis. The variables, which were limited only to one part of the examined population, such as PrEP, the number of recreational drugs and frequency of their use

*tics for Windows, version 23* (*Armonk, NY, IBM Corp.*) je korišćen za analizu baze podataka.

## Rezultati

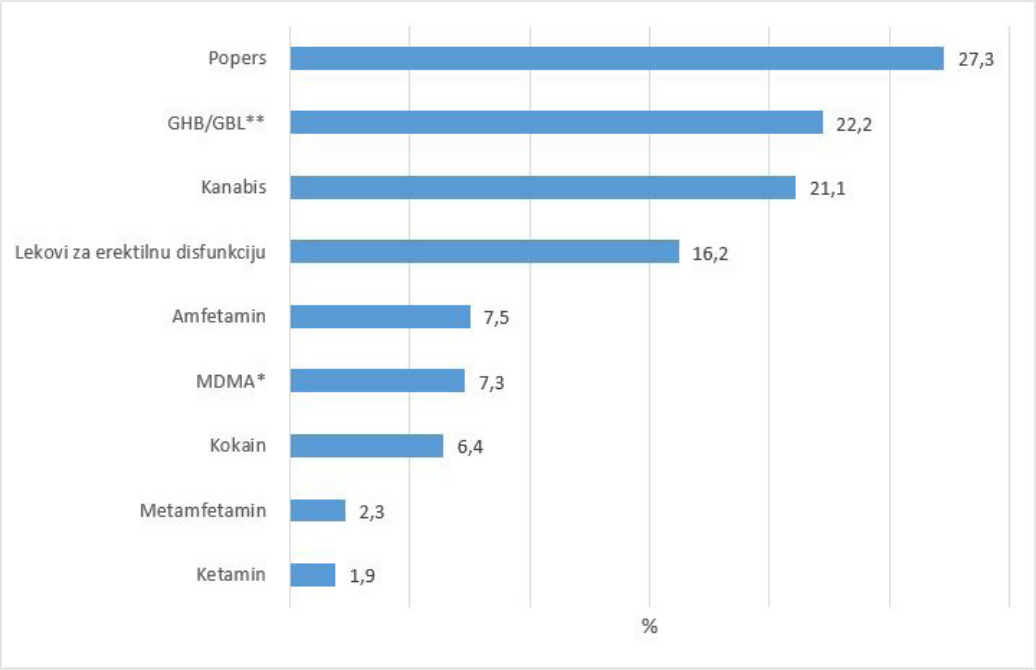
U studiju je uključeno 469 MSM osoba, od kojih je 48,6% koristilo neku rekreativnu drogu, a prevalencija hemseksa je iznosila 26,2%. Najveći broj ispitanika je koristio popers (23,7%), zatim GHB/GBL (22,2%), marihuanu (21,1%) i lekove za erektilnu disfunkciju (16,2%). Upotreba ostalih droga poput ketamina, metamfetamina, kokaina, MDMA i amfetamina je registrovana u manjem procentu od 1,9% do 7,5% (Grafikon 1).

Najveći broj ispitanika je bio starosne dobi između 26 i 45 godina (70,4%), a procenat onih sa nižim i višim stepenom obrazovanja je bio sličan (49,9% vs. 50,1%), dok je 79,7% ispitanika bilo zaposleno (Tabela 1). Prema rezultatima univarijantne logističke regresione analize ispitanici koji su praktikovali hemseks (122) u odnosu na one koji ga nisu praktikovali (346 ispitanika) su bili statistički značajno češće zaposleni (p<0,001), dolazili su kod lekara usled simptoma PPI ili podatka o izlaganju PPI (p<0,002), konzumirali su veće količine alkohola (p<0,001) i veći broj rekreativnih droga (p<0,001). Osobe koje su praktikovale hemseks su češće bile HIV pozitivne (p=0,053) i češće su koristile PrEP (p<0,001). S druge strane ovi ispitanici su znatno ređe koristili droge u toku poslednjih šest meseci u poređenju sa ispitanicima koji nisu praktikovali hemseks (p=0,007). Ispitanici u poređenim grupama nisu se razlikovali prema uzrastu, obrazovanju i podatku o tome kada su imali poslednji seksualni odnos bez upotrebe droga – „sober seks" (Tabela 1).

Prema rezultatima prikazanim u Tabeli 2, ispitanici koji su praktikovali hemseks, u poređenju sa onima koji ga nisu praktikovali, tokom poslednjih šest meseci imali su veći broj seksualnih partnera (p<0,001), analne seksualne odnose bez upotrebe kondoma (p<0,001), učestvovali su u grupnom seksu (p<0,001), imali su neku bakterijsku PPI u poslednjih godinu dana (p<0,001), novodijagnostikovanu bakterijsku PPI (p<0,001) i češće su pripadali osobama sa ponovnim PPI – imali su više od jedne bakterijske PPI u poslednjih godinu dana (p<0,001).

Od bakterijskih PPI kod svih ispitanika sifilis je bio najčešće dijagnostikovan – 122 (26%), potom gonoreja (kod 41 ispitanika – 8,9%) i hlamidijaza (kod 16 ispitanika -3,5%). Od ostalih PPI genitalne bradavice su dijagnostikovane kod 22 (4,8%) pacijenta, majmunske boginje kod 6 (1,3%), *molluscum contagiosum* infekcija kod 3 (0,6%) i genitalni herpes kod 1 (0,2%) pacijenta.

Rezultati multivarijantne logističke regresione analize su prikazani u Tabeli 3. U odnosu na osobe koje nisu praktikovale hemseks, ispitanici koji su




MDMA (ekstazi – 3,4-metilendioksimetamfetamine); GHB/GBL (gama-hidroksibutirat/gama-butirolakton)

**Grafikon 1.** Prevalencija (%) upotrebe rekreativnih droga tokom poslednjih 6 meseci među 469 muškaraca koji su imali seksualne odnose sa muškarcima

were added one by one to the new models of multivariate analysis. The selection method was the backward Wald test. All p values were based on the two-tailed test, while the values of $p < 0.05$ were considered to be statistically significant. The software package IBM SPSS Statistics for Windows, version 23 (Armonk, NY, IBM Corp.) was used for the analysis of database.

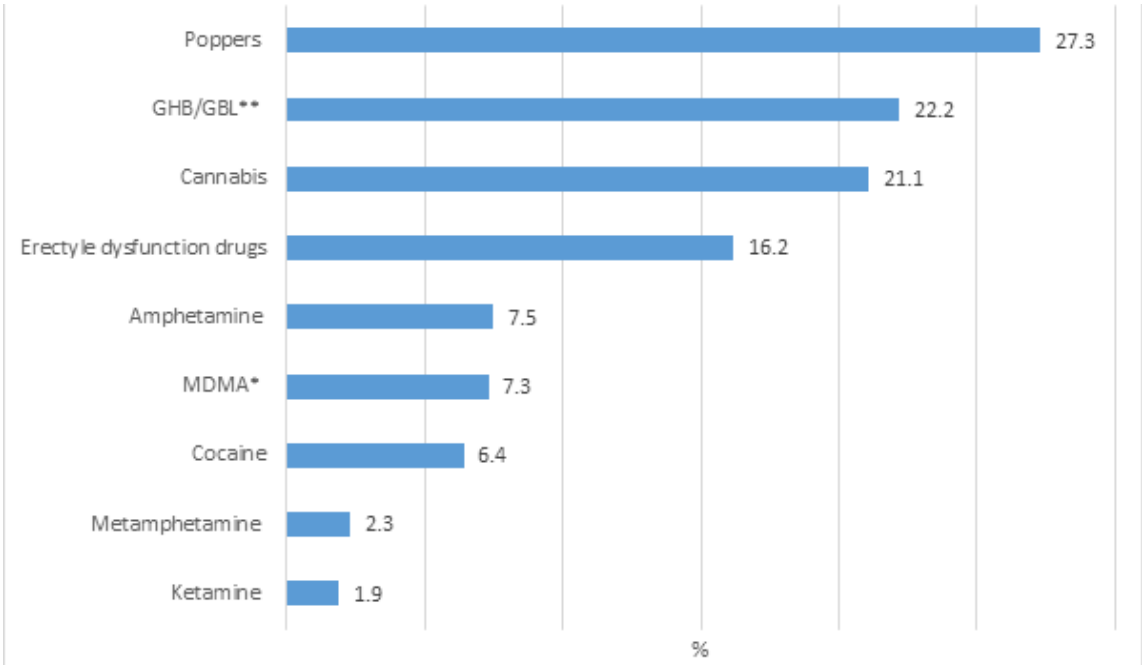
## Results

469 MSM were included in the study, 48.6% of whom used recreational drugs, while the prevalence of chemsex was 26.2%. The largest number of participants used poppers (23.7%), followed by GHB/GBL (22.2%), marijuana (21.1%) and drugs for erectile dysfunction (16.2%). The use of other drugs such as ketamine, methamphetamine, cocaine, MDMA and amphetamine was registered in smaller percentages, from 1.9% to 7.5% (Graph 1).

The largest number of participants belonged to the age groups between 26 and 45 years (70.4%), while the percentage of those participants with a lower and higher level of education was similar (49.9% vs. 50.1%), while 79.7% of respondents were employed (Table 1). According to the results of univariate logistic regression analysis, the participants who practiced chemsex (122) in comparison to those who did not practice it (346 respondents) were more often employed and it was statistically significant ($p<0.001$), came to the doctor due to the symptoms of STIs or data on the exposure to STIs ($p<0.002$), they consumed greater amounts of alcohol ($p<0.001$) and a larger number of recreational drugs ($p<0.001$). Persons who practiced chemsex were more often HIV positive ($p = 0.053$) and they used PrEP more often ($p < 0.001$). On the other hand, these participants used drugs significantly less often during the last six months compared to those respondents who did not practice chemsex ($p = 0.007$). The participants in the compared groups did not differ according to age, education and data related to the fact when they had the last sexual intercourse without the use of drugs – "sober sex" (Table 1).

According to the results shown in Table 2, the participants who practiced chemsex in comparison to those who did not practice it in the last six months had a higher number of sexual partners ($p < 0.001$), anal sexual relations without using a condom ($p< 0.001$), participated in group sex ($p < 0.001$), had some bacterial sexually transmitted infection in the last year ($p < 0.001$), newly diagnosed bacterial STI ($p < 0.001$) and they belonged to persons with repeated STIs – had more than one bacterial STI in the last year ($p < 0.001$).

Of all bacterial STIs in all participants, syphilis was most often diagnosed – 122 (26%), followed by gonorrhea (in 41 participants – 8.9%) and




MDMA (ecstasy – 3,4- Methylenedioxymethamphetamine); GHB/GBL (gamma-hydroxybutyrate)/gamma-butyrolactone)

**Figure 1.** Prevalence (%) of individual recreational drug use in the past six months among 469 males who have sex with males

**Tabela 1.** Distribucija ispitinika koji su praktikovali hemseks i onih koji nisu u odnosu na sociodemografkse i neke druge karakteristike

| Varijable | Ispitanici koji su praktikovali hemseks* (n=123) Broj (%) | Isptanici koji nisu praktikovali hemseks (n=346) Broj (%) | p vrednost** |
|---|---|---|---|
| **Uzrast (godine):** | | | |
| **≤ 25** | 13 (10,6) | 61 (17,6) | 0,499 |
| **26-35** | 52 (42,3) | 117 (33,8) | |
| **36-45** | 52 (42,3) | 109 (31,5) | |
| **45+** | 6 (4,9) | 59 (17,1) | |
| **Dužina trajanja obrazovanja (godine):** | | | |
| **≤ 12** | 58 (47,2) | 176 (50,9) | 0,480 |
| **>12** | 65 (52,8) | 170 (49,1) | |
| **Zaposlenost** | 111 (90,2) | 263 (76,0) | <0,001 |
| **Razlog posete lekaru:** | | | |
| **Simptomi PPI** | 46 (37,4) | 83 (24,0) | 0,002 |
| **Izloženost PPI** | 26 (21,1) | 54 (15,6) | |
| **Simptomi nevezani sa PPI** | 51 (41,5) | 209 (60,4) | |
| **Konzumiranje alkohola u poslednjih godinu dana#:** | | | |
| **Manje rizično pijenje** | 73 (59,3) | 272 (78,6) | <0,001 |
| **Rizično pijenje** | 45 (36,6) | 72 (20,8) | |
| **Visoko rizično pijenje** | 5 (4,1) | 2 (0,6) | |
| **Broj rekreativnih droga korišćenih u poslednjih šest meseci ≠:** | | | |
| **1** | 19 (15,4) | 80 (76,2) | <0,001 |
| **2** | 28 (22,0) | 21 (20,0) | |
| **3 – 8** | 76 (62,6) | 4 (3,8) | |
| **Učestalost upotrebe rekreativnih droga u poslednjih šest meseci:** | | | |
| **Jednom mesečno** | 76 (61,8) | 53 (50,5) | 0,007 |
| **2-4 puta mesečno** | 36 (29,3) | 27 (25,7) | |
| **2-3 puta nedeljno** | 9 (7,3) | 19 (18,1) | |
| **≥ 4 puta mesečno** | 2 (1,6) | 6 (5,7) | |
| **Poslednji seksualni odnos bez upotrebe droga (engl. *sober sex*):** | | | |
| **Prošlog meseca** | 85 (69,1) | 78 (74,3) | 0,397 |
| **Pre više od 3 meseca** | 20 (16,3) | 16 (15,2) | |
| **Pre više od 6 meseci** | 9 (7,3) | 4 (3,8) | |
| **Pre više od godinu dana** | 9 (7,3) | 7 (6,7) | |
| **HIV pozitivan status** | 60 (48,8) | 134 (38,7) | 0,053 |
| **Upotreba PrEP-a** | 11/63 (17,5) | 9/212 (4,2) | <0,001 |

PPI – polno prenosive infekcije; HIV – virus humane imunodeficijencije; PrEP – Pre-ekspoziciona profilaksa za HIV. *Upotreba jedne ili više seksualizovanih droga (GHB/GBL, kristalni metamfetamin, mefedron, ekstazi, amfetamin, kokain i ketamin); **Prema rezultatima univarijantne logističke regresione analize; #Konzumiranje alkohola je bazirano prema odgovorima na prva dva pitanja iz skraćenog upitnika Svetske zdravstvene organizacije AUDIT (engl. *Alcohol Use Disorders Identification Test*, test za identifikaciju poremećaja upotrebe alkohola); Manje rizično pijenje alkohola: skor ≤1, rizično pijenje: skor >1 prema drugom pitanju iz upitnika i visoko rizično pijenje: skor ≥6 (10); ≠ Upotreba hemseksa i/ili nekih drugih rekreativnih droga: kanabis, popers I lekovi za erektilnu disfunkciju;

praktikovali hemseks su bili značajno češće zaposleni (UO=2,50; 95%IP=1,19-5,26; p=0,015), imali su veći broj seksualnih partnera u poslednjih šest meseci (UO=1,39; 95%IP=1,14-1,72; p=0,002), češće su praktikovali analne seksualne odnose bez upotrebe kondoma (UO=3,23; 95%IP=1,64-6,25; p=0,001) i grupni seks tokom poslednjih šest meseci (UO=4,35; 95%IP=2,38-7,69; (p<0,001), konzumirali su veću količinu alkohola (UO=2,50; 95%IP=1,54-4,00; (p<0,001) i češće su imali neku bakterijsku PPI

**Table 1.** Distribution of partcicipants who practiced chemsex and those who did not according to socio-demographic and some other characteristics

| Variable | Engaged in chemsex* (n=123) No (%) | Not engaged in chemsex (n=346) No (%) | p value** |
|---|---|---|---|
| **Age groups (years):** | | | |
| **≤ 25** | 13 (10.6) | 61 (17.6) | 0.499 |
| **26-35** | 52 (42.3) | 117 (33.8) | |
| **36-45** | 52 (42.3) | 109 (31.5) | |
| **45+** | 6 (4.9) | 59 (17.1) | |
| **Education (years):** | | | |
| **≤ 12** | 58 (47.2) | 176 (50.9) | 0.480 |
| **>12** | 65 (52.8) | 170 (49.1) | |
| **Employed** | 111 (90.2) | 263 (76.0) | <0.001 |
| **Reason for visiting a doctor:** | | | |
| **STI related symptoms** | 46 (37.4) | 83 (24.0) | 0.002 |
| **STI exposure** | 26 (21.1) | 54 (15.6) | |
| **No STI related symptoms** | 51 (41.5) | 209 (60.4) | |
| **Alcohol consumption in the last year#:** | | | |
| **Low risk drinking** | 73 (59.3) | 272 (78.6) | <0.001 |
| **Hazardous drinking** | 45 (36.6) | 72 (20.8) | |
| **High risk drinking** | 5 (4.1) | 2 (0.6) | |
| **Number of recreational drugs used in the last six months ≠:** | | | |
| **1** | 19 (15.4) | 80 (76.2) | <0.001 |
| **2** | 28 (22.0) | 21 (20.0) | |
| **3 – 8** | 76 (62.6) | 4 (3.8) | |
| **Frequency of recreational drug use in the last six months:** | | | |
| **Once per month** | 76 (61.8) | 53 (50.5) | 0.007 |
| **2-4 times per month** | 36 (29.3) | 27 (25.7) | |
| **2-3 times per week** | 9 (7.3) | 19 (18.1) | |
| **≥ 4 times per week** | 2 (1.6) | 6 (5.7) | |
| **The last sober sex¶ among drug users:** | | | |
| **Last month** | 85 (69.1) | 78 (74.3) | 0.397 |
| **Before more than 3 months** | 20 (16.3) | 16 (15.2) | |
| **Before more than 6 months** | 9 (7.3) | 4 (3.8) | |
| **Before a year** | 9 (7.3) | 7 (6.7) | |
| **HIV positive** | 60 (48.8) | 134 (38.7) | 0.053 |
| **On PrEP** | 11/63 (17.5) | 9/212 (4.2) | <0.001 |

STI – Sexually Transmitted Infection; HIV – Human Immunodeficiency Viruses; PrEP – Pre-Exposure Prophylaxis of HIV.*Use of one of more of GHB/GBL, crystal methamphetamine, mephedrone, ecstasy, amphetamine, cocaine and ketamine. **According to univariate logistic regression analysis. #Alcohol consumption is based on the first two questions of the WHO AUDIT questionnaire. Lower risk drinking is indicated by a score ≤1, hazardous drinking is indicated by a score >1 on question 2 and higher risk drinking is indicated by a score ≥6 (10); ≠ Use of chemsex and/or some other recreational drugs: cannabis, poppers and erectile dysfunction drugs; ¶ Sex without the drugs

chlamydiasis (in 16 participants -3.5%). Of the other STIs, genital warts were diagnosed in 22 (4.8%) patients, monkey pox in 6 (1.3%), moluscum contagiosum in 3 (0.6%) and genital herpes in 1 patient (0.2%).

The results of multivariate logistic regression analysis are shown in Table 3. In comparison to persons who did not practice chemsex, the participants who practiced chemsex were significantly more often employed (OR=2.50; 95%CI=1.19-5.26; p=0.015), had a higher number of sexual partners in the last six months (OR = 1.39; 95%CI=1.14-1.72; p=0.002), they practiced anal sex without using a condom more often (OR

**Tabela 2.** Distribucija ispitanika koji su praktikovali hemseks i onih koji nisu u odnosu na seksualnu aktivnost, rizično seksualno ponašanje i dijagnozu bakterijske PPI

| Varijable | Ispitanici koji su praktikovali hemseks* (n=123) Broj (%) | Isptanici koji nisu praktikovali hemseks (n=346) Broj (%) | p vrednost** |
|---|---|---|---|
| **Broj seksualnih partnera u poslednjih šest meseci:** | | | |
| **1-3** | 29 (23,6) | 188 (54,3) | <0,001 |
| **4-9** | 39 (31,7) | 101 (29,2) | |
| **10+** | 55 (44,7) | 57 (16,5) | |
| **Analni seks bez upotrebe kondoma u poslednjih šest meseci** | 109 (88,6) | 213 (6,6) | <0,001 |
| **Grupni seks u poslednjih šest meseci** | 72 (58,5) | 50 (14,5) | <0,001 |
| **Bakterijske PPI u poslednjih godinu dana** | 65 (52,8) | 90 (26,0) | <0,001 |
| **Novodijagnostikovana bakterijska PPI** | 65 (52,8) | 113 (32,7) | <0,001 |
| **Ponovno obolevanje od bakterijske PPI** | 34 (27,6) | 25 (7,2) | <0,001 |

PPI – polno prenosive infekcije; *Upotreba jedne ili više seksualizovanih droga (GHB/GBL, kristalni metamfetamin, mefedron, ekstazi, amfetamin, kokain i ketamin); **Prema rezultatima univarijantne logističke regresione analize

u poslednjih godinu dana (UO=2,70; 95%IP=1,61-4,54; p<0,001). Učestalost upotrebe rekreativnih droga je bila niža kod osoba koje su praktikovale hemseks (UO=0,59; 95%IP=0,41-0,88; p=0,009).

## Diskusija

Iako je sproveden veliki broj istraživanja o prevalenciji hemseksa među MSM populacijom, njihove rezultate je teško porediti zbog različitih metoda istraživanja kako u odnosu na definisanje seksualizovanih droga (uži ili širi smisao), tako i u odnosu na karakteristike ispitanika (pripadnici opšte MSM populacije ili pacijenti klinika za polne bolesti). Sistematski pregled literature pokazuje da se prevalencija hemseksa među MSM populacijom kreće od 10% do 94% (2). Prema rezultatima našeg istraživanja 26,2% MSM ispitanika je praktikovalo hemseks, što je u korelaciji sa rezultatima drugih istraživanja sprovedenih među pacijentima klinika za polne bolesti.

Među MSM osobama koje su posetile klinike za polne bolesti u Dablinu 27% je praktikovalo hemseks (11), a u Velikoj Britaniji 21,8% pacijenata (1). Nešto manji procenat MSM osoba koje su praktikovale hemseks registrovan je među pacijentima klinika za polne bolesti u Amsterdamu – 17,6% (12) i Oslu – 17% (13). U našem istraživanju najveći broj ispitanika (84,6%) je koristilo GHB/GBL. Većina studija je opisala da je među korisnicima usluga klinika za polne bolesti ova droga najčešće praktikovana i to kod 57% pacijenata u Dablinu (11), 56% u Brajtonu (14) i 93% u Amsterdamu

**Tabela 3.** Rezultati multivarijantne logističke regresione analize* (ispitanici koji su praktikovali hemseks vs. ispitanici koji nisu praktikovali hemseks)

| Varijable | Unakrsni odnos | 95% interval poverenja | p vrednost* |
|---|---|---|---|
| **Zaposlenost** | 2,50 | 1,19-5,26 | 0,015 |
| **Broj seksualnih partnera u poslednjih šest meseci** | 1,39 | 1,14-1,72 | 0,002 |
| **Analni seks bez upotrebe kondoma u poslednjih šest meseci** | 3,23 | 1,64-6,25 | 0,001 |
| **Grupni seks u poslednjih šest meseci** | 4,35 | 2,38-7,69 | <0,001 |
| **Konzumiranje alkohola u poslednjih godinu dana** | 2,50 | 1,54-4,00 | <0,001 |
| **Bakterijska PPI u poslednjih godinu dana** | 2,70 | 1,61-4,54 | <0,001 |
| **Učestalost upotrebe rekreativnih droga** | 0,59 | 0,41-0,88 | 0,009 |

PPI – polno prenosive infekcije; *Prema rezultatima multivarijantne logističke regresione analize

**Table 2.** Distribution of participants who practiced chemsex and those who did not according to their sexual activity, sexual risk behaviours and diagnosis of bacterial STI

| Variable | Engaged in chemsex* (n=123) No (%) | Not engaged in chemsex (n=346) No (%) | p value** |
|---|---|---|---|
| **Number of sex partners in the last six months:** | | | |
| **1-3** | 29 (23.6) | 188 (54.3) | <0.001 |
| **4-9** | 39 (31.7) | 101 (29.2) | |
| **10+** | 55 (44.7) | 57 (16.5) | |
| **Condomless anal sex in the last six months** | 109 (88.6) | 213 (6.6) | <0.001 |
| **Group sex in the last six months** | 72 (58.5) | 50 (14.5) | <0.001 |
| **Bacterial STI diagnosis in the last year** | 65 (52.8) | 90 (26.0) | <0.001 |
| **Current bacterial STI diagnosis** | 65 (52.8) | 113 (32.7) | <0.001 |
| **Recurrent bacterial STI** | 34 (27.6) | 25 (7.2) | <0.001 |

STI - Sexually Transmitted Infections; *Use of one of more of GHB/GBL, crystal methamphetamine, mephedrone, ecstasy, amphetamine, cocaine and ketamine. **According to univariate logistic regression analysis

= 3.23; 95CI=1.64-6.25; p=0.001) and group sex during the last six months (OR=4.35; 95%CI=2.38-7.69; (p < 0.001), consumed a greater amount of alcohol (OR=2.50; 95%CI=1.54-4.00; (p<0.001) and they had more often one of STIs in the last year (OR=2.70; 95%CI=1.61-4.54; p < 0.001). The frequency of recreational drug use was lower in persons who practiced chemsex (OR = 0.59; 95%CI 0.41-0.88; p = 0.009).

## Discussion

Although a large number of studies have been conducted on the prevalence of chemsex in the population of MSM, their results are difficult to compare due to different study methods related to the definition of sexualized drugs (narrower or broader sense), as well as related to the characteristics of participants (members of the general MSM population or patients from clinics for sexually transmitted diseases). A systematic literature review has shown that the prevalence of chemsex in the MSM population ranges from 10% to 94% (2). According to the results of our study, 26.2% of MSM practiced chemsex, which is in correlation with the results of other studies conducted among patients from clinics for venereal diseases.

Among MSM who visited clinics for venereal diseases in Dublin, 27% practiced chemsex (11), and in Great Britain 21.8% of patients (1). A slightly smaller percentage of MSM who practiced chemsex, was registered among patients from clinics for venereal diseases in Amsterdam – 17.6% (12), and Oslo – 17% (13). In our study, the largest number of participants (84.6%) used GHB/GBL. The majority of studies described that this drug was

**Table 3.** Results of multivariate logistic regression analysis* (participants who practiced chemsex vs. participants who did not practice it)

| Varijable | Unakrsni odnos | 95% interval poverenja | p vrednost* |
|---|---|---|---|
| **Employed** | 2.50 | 1.19-5.26 | 0.015 |
| **Number of sex partners in the last six months** | 1.39 | 1.14-1.72 | 0.002 |
| **Condomless anal sex in the last six months** | 3.23 | 1.64-6.25 | 0.001 |
| **Group sex in the last six months** | 4.35 | 2.38-7.69 | <0.001 |
| **Alcohol consumption** | 2.50 | 1.54-4.00 | <0.001 |
| **Bacterial STI diagnosis in the last year** | 2.70 | 1.61-4.54 | <0.001 |
| **Frequency of recreational drug use** | 0.59 | 0.41-0.88 | 0.009 |

STI – Sexually transmitted infection; *According to the results of multivariate logistic regression analysis

(12). Podaci iz istraživanja sprovedenog u Australiji pokazali su da je samo 5,4% MSM osoba koristilo GHB/GBL (15). Iako je upotreba amfetamina zabeležena kod samo 2,3% naših ispitanika, ova droga je na drugom mestu po učestalosti upotrebe tokom hemseksa – koristi je i do 22% osoba (16) a najčešće se unosi intravenskim putem (17). Prema rezultatima našeg istraživanja niko od ispitanika nije upotrebljavao intravenske droge u toku poslednjih šest meseci.

GHB/GBL predstavlja noviju psihoaktivnu supstancu u Republici Srbiji koja je veoma popularna među MSM populacijom (9). I pored pozitivnih efekata na seksualno ponašanje (povećava seksualno zadovoljstvo i redukuje inhibicije) ova droga može izazvati zavisnost a predoziranje je praćeno povraćanjem, problemima sa disanjem, halucinacijama i gubitkom svesti, a može nastupiti i smrt (18). S obzirom na to, lekari i korisnici ove droge u našoj sredini bi trebalo da budu dobro upoznati sa njenim neželjenim dejstvima.

Upotreba većeg broja droga (tri ili više) tokom hemseksa je registrovana kod 62,6% naših ispitanika i predstavlja prediktor za visoko rizično seksualno ponašanje i PPI (19). *Sewell* i saradnici (1) su opisali u svojoj studiji da je 25% MSM osoba koristilo veći broj droga. Istraživanje sprovedeno u Velikoj Britaniji među 1.138 MSM osoba je pokazalo da je 47% ispitanika koristilo tri i/ili više droga, a čak 21% je koristilo pet i/ili više različitih psihoaktivnih supstanci (19).

Prema rezultatima našeg istraživanja osobe koje su praktikovale hemseks u odnosu na one koje ga nisu praktikovale su bile znatno češće zaposlene, imale su veći broj seksualnih partnera u toku prethodnih šest meseci, praktikovale su grupni seks i analne seksualne odnose bez upotrebe kondoma, konzumirale su veće količine alkohola i znatno češće imale neku bakterijsku PPI u poslednjih godinu dana. Jedino je učestalost upotrebe rekreativnih droga bila manja u grupi osoba koje su praktikovale hemseks.

Podatak da su korisnici hemseksa bili znatno češće zaposleni i imali redovan prihod mogla bi objasniti njihovu veću mogućnost da nabave droge. Visok stepen zaposlenosti MSM osoba koje praktikuju hemseks registrovan je i u Velikoj Britaniji – 79,7% (1) i Norveškoj – 83,9% (14).

Prema našim rezultatima MSM osobe koje su praktikovale hemseks imale su visoko rizično seksualno ponašanje i češće su obolevale od bakterijske PPI u toku poslednjih godinu dana što je u korelaciji sa podacima iz literature (1,6,11-13). *Glynn* i saradnici (11) su opisali da je ⅓ MSM osoba koje su praktikovale hemseks imala više od 10 partnera tokom prethodne godine i nije koristila kondom tokom analnog seksualnog odnosa. Prema podacima *Druckler*-a i saradnika 42,4% osoba koje su praktikovale hemseks u Amsterdamu je imala više od 16 partnera tokom poslednjih šest meseci i 84,3% njih nije koristilo kondom za analni seks (12). Istraživanje sprovedeno u Oslu je pokazalo da je 60% MSM osoba koje su praktikovale hemseks imalo preko 11 seksualnih partnera tokom prethodnih godinu dana a 84% njih je učestvovalo u grupnom seksu (13). Naši ispitanici koji su praktikovali hemseks su češće bili HIV pozitivni, koristili su PrEP i posetili su našu ustanovu zbog simptoma PPI ili izlaganja PPI. Ovo je u skladu sa rezultatima iz Amsterdama gde je 1/3 osoba koje su praktikovale hemseks bila HIV pozitivna, 25,5% ispitanika je koristilo PrEP i došli su kod lekara zbog simptoma PPI ili izlaganja PPI (12). *Hagazi* i saradnici su objavili da su HIV pozitivne MSM osobe znatno češće praktikovale hemseks u odnosu na HIV negativne osobe (14). Više od polovine naših ispitanika koji su praktikovali hemseks imali su neku bakterijsku PPI u prethodnih godinu dana, a sifilis je bio najčešće registrovan. Rezultati studije koje su sproveli *Glynn* i saradnici (11) su pokazali da je 47% MSM osoba koje su praktikovale hemseks lečeno od neke bakterijske PPI, a gonoreja je bila najčešće dijagnostikovana. Istraživanje iz Norveške (13) je pokazalo da je među osobama koje su praktikovale hemseks najčešće dijagnostikovana hlamidijaza (26,4%).

Upotreba veće količine alkohola među našim ispitanicima koji su praktikovali hemseks mogla se i očekivati s obzirom na to da je konzumiranje alkohola prepoznato kao faktor koji dodatno doprinosi riziku za dobijanje PPI i HIV-a (20,21).

Češća upotreba rekreativnih droga među našim ispitanicima koji nisu praktikovali hemseks mogla bi se objasniti činjenicom da su oni koristili znatno češće kanabis (57,1% ih je koristilo 2 do 3 puta nedeljno, a 87,5% više od 4 puta nedeljno). Kanabis je najčešće korišćena rekreativna droga u Srbiji (8) i druga po učestalosti korišćenja među MSM populacijom (22). *Bruce* i saradnici su opisali da 23% MSM osoba svakodnevno koristi kanabis (20). Nisu postojale razlike među našim ispitanicima prema podatku o poslednjem seksualnom odnosu kada nisu koristili nikakve droge. Većina

most often used among users of services of clinics for venereal diseases, that is, in 57% of patients in Dublin (11), 56% in Brighton (14) and 93% in Amsterdam (12). Data from one study, which was conducted in Australia, showed that only 5.4% of MSM used GHB/GBL (15). Although the use of amphetamine was registered only in 2.3% of our participants, this drug takes second place according to the frequency of use during chemsex – it is used by up to 22% of people (16), and it is most often administered intravenously (17). According to the results of our study, none of the participants used intravenous drugs in the last six months.

GHB/GBL is a newer psychoactive substance in the Republic of Serbia, which is very popular in the population of MSM (9). Although it has some positive effects on sexual behavior (increases sexual pleasure and reduces inhibitions), this drug can cause addiction, while overdose is accompanied by vomiting, problems with breathing, hallucinations, loss of consciousness, and death can occur, as well (18). Therefore, doctors and users of this drug in our environment should be well aware of its side effects.

The use of a larger number of drugs (three or more) during chemsex was registered in 62.6% of our participants and it is a predictor of high-risk sexual behavior and STIs (19). *Sewell et al*. (1) described in their study that 25% of MSM used more drugs. A study, which was conducted in Great Britain among 1,138 MSM, showed that 47% of participants used three and/or more drugs, and even 21% used five and/or more different psychoactive substances (19).

According to the results of our study, the participants, who practiced chemsex in comparison to those who did not practice it, were employed significantly more often, had a greater number of sexual partners during the last six months, practiced group sex and anal sex without condoms, consumed greater amounts of alcohol and had a bacterial STI significantly more often in the last year. Only the frequency of use of recreational drugs was lower in the group of persons who practiced chemsex.

The fact that the users of chemsex were employed significantly more often and had a regular income could explain the greater possibility of acquiring drugs. A high level of employment of MSM who practiced chemsex was also registered in Great Britain – 79.7% (1) and Norway – 83.9% (14).

According to our results, MSM who practiced chemsex were engaged in high-risk sexual behavior and suffered from bacterial STIs more often in the last year, which is in correlation with literature data (1,6,11-13). *Glynn et al* (11) described that 1/3 of MSM who practiced chemsex had more than 10 partners during the previous year and did not use a condom during anal sexual intercourse. According to the data of *Druckler et al*, 42.4% of persons who practiced chemsex in Amsterdam had more than 16 partners during the last six months and 84.3% of them did not use a condom for anal sex (12). A study, which was conducted in Oslo, showed that 60% of MSM who practiced chemsex had more than 11 sexual partners during the last year and 84% of them participated in group sex (13). Our participants who practiced chemsex were more often HIV positive, they used PrEP and they visited our institution due to the symptoms of STIs or exposure to STIs. This is in accordance with the results from Amsterdam where 1/3 of persons who practiced chemsex were HIV positive, 25.5% of participants used PrEP and they visited doctors due to the symptoms of STIs or exposure to STIs (12). *Hagazi* and associates published that HIV positive MSM significantly more often practiced chemsex in comparison to HIV negative persons (14). More than half of our participants who practiced chemsex had some bacterial STI in the previous year, while syphilis was registered most frequently. The results of a study by *Glynn et al.* (11) showed that 47% of MSM who practiced chemsex were treated for some bacterial STI, while gonorrhea was most frequently diagnosed. A study from Norway (13) showed that Chlamydia (26.4%) was most frequently diagnosed among persons who practiced chemsex.

The use of a greater amount of alcohol among our participants who practiced chemsex could be expected because alcohol consumption is recognized as a factor that additionally contributes to the risk of getting STI and HIV (20,21).

The frequent use of recreational drugs among our participants who did not practice chemsex could be explained by the fact that they used cannabis significantly more often (57.1% used them 2 to 3 times a week, and 87.5% more than 4 times a week). Cannabis is the most frequently used recreational drug in Serbia (8) and the second most frequently used in the MSM population (22). *Bruce et al.* described that 23% of MSM used

naših ispitanika (oko 70%) je rekla da su poslednji seks bez upotrebe droga imali tokom prethodnih mesec dama, što je u skladu sa podacima iz Amsterdama gde je ovaj broj iznosio 87% (12).

U našem istraživanju nova bakterijska PPI je registrovana kod 52,8% ispitanika koji su praktikovali hemseks. Čak 27,6% njih je pripadalo osobama sa ponovnim obolevanjem od bakterijske PPI u poslednjih godinu dana, a sifilis je registrovan kod 35% ispitanika. Visoka prevalencija sifilisa je u skladu sa epidemiološkom situacijom u našoj zemlji, gde je ova bolest u kontinuiranom porastu naročito među pripadnicima MSM populacije (23). Ranije sprovedena studija u Beogradu (24) među osobama sa ponovnim obolevanjem od PPI je pokazala da ove osobe praktikuju visoko rizična seksualna ponašanja, češće koriste alkohol i psihoaktivne supstance i imaju specifične dimenzije ličnosti koje prate niska tolerancija frustracija i agresivno ponašanje. Naime, ponašanje osoba koje ponovno obolevaju od PPI je u skladu sa njihovim samokonceptom ličnosti što čini njihov tretman otežanim i ukazuje na značaj primene preventivnih mera za PPI (24).

Glavno ograničenje našeg istraživanja je to što je sprovedeno među pacijentima koji su dolazili u zdravstvenu ustanovu, te je pitanje da li se dobijeni rezultati moguodnositi i na opštu MSM populaciju u Srbiji.

## Zaključak

MSM osobe koje praktikuju hemseks imaju visoko rizično seksualno ponašanje i češće obolevaju od bakterijskih PPI. Sve više prisutan fenomen hemseksa među MSM populacijom ukazuje na značaj podizanja svesti o ovoj pojavi kako među pripadnicima ove vulnerabilne grupe, tako i među zdravstvenim radnicima. Poruke o štetnosti hemseksa trebalo bi da dopru do što većeg broja pripadnika MSM populacije kako preko javnih zdravstvenih servisa, tako i preko društvenih mreža i nevladinih organizacija koje rade sa ovom osetljivom populacijom. MSM osobe bi trebalo da budu upoznate sa činjenicom da je praktikovanje hemseksa povezano sa visoko rizičnim seksualnim ponašanjem i prenošenjem PPI, kao i sa nastankom zavisnosti, predoziranjem pa čak i smrtnim ishodom. Zdravstveni radnici koji rade sa MSM populacijom bi trebalo da budu edukovani o dejstvima seksualizovanih droga i da budu obučeni u pružanju psihološke podrške korisnicima. Savetovanje pacijenata o delovanju ovih droga bi trebalo da se ponudi svim pacijentimakoji dolaze u klinike za polne prenosive bolesti.

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

## Reference


1. Sewell J, Miltz A, Lampe FC, Cambiano V, Speakman A, Phillips AN, et al. Poly drug use, chemsex drug use, and associations with sexual risk behaviour in HIV-negative men who have sex with men attending sexual health clinics. Int J Drug Policy 2017;43: 33-43. http://doi: 10.1016/j.drugpo.2017.01.001.
2. Tomkins A, George R, Kliner M. Sexualised drug taking among men who have sex with men: a systematic review. Perspect Public Health 2019;139(1):23-33. http:// doi: 10.1177/1757913918778872.
3. Stuart D. Chemsex: origins of the world, a history of the phenomenon and a respect to the culture. Drugs Alcohol Today 2019;19(1):3-10. https://doi.org/10.1108/DAT-10-2018-0058
4. McCarty-Caplan D, Jantz I, Swartz J. MSM and drug use a latent class analysis of drug use and related sexual risk behaviors. Aids Behav 2014;18(7):1339-51. https:// doi: 10.1007/s10461-013-0622-x.
5. European monitoring centre for drugs and drug addiction (EMCDDA). European Drug Report 2018: Trends and Developments. Available at: http://www.emcdda.europa.eu/system/files/publications/8585/20181816_TDAT18001ENN_PDF.pdf/. Accessed February 16, 2023.
6. Evers YJ, Van Liere GAFS, Hoebe CJPA, Dukers-Muijrers NHTM. Chemsex among men who have sex with men living outside major cities and associations with sexually transmitted infection: a cross-sectional study in the Netherlands. PLoS ONE 2019;14(5):e0216732. https:// doi: 10.1371/journal.pone.0216732.
7. Bourne A, Reid D, Hickson F, Torres-Rueda S, Steinberg P, Weatherburn P. "Chemsex" and harm reduction need among gay men in South London. Int J Drug Policy 2015;26(12):1171-6. https:// doi: 10.1016/j.drugpo.2015.07.013.
8. European Monitoring Centre for Drugs and Drug Addiction. Serbia, National Drug Report 2017. Publications Office of the European Union, Luxembourg, 2017.
9. Kurcevič E, Lines R. New psychoactive substances in Eurasia; a qualitative study of people who use drugs and harm reduction services in six countries. Harm Reduct J 2020;17(1). 94. https:// doi: 10.1186/s12954-020-00448-2.
10. Babor T, Higgins-Biddle JC, Sounders JB, Monteiro MG. The alcohol use disorder identification test. Guidelines for use in primary care. Department of Mental Health and Substance Dependence, World Health Organization, 2001.
11. Glynn RW, Byrne N, O'Dea S, Shanley A, Codd M, Keenan E, et al. Chemsex, risk behaviours and sexually transmitted

cannabis daily (20). There were no differences between our participants regarding data on the last sexual intercourse when they did not use any drugs. The majority of our participants (about 70%) said that they had last sex without the use of drugs during the previous month, which is in accordance with the results from Amsterdam, where this number amounted to 87% (12).

In our study, a new bacterial STI was registered in 52.8% of respondents who practiced chemsex. Even 27.6% of them had repeated STI in the last year, while syphilis was registered in 35% of participants. The high prevalence of syphilis is in accordance with the epidemiological situation in our country, where the number of new cases of this disease continuously rises, especially in the MSM population (23). An earlier study, which was conducted in Belgrade (24) among persons with recurrent STI, showed that these persons practiced high-risk sexual behaviors, used alcohol and psychoactive substances more frequently and had specific personality dimensions accompanied by low tolerance of frustrations and aggressive behavior. Namely, the behavior of persons who repeatedly suffered from STIs was in accordance with their self-concept of personality, which made their treatment more difficult and pointed to the significance of prevention measures for STIs (24).

The main limitation of our study is that it was conducted among patients who came to the health institution, and therefore, the question arises whether the obtained results can be applied to the general MSM population in Serbia.

## Conclusion

MSM who practice chemsex are engaged in high-risk sexual behavior and they suffer from bacterial STIs more frequently. The increasingly present phenomenon of chemsex in the MSM population indicates the importance of raising awareness about this phenomenon both among the members of this vulnerable group and among healthcare workers. Messages about the harmfulness of chemsex should reach as many members of the MSM population as possible through public health services, as well as through social media and non-governmental organizations which work with this vulnerable population. MSM should be acquainted with the fact that practicing chemsex is associated with high-risk sexual behavior and transmission of STIs, as well as addiction, overdose and even death. Healthcare workers who work with the MSM population should be educated about the effects of sexualized drugs and trained to provide psychological support to users. Patient counseling about the effects of these drugs should be offered to all patients who come to clinics for venereal diseases.

## Competing interests

The authors declared no competing interests.

## References


1. Sewell J, Miltz A, Lampe FC, Cambiano V, Speakman A, Phillips AN, et al. Poly drug use, chemsex drug use, and associations with sexual risk behaviour in HIV-negative men who have sex with men attending sexual health clinics. Int J Drug Policy 2017;43: 33-43. http://doi: 10.1016/j.drugpo.2017.01.001.
2. Tomkins A, George R, Kliner M. Sexualised drug taking among men who have sex with men: a systematic review. Perspect Public Health 2019;139(1):23-33. http:// doi: 10.1177/1757913918778872.
3. Stuart D. Chemsex: origins of the world, a history of the phenomenon and a respect to the culture. Drugs Alcohol Today 2019;19(1):3-10. https://doi.org/10.1108/DAT-10-2018-0058
4. McCarty-Caplan D, Jantz I, Swartz J. MSM and drug use a latent class analysis of drug use and related sexual risk behaviors. Aids Behav 2014;18(7):1339-51. https:// doi: 10.1007/s10461-013-0622-x.
5. European monitoring centre for drugs and drug addiction (EMCDDA). European Drug Report 2018: Trends and Developments. Available at: http://www.emcdda.europa.eu/system/files/publications/8585/20181816_TDAT18001ENN_PDF.pdf/. Accessed February 16, 2023.
6. Evers YJ, Van Liere GAFS, Hoebe CJPA, Dukers-Muijrers NHTM. Chemsex among men who have sex with men living outside major cities and associations with sexually transmitted infection: a cross-sectional study in the Netherlands. PLoS ONE 2019;14(5):e0216732. https:// doi: 10.1371/journal.pone.0216732.
7. Bourne A, Reid D, Hickson F, Torres-Rueda S, Steinberg P, Weatherburn P. "Chemsex" and harm reduction need among gay men in South London. Int J Drug Policy 2015;26(12):1171-6. https:// doi: 10.1016/j.drugpo.2015.07.013.
8. European Monitoring Centre for Drugs and Drug Addiction. Serbia, National Drug Report 2017. Publications Office of the European Union, Luxembourg, 2017.
9. Kurcevič E, Lines R. New psychoactive substances in Eurasia; a qualitative study of people who use drugs and harm reduction services in six countries. Harm Reduct J 2020;17(1). 94. https:// doi: 10.1186/s12954-020-00448-2.
10. Babor T, Higgins-Biddle JC, Sounders JB, Monteiro MG. The alcohol use disorder identification test. Guidelines for use in primary care. Department of Mental Health

infections among men who have sex with men in Dublin, Ireland. Int J Drug Policy 2018; 52: 9-15. https:// doi: 10.1016/j.drugpo.2017.10.008.

12. Druckler S, van Rooijen MS, de Vries HJC. Chemsex among men who have sex with men: a sexualized drug use survey among clients of the sexually transmitted infection outpatient clinic and users of a gay dating app in Amsterdam, the Netherlands. Sex Transm Dis 2018; 45(5): 325-331. https:// doi: 10.1097/OLQ.0000000000000753.
13. Amundsen E, Haugstvedt A, Skogen V, Berg RC. Health characteristics associated with chemsex among men who have sex with men: results from a cross-sectional clinic survey in Norway. PLoS One 2022; 17(10): e0275618. https:// doi: 10.1371/journal.pone.0275618.
14. Hegazi A, Lee MJ, Whittaker W, Green S, Simms R, Cutts R, et al. Chemsex and the city: sexualised substance use in gay bisexual and other men who have sex with men attending sexual health clinics. Int J STD & AIDS 2017;28(4): 362-366. https:// doi: 10.1177/0956462416651229.
15. Hammoud MA, Bourne A, Maher L, Jin F, Haire B, Lea T, et al. Intensive sex partying with gamma-hydroxybutyrate: factors associated with using gamma-hydroxybutyrate for chemsex among Australian gay and bisexual men – results from the Flux Study. Sex Health 2018;15(2): 123-134. https:// doi: 10.1071/SH17146.
16. Maxwell S, Shahmanesh M, Gafos M. Chemsex behaviours among men who have sex with men: a systematic review of the literature. IntJ Drug Policy 2019; 63: 74-89. https:// doi: 10.1016/j.drugpo.2018.11.014.
17. Bowden-Jones O, Whitelock C, Abdulrahim D, Hemmings S, Margetts A, Crawford M. Prevalence of HIV risk-related drug use and sexual activity among men who have sex with men attending a specialist UK club drug clinic. Drugs Alcohol Today 2017; 17(1): 50-59. https:// DOI:10.1108/DAT-01-2017-0001.
18. Hockenhull J, Murphy KG, Paterson S. An observed rise in gamma-hydroxybuturate associated deaths in London: evidence to suggest a possible link with concomitant rise in chemsex. Forensic Sci Int 2017; 270: 93-97. https:// doi: 10.1016/j.forsciint.2016.11.039.
19. Daskalopoulou M, Rodger A, Phillips AN, Sherr L, Speakman A, Collins S, et al. Recreational drug use, polydrug use, and sexual behaviour in HIV-diagnosed men who have sex with men in the UK: Results from the cross-sectional ASTRA study. Lancet HIV 2014; 1(1): e22-31. https:// doi: 10.1016/S2352-3018(14)70001-3.
20. Gorbach PM, Javanbakht M, Shover CL, Bolan RK, Ragsdale A, Shoptaw S. Associations between cannabis use, sexual behavior, and sexually transmitted infections/human immunodeficiency virus in a cohort of young men who have sex with men. Sex Transm Dis 2019; 46(2):105-11. https:// doi: 10.1097/OLQ.0000000000000919.
21. Bruce D, Kahana S, Harper GW, Fernández MI, ATN. Alcohol use predicts sexual risk behavior with HIV-negative or partners of unknown status among young HIV-positive men who have sex with men. AIDS Care 2013; 25(5): 559-65. https:// doi: 10.1080/09540121.2012.720363.
22. Woolf SE, Maisto SA. Alcohol use and risk of HIV infection among men who have sex with men. AIDS Behav 2009; 13(4):757-82. https:// doi: 10.1007/s10461-007-9354-0.
23. Bjekić M, Šipetić-Grujičić S, Begović-Vuksanović B, Rafailović N, Vlajinac H. Syphilis resurgence in Belgrade, Serbia in the new millennium: an outbreak in 2014. Cent Eur J Public Health 2017;25(4):277-81. https:// doi: 10.21101/cejph.a4525.
24. Bjekić M, Lečić-Toševski D, Vlajinac H. Personality dimensions of sexually transmitted disease repeaters assessed with the Millon Clinical Multiaxial Inventory. J Eur Acad Dermatol Venereol 2002:16(1):63-5. https:// doi: 10.1046/j.1468-3083.2002.00367.x.



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and Substance Dependence, World Health Organization, 2001.

11. Glynn RW, Byrne N, O'Dea S, Shanley A, Codd M, Keenan E, et al. Chemsex, risk behaviours and sexually transmitted infections among men who have sex with men in Dublin, Ireland. Int J Drug Policy 2018; 52: 9-15. https:// doi: 10.1016/j.drugpo.2017.10.008.
12. Druckler S, van Rooijen MS, de Vries HJC. Chemsex among men who have sex with men: a sexualized drug use survey among clients of the sexually transmitted infection outpatient clinic and users of a gay dating app in Amsterdam, the Netherlands. Sex Transm Dis 2018; 45(5): 325-331. https:// doi: 10.1097/OLQ.0000000000000753.
13. Amundsen E, Haugstvedt A, Skogen V, Berg RC. Health characteristics associated with chemsex among men who have sex with men: results from a cross-sectional clinic survey in Norway. PLoS One 2022; 17(10): e0275618. https:// doi: 10.1371/journal.pone.0275618.
14. Hegazi A, Lee MJ, Whittaker W, Green S, Simms R, Cutts R, et al. Chemsex and the city: sexualised substance use in gay bisexual and other men who have sex with men attending sexual health clinics. Int J STD & AIDS 2017;28(4): 362-366. https:// doi: 10.1177/0956462416651229.
15. Hammoud MA, Bourne A, Maher L, Jin F, Haire B, Lea T, et al. Intensive sex partying with gamma-hydroxybutyrate: factors associated with using gamma-hydroxybutyrate for chemsex among Australian gay and bisexual men – results from the Flux Study. Sex Health 2018;15(2): 123-134. https:// doi: 10.1071/SH17146.
16. Maxwell S, Shahmanesh M, Gafos M. Chemsex behaviours among men who have sex with men: a systematic review of the literature. IntJ Drug Policy 2019; 63: 74-89. https:// doi: 10.1016/j.drugpo.2018.11.014.
17. Bowden-Jones O, Whitelock C, Abdulrahim D, Hemmings S, Margetts A, Crawford M. Prevalence of HIV risk-related drug use and sexual activity among men who have sex with men attending a specialist UK club drug clinic. Drugs Alcohol Today 2017; 17(1): 50-59. https:// DOI:10.1108/DAT-01-2017-0001.
18. Hockenhull J, Murphy KG, Paterson S. An observed rise in gamma-hydroxybuturate associated deaths in London: evidence to suggest a possible link with concomitant rise in chemsex. Forensic Sci Int 2017; 270: 93-97. https:// doi: 10.1016/j.forsciint.2016.11.039.
19. Daskalopoulou M, Rodger A, Phillips AN, Sherr L, Speakman A, Collins S, et al. Recreational drug use, polydrug use, and sexual behaviour in HIV-diagnosed men who have sex with men in the UK: Results from the cross-sectional ASTRA study. Lancet HIV 2014; 1(1): e22-31. https:// doi: 10.1016/S2352-3018(14)70001-3.
20. Gorbach PM, Javanbakht M, Shover CL, Bolan RK, Ragsdale A, Shoptaw S. Associations between cannabis use, sexual behavior, and sexually transmitted infections/human immunodeficiency virus in a cohort of young men who have sex with men. Sex Transm Dis 2019; 46(2):105-11. https:// doi: 10.1097/OLQ.0000000000000919.
21. Bruce D, Kahana S, Harper GW, Fernández MI, ATN. Alcohol use predicts sexual risk behavior with HIV-negative or partners of unknown status among young HIV-positive men who have sex with men. AIDS Care 2013; 25(5): 559-65. https:// doi: 10.1080/09540121.2012.720363.
22. Woolf SE, Maisto SA. Alcohol use and risk of HIV infection among men who have sex with men. AIDS Behav 2009; 13(4):757-82. https:// doi: 10.1007/s10461-007-9354-0.
23. Bjekić M, Šipetić-Grujičić S, Begović-Vuksanović B, Rafailović N, Vlajinac H. Syphilis resurgence in Belgrade, Serbia in the new millennium: an outbreak in 2014. Cent Eur J Public Health 2017;25(4):277-81. https:// doi: 10.21101/cejph.a4525.
24. Bjekić M, Lečić-Toševski D, Vlajinac H. Personality dimensions of sexually transmitted disease repeaters assessed with the Millon Clinical Multiaxial Inventory. J Eur Acad Dermatol Venereol 2002:16(1):63-5. https:// doi: 10.1046/j.1468-3083.2002.00367.x.



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# STAVOVI ZAPOSLENIH O NAČINU UPRAVLJANJA I ORGANIZOVANJA PROCESA RADA U ZAVODU ZA ANTIRABIČNU ZAŠTITU - PASTEROV ZAVOD, NOVI SAD

**Dragana Gazibara[*1,2], Marko Ključar[3], Andrea Stojšić[4], Dragana Mijatović[5], Pavle Banović[2,3]**

[1] Služba za obezbeđenje i kontrolu kvaliteta, Pasterov zavod Novi Sad, Novi Sad, Republika Srbija
[2] Medicinski fakultet Novi Sad, Univerzitet u Novom Sadu, Novi Sad, Republika Srbija
[3] Odsek za pravne, ekonomsko-finansijske, tehničke i druge slične poslove, Pasterov zavod Novi Sad, Republika Srbija
[4] Služba za prevenciju i sprečavanje širenja besnila i drugih zaraznih bolesti, Pasterov zavod Novi Sad, Republika Srbija
[5] Služba za istraživanje i praćenje kretanja besnila i drugih zoonoza, Pasterov zavod Novi Sad, Republika Srbija

[*] Korespondencija: dr med. Dragana Gazibara, Služba za obezbeđenje i kontrolu kvaliteta, Pasterov zavod Novi Sad, 21000 Novi Sad, Republika Srbija; Medicinski fakultet Novi Sad, Univerzitet u Novom Sadu, 21000 Novi Sad, Republika Srbija; e-mail: 906005d23@mf.uns.ac.rs

**SAŽETAK**

**Uvod/Cilj:** Menadžment u zdravstvu igra ključnu ulogu u unapređenju poslovanja zdravstvenih ustanova, integraciji tehnologije i razvoju ljudskih resursa. Cilj našeg istraživanja je bio da se ispitaju stavovi zaposlenih u Zavodu za antirabičnu zaštitu - Pasterov zavod, Novi Sad (ZARZ Pasterov zavod, Novi Sad) o samoj organizaciji, organizacionoj klimi (tj. atmosferi i odnosima koji vladaju u organizaciji među zaposlenima, prvenstveno između rukovodilaca i ostalih članova kolektiva) i rukovođenju.
**Metode:** Sprovedeno je istraživanje među 19 zaposlenih, na platformi *Google form*, koristeći modifikovanu verziju upitnika *The Work Design Questionnaire* koji sadrži 8 demografskih pitanja o ispitaniku i 26 pitanja (tvrdnji) koja se odnose na predmet istraživanja. Respondenti, koji su činili 86,4% od ukupno 22 zaposlena, iskazali su nivo saglasnosti sa tvrdnjom koristeći skalu sa ocenamaod 1 do 5.
**Rezultati:** Većina ispitanika smatra da su funkcije, ciljevi i odgovornosti unutar Pasterovog zavoda-Novi Sad, jasno definisani. Stav zaposlenih je da postoji prostor za povećanje učešća zaposlenih u donošenju odluka.
**Zaključak:** Neophodno je uvođenje participativnijeg pristupa u procesu donošenja odluka u ustanovi i implementacija mera usmerenih ka maksimalnom korišćenju sposobnosti zaposlenih, unapređenju komunikacije i informisanja zaposlenih, uključivanje zaposlenih u proces odlučivanja, jačanju međusobnog poverenja i razvoju timskog duha kako bi se unapredila efikasnost ustanove i postiglo održivo poboljšanje organizacione klime i rada rukovodstva u Pasterovom zavodu-Novi Sad.

**Ključne reči:** upravljanje u zdravstvu, organizaciona struktura, angažovanost zaposlenih, organizaciona klima

## Uvod

Menadžment u zdravstvu predstavlja instrument za unapređenje poslovanja zdravstvenih ustanova i značajan je faktor za podsticaj i primenu tehnologije, znanja i veština. Zadatak zdravstvenog menadžmenta je razumevanje zahteva i potreba i praćenje teorijskih i praktičnih trendova u ovoj oblasti, kao i pronalaženje modela za implementaciju dostignuća iz oblasti menadžmenta u delatnost zdravstvenih ustanova (1).

Organizovanje je aktivnost menadžmenta koja obezbeđuje skladno povezivanje ljudi koji pribavljaju, raspoređuju i koriste sredstva za rad i materijal u cilju uspešnog poslovanja preduzeća (2). Zasniva se na podeli rada između učesnika u procesu poslovanja sa ciljem stvaranja organizacione strukture koja obuhvata aktivnosti i odnose zaposlenih i upravlja ljudskim resursima u cilju uspešnog poslovanja na duže staze (3).

Sve organizacije obuhvataju tri ključna elementa, i to: ciljeve, strukturu i ljude (4). Kada se analizira celokupna problematika organizacije, može se zaključiti da ona predstavlja namerno

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# EMPLOYEES' VIEWS ON THE WAYS OF MANAGING AND ORGANIZING WORK PROCESSES IN THE INSTITUTE FOR ANTI-RABIES PROTECTION - THE PASTEUR INSTITUTE, NOVI SAD

**Dragana Gazibara[*1,2], Marko Ključar[3], Andrea Stojšić[4], Dragana Mijatović[5], Pavle Banović[2,3]**

[1] Department of Quality Assurance and Quality Control, Pasteur Institute Novi Sad, Novi Sad, Republic of Serbia
[2] Faculty of Medicine, University of Novi Sad, Novi Sad, Republic of Serbia
[3] Department of Legal, Economic-Financial, Technical and Other Related Affairs, Novi Sad, Republic of Serbia
[4] Department of Prevention of Rabies and Other Infectious Diseases, Pasteur Institute Novi Sad, Novi Sad, Republic of Serbia.
[5] Department for Research & Monitoring of Rabies & Other Zoonoses, Pasteur Institute Novi Sad, Novi Sad, Republic of Serbia.

[*] Correspondence: Dragana Gazibara, MD, Department of Quality Assurance and Quality Control, Pasteur Institute Novi Sad, 21000 Novi Sad, Serbia; Faculty of Medicine, University of Novi Sad, 21000 Novi Sad, Serbia; e-mail: 906005d23@mf.uns.ac.rs

**SUMMARY**

**Introduction/Aim:** Management in healthcare plays a pivotal role in enhancing the operations of healthcare institutions, integrating technology, and developing human resources. The aim of our research was to examine the attitudes of employees in the Institute for anti-rabies protection - The Pasteur Institute, Novi Sad towards the organization itself, organizational climate (atmosphere and relations between employees, primarily managers and other members of the collective) and management.
**Methods:** A survey was conducted among 19 employees, using the GoogleForms platform, employing a modified version of The Work Design Questionnaire, which includes 8 demographic questions about the respondent and 26 questions related to the research topic. Respondents, constituting 86.4% of the total of 22 employees, expressed their agreement with the statements using a scale with grades from 1 to 5.
**Results:** The majority of respondents believe that functions, goals, and responsibilities within the Pasteur Institute, Novi Sad are clearly defined. The position of the employees is that there is room for increasing the participation of employees in decision-making.
**Conclusion:** It is necessary to introduce a more participatory approach in the decision-making process in the institution and implement measures aimed at the maximum use of employees' abilities, improvement of communication and information of employees, involvement of employees in the decision-making process, strengthening of mutual trust and development of team spirit in order to improve the efficiency of the institution and achieve sustainable improvement of organizational climate and leadership work in the Pasteur Institute, Novi Sad.

**Keywords:** Healthcare Management; Organizational Structure; Employee Engagement; Organizational Climate

## Introduction

Management in healthcare represents an instrument for improving the business operations of health institutions and it is an important factor for the encouragement and application of technology, knowledge and skills. The task of health management is to understand the requirements and needs and to follow theoretical and practical trends in this field, as well as to find models for the implementation of achievements from the field of management in the field of health institutions (1).

Organization is the management activity that ensures the harmonious connection of people who acquire, distribute and use resources and materials, which is aimed at successful business operations (2). It is based on the division of labor between the participants in the business process

konstruisani i veštački dizajniran entitet. Osnovne razlike između savremenih i tradicionalnih organizacija se mogu sagledati na osnovu više postulata, u zavisnosti koliki je fokus na podeli rada, centralizaciji i rasponu kontrole. Sam izbor organizacionog modela nije jednostavan i na njega utiču mnogi faktori poput veličine organizacije, delatnosti kojom se preduzeće bavi, kao i geografska rasprostranjenost preduzeća (5).

U Pasterovom zavodu zastupljen je participativni stil upravljanja. Ovaj stil primenjuju šefovi službi koji prikupljaju ideje od zaposlenih u svojim službama. S druge strane, zaposleni učestvuju u donošenju odluka, ali samo delimično, u granicama koje postavlja lider. Pored participativnog stila upravljanja, Pasterov zavod odlikuje linijska organizaciona struktura, koja potpada pod tradicionalne modele organizacionih struktura.

Takva organizaciona struktura predstavlja bazu za sve ostale modele koji svoje funkcionisanje zasnivaju na hijerarhiji odnosa i odgovornosti položaja unutar organizacije. Osnovu ovog modela čini hijerarhijski odnos svake pozicije u organizaciji, gde je svaki hijerarhijski nivo pod kontrolom višeg. Ova karakteristika pojednostavljuje komunikacione linije i lanac upravljanja, jer su za sve pozicije jasno određene odgovornosti. Ipak, ne postoji detaljna podela rada pa jedna osoba može raditi više različitih poslova. U skladu s time, za poslove izvan ovlašćenja pojedinca je odgovoran nadređeni na istoj liniji rukovođenja.

Utvrđivanje stila upravljanja, kao i adekvatnost odnosa rukovodstva sa zaposlenima u zdravstvanim ustanovama je od strateške važnosti za poslovanje same ustanove (5). Funkcija organizovanja je važna za svako preduzeće i ona se ne završava definisanjem organizacione strukture, već je neophodna tokom čitavog postojanja preduzeća zbog dinamike savremenog poslovanja.

Cilj našeg istraživanja je bio da se ispitaju stavovi zaposlenih u Zavodu za antirabičnu zaštitu - Pasterov zavod, Novi Sad (ZARZ Pasterov zavod, Novi Sad) o samoj organizaciji, organizacionoj klimi (tj. atmosferi i odnosima koji vladaju u organizaciji među zaposlenima, prvenstveno između rukovodilaca i ostalih članova kolektiva) i rukovođenju.

## Metode

Istraživanje je sprovedeno u periodu 21–28.03.2023. godine u vidu anonimne ankete na platformi *Google form*, gde je zaposlenima data mogućnost da se izjasne odgovaranjem na pitanja na temu samoprocene o načinu upravljanja i organizovanja u zdravstvenoj ustanovi, u vidu deskriptivne studije. Anketni upitnik je modifikovana vezija upitnika *The Work Design Questionnaire* (6) i sadrži 8 pitanja koja se odnose na osnovne demografske podatke o zaposlenom i 26 pitanja (tvrdnji) koja se odnose na predmet istraživanja (Prilog 1). Pored svake stavke nalazi se skala sa ocenama (Likertova skala) od 1 do 5, koje treba zaokružiti u skladu sa stepenom u kojem se ispitanik slaže sa navedenim tvrdnjama: 1 – uopšte se ne slažem; 2 – ne slažem se; 3– niti se slažem, niti se ne slažem; 4 – slažem se; 5 – potpuno se slažem.

Istraživanje je sprovedeno u zdravstvenoj ustanovi kombinovane zdravstvene zaštite ZARZ Pasterov zavod, Novi Sad. Uzorak se sastojao od 19 ispitanika, što je predstavljalo reprezentativan uzorak od ukupno 22 zaposlena (19/22; 86,4%). Upitnici su podeljeni među zaposlenim radnicima ustanove i u cilju dobijanja što objektivnijih rezultata, istraživanje je obuhvatilo zaposlene iz različitih sektora, odnosno radnih jedinica i različitih nivoa organizacione strukture od rukovodioca do izvršioca. Odgovarali su na pitanja zdravstveni radnici svih profila stručnosti raznih medicinskih specijalnosti (lekari-specijalisti, na specijalizaciji, lekari opšte medicine, viši medicinski kadrovi, srednji medicinski kadrovi), zaposleni iz upravljačkog menadžmenta, tehničko osoblje ZARZ Pasterov zavod, Novi Sad i ostali koji obavljaju poslove koji nisu iz oblasti medicine. Izbor anketiranih radnika nije formiran prema određenom kriterijumu, već je istraživanje sprovedeno po principu slučajnog uzorka.

Kompletna statistička analiza podataka je urađena u programu za statističku analizu *GraphPad Prism* verzija 8.0.1 (*GraphPad Software Inc., La Jolla*, Kalifornija, Sjedinjene Američke Države). Sve atributivne varijable su predstavljene u obliku frekfencija pojedinih kategorija, a statistička značajnost učestalosti između pojedinih kategorija je testirana kombinovanim $\chi^2$ testom sa post hok analizom. *Yates*-ova korekcija je korišćena uslučaju da je zapojedinu varijablu zabeleženo 5 ili manje unosa.

Ovo istraživanje je izvršeno u skladu sa Helsinškom deklaracijom i odobreno od strane Etičkog odbora ZARZ Pasterov zavod Novi Sad (odobrenje broj 10-110/1 od 17.03.2023. godine).

with the aim of creating an organizational structure, which includes activities and relations between employees and manages human resources aimed at successful business operations on a long-term basis (3).

All organizations include three key elements: goals, structure and people (4). When the issue of organization is analyzed as a whole, it can be concluded that it represents a deliberately constructed and artificially designed entity. The basic differences between modern and traditional organizations can be perceived based on several postulates, depending on how much they focus on division of labor, centralization and span of control. The choice of the organizational model itself is not simple and it is influenced by numerous factors such as the size of the organization, the activities it is engaged in, as well as the geographical span of the organization (5).

The participatory management style is present in the Pasteur Institute. This style is applied by heads of departments who collect ideas from employees in their departments. On the other hand, employees participate in decision-making, but only partially, within the limits set by the leader. In addition to the participatory style of management, the linear organizational structure is characteristic of the Pasteur Institute, and it falls under the traditional models of organizational structures.

Such an organizational structure is the basis for all other models that base their operations on the hierarchy of relationships and responsibilities of positions within that organization. The basis of this model is the hierarchical relationship of each position within the organization, where each hierarchical level is under the control of a higher one. This characteristic facilitates communication lines and the chain of management, because all positions have clearly defined responsibilities. However, there is no detailed division of labor, and therefore, one person can do several different jobs. Accordingly, the superior on the same line of management is responsible for tasks beyond the authority of an individual.

Determining the management style, as well as the adequacy of relations between management and employees in healthcare institutions is of strategic importance for the operations of the institution itself (5). The organizing function is important for every company and it does not end with the definition of organizational structure, but it is necessary throughout the entire existence of the company due to the dynamics of modern business.

The aim of our study was to examine the attitudes of employees at the Institute for Anti-Rabies Protection – Pasteur Institute, Novi Sad towards the organization itself, organizational climate (atmosphere and relations that prevail in the organization among employees, primarily between managers and other members of the collective) and management.

## Methods

The research was conducted as a descriptive study in the period March 21$^{st}$ - March 28$^{th}$, 2023 using the anonymous survey on the platform Google form, where the employees were given the opportunity to answer self-assessment questions about management and organization in the healthcare institution. The survey questionnaire is a modified version of the questionnaire The Work Design Questionnaire (6) and it includes 8 questions related to the basic demographic data about the employee and 26 questions (statements) related to the subject of the study (Appendix 1). Next to each item there is a scale with marks (Likert scale) from 1 to 5, which should be circled according to the degree to which the respondent agrees with the given statements: 1 – Strongly disagree; 2 – Disagree; 3 – Neither agree nor disagree; 4 – Agree; 5 – Strongly agree.

The study was conducted in the health institution of combined healthcare, the Pasteur Institute in Novi Sad. Of the total of 22 employees, the sample included 19 respondents, which was a representative sample (19/22; 82.4%). The questionnaires were handed out among the employees of the institution and in order to obtain as objective results as possible, the study included different sectors, that is, work units and different levels of organizational structure, from managers to employees. Health workers of all profiles belonging to different medical specialties (doctors-specialists, doing specialization, general practitioners, medical staff who graduated from vocational academies, and medical staff with secondary education), employees from the management sector, technical staff from the Pasteur Institute, Novi Sad and other non-medical staff answered the questions. The selection of

## Rezultati

Većinu ispitanika su činile osobe ženskog pola (13/19;68,4%). Ipak, statistički značajna razlika u učestalosti ženskog naspram muškog pola nije uočena ($\chi^2(1) = 1,30$; $p > 0,05$). Najviše ispitnika je pripadalo starosnim kategorijama 28-37 godina (7/19; 36,8%) i 38-47 godina(7/19; 36,8%). Uočena je statistički značajna razlika u učestalosti starosnih kategorija ($\chi^2(4) = 11,3$; $p < 0,05$).

Prosečna dužina radnog staža zaposlenih je bila 16,2 godina (95%CI: 14,8-17,6 godina). Najviše zaposlenih je imalo dužinu radnog straža od 11 do 15 godina (6/19; 31,6%) i 6-10 godina (5/19; 26,32%). Iako nije uočena značajna razlika u dužini radnog staža među zaposlenima ($\chi^2(5) = 10,1$; $p > 0,05$).

Najviše zaposlenih je imaloo brazovanjena nivou srednje škole (7/19; 36,8%) i visoke škole (6/19; 31,6%), dok su prirodne nauke bile najučestalija klasifikacija (10/19; 52,6%). Većina ispitanika (11/19; 57,9%) se izjasnila da je tokom rada uZARZ Pasterov zavod, Novi Sad napredovala. Nije uočena značajna razlika u učestalosti pojedinih kategorija nivoa obrazovanja ($\chi^2(3) = 4,36$; $p > 0,05$), pripadnosti kategoriji zanimanja ($\chi^2(3) = 2,11$; $p > 0,05$), kao ni u učestalosti napredovanja među zaposlenima ($\chi^2(1) = 0,47$; $p > 0,05$).

Najviše zaposlenih je bilo u kategoriji radnika (13/19; 68,4%), dok su po 2 ispitanika imala niži, srednji i viši nivo organizacione strukture (2/19; 10,5%). Posledično uočena je značajna razlika u distribuciji zaposlenih prema nivou organizacione strukture ($\chi^2(3) = 17,4$; $p < 0,05$). Svi ispitanici su se izjasnili da rade u državnom tipu organizacije ili javnom preduzeću (19/19; 100%).

Od ukupno 26 tvrdnji ponuđenih u upitniku, značajna razlika u distribuciji odgovora je identifikovana u 16 tvrdnji (Tabela 1). Najučestaliji stavovi zaposlenih kod svih tvrdnji su bili afirmativni (tj. „Potpuno se slažem" i/ili „Slažem se"), osim kod tvrdnje „Imamo poverenja jedni u druge" gde se podjednak broj ispitanika (n = 6) izjasnio sa „Slažem se" i „Ne slažem se".

## Diskusija

Većinaza poslenih je smatrala da u organizaciji ZARZ Pasterov zavod, Novi Sad postoje jasno definisane funkcije zaposlenih. Ta tvrdnja je jedina u kojoj je stav kolektiva izuzetno homogen, te je posledično uočena i visoko značajna razlika u učestalosti stava „Slažem se"i „Potpuno se slažem" naspram svih drugih opcija. Definisanje funkcije zaposlenih je rezultat administrativnog delovanja i može se smatrati faktorom koji na zaposlenog deluje spolja i nije pod uticajem pojedinca, već celokupnog rukovodstva (7). Stavovi zaposlenih ukazuju da je rukovodstvo ZARZ Pasterov zavod, Novi Sad adekvatno izvršilo procenu karakteristika pojedinaca i u skladu s time definisalo njihove funkcije. U prilog poziciji da je rukovodstvo ZARZ Pasterov zavod, Novi Sad izvršilo primerenu procenu zaposlenih je i najučestaliji stav da su njihovi ciljevi konkretni, da imaju efikasan sistem rada, kao i da su im odgovornosti precizno definisane.

S druge strane, nije uočena značajna razlika u učestalosti specifičnog stava po pitanju tvrdnji da se sposobnosti ljudi koriste do maksimuma, kao i da je svaki korak njihovog radnog procesa neophodan. Izostanak homogenosti u stavovima prema ovim tvrdnjama indikuje da postoji prostor za poboljšanje rada rukovodstva u ovim poljima, te da treba razmotriti postojanje potrebe za reevaluacijom korišćenja radnih kapaciteta pojedinaca, kao i identifikacija faza rada koje zaposleni smatraju suvišnim, nakon čega treba izvršiti analizu potrebe za uklanjanjem istih.

Izostanak homogenosti u stavu kolektiva je uočen i kod tvrdnje da svi zaposleni imaju mogućnost da utiču na odluke. Takav nalaz traži pažnju rukovodstva, s obzirom da ograničenje zaposlenih u okvirima odlučivanja dovodi do osećaja nedostatka kontrole nad radnom sredinom, čineći pojedinca osetljivim na stresore koji indukuju sindrom sagorevanja (8,9). Učestvovanje zaposlenih u odlučivanju o pitanjima koja se tiču radnog okruženja igra važnu ulogu u prevenciji sindroma sagorevanja i osećaja opterećenja (8,9). Protektivni efekat sposobnosti odlučivanja o svom radu je jasno prikazan na modelu četiri obrazovne bolnice u Ardabilu (Islamska Republika Iran) (10), gde je uočeno da su medicinske sestre znatno zadovoljnije svojim poslom u poređenju sa administrativnim radnicima. Iako je mentalno opterećenje medicinskih sestara značajno veće u odnosu na administrativne radnike, one takođe ostvaruju i veću kontrolu nad svojim poslom u poređenju sa kohortom iz administracije (10).

Jedno od mogućih rešenja za poboljšanje zatečene situacije je revizija organizacione strukture ustanove po službama, kao i kontrolisanje da li se održavaju redovni sastanci šefova sa zaposlenima u službama. Uzevši u obzir veličinu kolektiva, postoji

surveyed employees was not based on a certain criterion, however, the study was conducted according to the principle of random sampling.

The complete statistical analysis of data was carried out in the program for statistical analysis GraphPad Prism version 8.0.1 (GraphPad Software Inc., La Jolla, California, the United States of America). All attribute variables were presented in the form of frequencies of certain categories, while the statistical significance of the frequency between certain categories is tested with a $\chi^2$ test with post hoc analysis. Yates's correction was used when 5 or fewer entries were recorded for a particular variable. The existence of trends between certain groups of variables was examined using the correlation method. The analysis of the frequency of parameters was estimated at the level of statistical significance of $p < 0.05$.

This study was conducted in accordance with the Helsinki Declaration and approved by the Ethics Committee of the Pasteur Institute Novi Sad (number 10-110/1, March 17th, 2023).

## Results

The majority of respondents were female (13/19; 68.4%). However, statistically significant difference between the frequency of female and male gender was not noticed ($\chi^2(1) = 1.30$; $p > 0.05$). The majority of respondents belonged to the age groups 28-37 years (7/19; 36.8%) and 38-47 years (7/19; 36.84%). Statistically significant difference was observed in the frequency of age groups ($\chi^2(4) = 11.3$; $p < 0.05$).

The average length of service was 16.21 years (95% CI: 14.8 – 17.6 years). The majority of employees worked from 11 to 15 years (6/19; 31.6%) and 6-10 years (5/19; 26.3%). Although there was no significant difference regarding the length of service between the employees ($\chi^2(5) = 10.12$; $p > 0.05$).

The majority of employees had secondary school (7/19; 36.8%) and university education (6/19; 31.6%), while natural sciences were the most frequent classification (10/19; 52.6%). The majority of respondents (11/19; 57.9%) stated that they were promoted during their work at the Pasteur Institute in Novi Sad. There was no significant difference in the frequency of certain categories of educational levels ($\chi^2(3) = 4.36$; $p > 0.05$), category of occupation ($\chi^2(3) = 2.11$; $p > 0.05$), as well as in the frequency of advancement ($\chi^2(1) = 0.47$; $p > 0.05$) among the employees.

The majority of employees were in the category of workers (13/19; 68.4%), whereas 2 respondents had a lower, middle and higher level of organizational structure (2/19; 10.5%). As a result, a significant difference was observed in the distribution of employees according to the level of organizational structure ($\chi^2(3) = 17.4$; $p < 005$). All respondents stated that they worked in state organizations or public companies (19/19; 100%).

Out of the total of 26 statements offered in the questionnaire, a significant difference in the distribution of responses was identified in 16 cases (Table 1). The most frequent views of employees for all statements were affirmative (I strongly agree and/or I agree), except for the statement "We trust each other", where the equal number of respondents (n = 6) chose "I agree" and "I disagree".

## Discussion

The majority of employees think that employees' functions are clearly defined in the organization of the Pasteur Institute in Novi Sad. This is the only statement in which the attitude of the collective is extremely homogenous, and consequently, a highly significant difference was observed in the frequency of the attitude "I agree" and "I strongly agree" compared to all other options. Defining the employees' function is the result of administrative actions and can be a factor that has influence on the employee from outside and is not under the influence of an individual, but the entire management (7). The employees' views indicate that the management of the Pasteur Institute in Novi Sad made adequate estimates of the individual characteristics and in accordance with that defined their functions. The position that the management of the Pasteur Institute in Novi Sad made adequate estimates of employees is supported by the most frequent views that their goals are concrete, that they have an efficient system of work and that their responsibilities are precisely defined.

On the other hand, there was no significant difference in the frequency of specific attitude regarding the statements that people's abilities are used to the maximum, as well as that every step of their work process is necessary. The absence of homogeneity of attitudes towards these statements indicates that there is room

**Tabela 1.** Najučestaliji stavovi zaposlenih (n=19) o načinu upravljanja i organizovanja procesa rada u Zavodu za antirabičnu zaštitu - Pasterov zavod, Novi Sad

| Redni broj | Tvrdnja | Najučestaliji stav | Hi-kvadrat test |
|---|---|---|---|
| **1.** | Naši radni zadaci su jasno definisani | Slažem se (9/19; 47,4%)<br>Potpuno se slažem (8/19; 42,1%) | $\chi^2(4) = 19,68$;<br>$p < 0,001$ ** |
| **2.** | Naši ciljevi su konkretni | Potpuno se slažem (11/19; 57,9%) | $\chi^2(4) = 12,9$;<br>$p < 0,05$ * |
| **3.** | Naše odgovornosti su precizno definisane | Potpuno se slažem (11/19; 57,9%) | $\chi^2(4) = 12,9$;<br>$p < 0,05$* |
| **4.** | Sposobnosti ljudi se koriste do maksimuma | Potpuno se slažem (7/19; 36,8%)<br>Slažem se (7/19; 36,8%) | $\chi^2(4) = 7,83$;<br>$p > 0,05$ |
| **5.** | Držimo sastanke koji su produktivni | Slažem se (9/19; 47,4%) | $\chi^2(4) = 11,75$;<br>$p < 0,05$* |
| **6.** | Zadatke obavljamo u predviđenom roku | Potpuno se slažem (10/19; 52,6%) | $\chi^2(4) = 26,25$;<br>$p < 0,05$* |
| **7.** | Imamo efikasan sistem rada | Slažem se (9/19; 47,4%) | $\chi^2(4) = 11,75$;<br>$p < 0,05$* |
| **8.** | Svesni smo faza u kojima dolazi do najdužihz astoja u radnom procesu | Potpuno se slažem (8/19; 42,1%)<br>Slažem se (8/19; 42,1%) | $\chi^2(4) = 15,25$;<br>$p < 0,05$* |
| **9.** | Posao se obavlja logičnim tokom | Slažem se (11/19; 57,9%) | $\chi^2(4) = 21,25$;<br>$p < 0,05$* |
| **10.** | Svaki korak našeg radnog procesa je neophodan | Slažem se (8/19;42,1%) | $\chi^2(4) = 9,25$;<br>$p > 0,05$ |
| **11.** | Ljudi koji rade na međusobno povezanim poslovima smešteni su blizu jedno drugom | Potpuno se slažem (9/19; 47,4%) | $\chi^2(4) = 18,25$;<br>$p < 0,05$* |
| **12.** | Sjajno je raditi u firmi kao aktivan član: zato što nam je zabavno | Potpuno se slažem (7/19; 36,8%)<br>Slažem se (7/19; 47,4%) | $\chi^2(4) = 9,75$;<br>$p < 0,05$* |
| **13.** | Sjajno je raditi u firmi kao aktivan član: proslavljamo uspehe | Slažemse (10/19;52,6%) | $\chi^2(4) = 12,58$;<br>$p < 0,05$* |
| **14.** | Sjajno je raditi u firmi kao aktivan član: jedni druge tretiramo kao ljude, a ne samo kao brojke | Slažem se (8/19; 52,63%) | $\chi^2(4) = 8,83$;<br>$p > 0,05$* |
| **15.** | Sjajno je raditi u firmi kao aktivan član: svi imaju mogućnost da utiču na odluke | Slažem se (6/19; 31,6%) | $\chi^2(4) = 4,08$;<br>$p > 0,05$ |
| **16.** | Sjajno je raditi u firmi kao aktivan član: imamo pravila ponašanja kojih se ridržavamo | Slažem se (10/19; 52,6%) | $\chi^2(4) = 14,75$;<br>$p < 0,05$* |
| **17.** | Sjajno je raditi u firmi kao aktivan član: imamo poverenja jedni u druge | Slažem se (6/19; 31,6%)<br>Ne slažem se (6/19; 31,6%) | $\chi^2(4) = 4,33$;<br>$p > 0,05$ |
| **18.** | Rukovodstvo naše firme: zainteresovano je za ono što mi imamo da kažemo | Slažem se (10/19;52,6%) | $\chi^2(4) = 22,25$;<br>$p < 0,05$* |
| **19.** | Rukovodstvo naše firme: konsultuje nas pre nego što se odluči za neku promenu koja će direktno uticati na naš rad | Potpuno se slažem (7/19; 36,8%)<br>Slažem se (7/19; 36,8%) | $\chi^2(4) = 9,5$;<br>$p < 0,05$* |
| **20.** | Rukovodstvo naše firme: vodi računa o tome da nam prepusti i interesantne poslove | Slažem se (7/19; 36,8%) | $\chi^2(4) = 6,83$;<br>$p > 0,05$ |
| **21.** | Rukovodstvo naše firme: podstiče timski rad | Potpuno se slažem (8/19; 42,1%) | $\chi^2(4) = 6,83$;<br>$p > 0,05$ |
| **22.** | Rukovodstvo naše firme: ponaša se kao trener (posvećuje dovoljno vremena da bi nas obučilo za neke ključne operacije) | Potpuno se slažem (7/19; 36,8%) | $\chi^2(4) = 6,52$;<br>$p > 0,05$ |
| **23.** | Rukovodstvo naše firme: brine o našem profesionalnom razvoju u okviru firme | U potpunosti se slažem (10/19; 52,6%) | $\chi^2(4) = 19,25$;<br>$p < 0,05$(*) |
| **24.** | Rukovodstvo naše firme: rado sa nama deli važne informacije | U potpunosti se slažem (7/19; 47,4%)<br>Slažem se (7/19; 36,8%) | $\chi^2(4) = 9,08$;<br>$p > 0,05$ |
| **25.** | Rukovodstvo naše firme: osobe su koje poštujem | U potpunosti se slažem (14/19; 73,7%) | $\chi^2(4) = 34,25$;<br>$p < 0,05$(*) |

*razlika u učestalosti stavova je značajna; **razlika u učestalosti stavova je visoko značajna.

**Table 1.** The most frequent views of employees (n = 19) regarding the ways of managing and organizing the work process in the Institute for Anti-Rabies Protection – Pasteur Institute, Novi Sad

| Ordinal number | Statement | The most frequent view | chi-squared test |
|---|---|---|---|
| **1.** | Our work tasks are clearly defined | I agree (9/19; 47.4%)<br>I strongly agree (8/19; 42.1%) | $\chi^2(4) = 19.68$;<br>$p < 0.001$ ** |
| **2.** | Our goals are specific | I strongly agree (11/19; 57.9%) | $\chi^2(4) = 12.9$;<br>$p < 0.05$ * |
| **3.** | Our responsibilities are clearly defined | I strongly agree (11/19; 57.9%) | $\chi^2(4) = 12.9$;<br>$p < 0.05$* |
| **4.** | People's abilities are used to the maximum | I strongly agree (7/19; 36.8%)<br>I agree (7/19; 36.8%) | $\chi^2(4) = 7.83$;<br>$p > 0.05$ |
| **5.** | We hold meetings that are productive | I agree (9/19; 47.4%) | $\chi^2(4) = 11.75$;<br>$p < 0.05$* |
| **6.** | We perform tasks within the scheduled deadline | I strongly agree (10/19; 52.6%) | $\chi^2(4) = 26.25$;<br>$p < 0.05$* |
| **7.** | We have an efficient system of work | I agree (9/19; 47.37%) | $\chi^2(4) = 11.75$;<br>$p < 0.05$* |
| **8.** | We are aware of the phases with the longest delays in the work process | I strongly agree (8/19; 42.1%)<br>I agree (8/19; 42.11%) | $\chi^2(4) = 15.25$;<br>$p < 0.05$* |
| **9.** | The work is done in a logical way | I agree (11/19; 57.9%) | $\chi^2(4) = 21.25$;<br>$p < 0.05$* |
| **10.** | Each step of our work process is necessary | I agree (8/19; 42.1%) | $\chi^2(4) = 9.25$;<br>$p > 0.05$ |
| **11.** | People working in interrelated jobs are located close to each other | I strongly agree (9/19; 47.4%) | $\chi^2(4) = 18.25$;<br>$p < 0.05$* |
| **12.** | It is great to work in the company as an active member: because it is fun | I strongly agree (7/19; 36.8%)<br>I agree (7/19; 47.4%) | $\chi^2(4) = 9.75$;<br>$p < 0.05$* |
| **13.** | It is great to work in the company as an active member: we celebrate success | I agree (10/19; 52.6%) | $\chi^2(4) = 12.58$;<br>$p < 0.05$* |
| **14.** | It is great to work in the company as an active member: we treat each other as people, not just numbers | I agree (8/19; 52,63%) | $\chi^2(4) = 8,83$;<br>$p > 0,05$* |
| **15.** | It is great to work in the company as an active member: everyone is given the opportunity to influence decision | I agree (6/19; 31.6%) | $\chi^2(4) = 4.08$;<br>$p > 0.05$ |
| **16.** | It is great to work in the company as an active member: we have rules that we adhere to | I agree (10/19; 52.6%) | $\chi^2(4) = 14.75$;<br>$p < 0.05$* |
| **17.** | It is great to work in the company as an active member: we trust each other | I agree (6/19; 31.6%)<br>I disagree (6/19; 31.6%) | $\chi^2(4) = 4.33$;<br>$p > 0.05$ |
| **18.** | Management of our company: is interested in what we have to say | I agree (10/19; 52.6%) | $\chi^2(4) = 22.25$;<br>$p < 0.05$* |
| **19.** | Management of our company: consults us before deciding on a change that will directly affect our work | I strongly agree (7/19; 36.8%)<br>I agree (7/19; 36.8%) | $\chi^2(4) = 9.5$;<br>$p < 0.05$* |
| **20.** | Management of our company: takes care to leave interesting jobs to us | I agree (7/19; 36.8%) | $\chi^2(4) = 6.83$;<br>$p > 0.05$ |
| **21.** | Management of our company encourages teamwork | I strongly agree (8/19; 42.1%) | $\chi^2(4) = 6.83$;<br>$p > 0.05$ |
| **22.** | Management of our company: acts like a coach (dedicates enough time to train us for some key operations) | I strongly agree (7/19; 36.8%) | $\chi^2(4) = 6.52$;<br>$p > 0.05$ |
| **23.** | Management of our company: takes care of our professional development within the company | I strongly agree (10/19; 52.6%) | $\chi^2(4) = 19.25$;<br>$p < 0.05$(*) |
| **24.** | Management of our company: is happy to share important information with us | I strongly agree (7/19; 47.4%)<br>I agree (7/19; 36.8%) | $\chi^2(4) = 9.08$;<br>$p > 0.05$ |
| **25.** | I respect the management of our company | I strongly agree (14/19; 73.7%) | $\chi^2(4) = 34.25$;<br>$p < 0.05$(*) |

*difference in the frequency of views is significant; **difference in the frequency of views is highly significant.

mogućnost da je problem u komunikaciji i izjašnjavanju vezan za samo jednu službu, a ne celokupnu organizaciju, te je dalja analiza neophodna radi utvrđivanja koje su prepreke kod pojedinih zaposlenih da iskažu svoje mišljenjei zašto smatraju da se njihovo mišljenje ne uvažava u toku odlučivanja.

Uključivanje zdravstvenog osoblja u planiranje i implementaciju inovacija u tehnološkim i drugim organizacionim promenama ustanove je izuzetno važno. Iz perspektive zadovoljstva poslom, informisanje zaposlenih o predstojećim promenama najkorisnije je u ranijim fazama promene. Oni zdravstveni radnici koji su dobili informacije o organizacionim promenama u fazi planiranja promene osećali su se više poštovanim, imali su jači kolegijalni kapital, bili su zadovoljniji uticajem na radnom mestu i bili su zadovoljniji svojim menadžerima (11,12).

Analizom rezultata iz oblasti klime u organizaciji većinom odgovora ispitanika utvrđujemo da u organizaciji preovladava podsticajna atmosfera. Ipak, rezultati samoprocene ukazuju da je potrebno raditi na povećanju poverenja među zaposlenima. To se može postići projektovanjem svakog zaposlenog pojedinačno da se razvija u pravcu profesionalca, i da se razvija timski duh u svakoj službi, gde bi zajednički cilj i interes bili glavna preokupacija zaposlenih.

Da bi se poboljšao protok informacija potrebno je uticati na brzinu, kompletnost i jasnoću tokova informacija među zaposlenima, uzevši u obzir veliku mogućnost uticaja komunikacije na organizaciono ponašanje (13).

Globalizacija i napredak u informacionim tehnologijama i komunikacijama postavljaju izazove pred tradicionalne modele centralizovanog upravljanja. Evidentna je potreba za decentralizacijom u upravljanju zdravstvenim uslugama, gde se kao rešenje nudi model holakratije (14).

U kontekstu COVID-19 pandemije, nameće se pitanje o koristima autonomije u upravljanju zdravstvenim sistemima, koje naglašava značaj decentralizacije u rešavanju hitnih situacija.Prednosti primene holakratije u zdravstvenoj ustanovi su višestruke. Holakratija omogućava distribuirano donošenje odluka, omogućavajući zdravstvenim radnicima na različitim nivoima da donesu pravovremene odluke u okviru svojih uloga (14). Ovo može poboljšati odgovor na potrebe pacijenata i poboljšati ukupnu zdravstvenu zaštitu. Fleksibilnost i prilagodljivost holakratije mogu pomoći zdravstvenim ustanovama da se brzo prilagode situacijama koje se razvijaju, kao što su krize javnog zdravlja ili promene u demografiji pacijenata. Sa jasnim ulogama i odgovornostima, zdravstveni timovi mogu pojednostaviti komunikaciju i koordinaciju, što dovodi do efikasnije nege pacijenata. Naglasak holakratije na stalnom poboljšanju može doprineti unapređenju procesa zdravstvene zaštite (15). Krugovi u holakratiji olakšavaju kolaborativne napore među zdravstvenim timovima. Poboljšana komunikacija i zajedničke odgovornosti mogu podstaći kulturu timskog rada, što dovodi do zdravstvenih ishoda pacijenata (16). Autonomija koju daje holakratija može podstaći zdravstvene radnike da istraže inovativna rešenja za izazove nege pacijenata. Ovo može rezultirati implementacijom novih i efikasnih zdravstvenih usluga.

Pored toga, eksplicitna definicija uloga i odgovornosti holakratije obezbeđuje jasnu odgovornost, što je ključno za održavanje standarda bezbednosti pacijenata, te može pomoći u sprečavanju grešaka i poboljšanju kvaliteta nege (17). S druge strane, kod zdravstvenih radnika koji su navikli na tradicionalne hijerarhijske strukture prelazak na holakratiju mogao bi naići na otpor. Prevazilaženje ovog otpora zahteva efikasne strategije upravljanja promenama, a tranzicija može biti složena i može zahtevati značajno vreme i resurse za obuku i adaptaciju. Ako uloge i odgovornosti nisu dobro definisane ili ako je prisutan nedostatak komunikacije, postoji rizik od nastajanja nedosledne nege pacijenata. Zdravstvene ustanove moraju osigurati da se standardi nege pacijenata održavaju tokom tranzicije. Integracija holakratije u zdravstvenu ustanovu može predstavljati izazove u koegzistenciji sa postojećim hijerarhijskim strukturama. Balansiranje novog pristupa sa tradicionalnim linijama izveštavanja zahteva pažljivo razmatranje od strane menadžmenta.

Ograničenja sprovedene studije su ta da je u anketi učestvovao mali broj ispitanika, zaposlenih u ZARZ Pasterov zavod, Novi Sad.

## Zaključak

Na osnovu sprovedenog istraživanja o stavovima zaposlenih u ZARZ Pasterov zavod, Novi Sad o samoj organizaciji, klimi u organizaciji i rukovođenju može se zaključiti da većina zaposlenih smatra da su njihove funkcije jasno definisane, ciljevi konkretni, odgovornosti zaposlenih u organizaciji precizno definisane, kao i da je atmosfera u orga-

for improving the management's work in these fields, and that the existence of need for the re-evaluation of individual work capacities should be considered, as well as the identification of work phases that are thought to be redundant by the employees, after which the analysis of the need to remove them should be carried out.

The absence of homogeneity in the attitude of the collective was also observed for the statement that all employees have the opportunity to influence decisions. This finding requires the attention of the management, considering that the limitation of employees in decision-making processes leads to the feeling of lack of control over the work environment, thus making an individual sensitive to stressors that induce burnout syndrome (8,9). The participation of employees in making decisions about questions related to the work environment plays an important role in the prevention of burnout syndrome and feeling of a heavy workload (8,9). The protective effect of the ability to make decisions about one's work is clearly shown in the model of four educational hospitals in Ardabil (Islamic Republic of Iran) (10), where it was found that nurses were significantly more satisfied with their work compared to administrative workers. Although the mental workload is significantly higher compared to administrative workers, they also exercise more control over their work compared to the administrative cohort (10).

One of the possible solutions to improve the existing situation is the revision of organizational structure of the institution by departments, as well as controlling whether regular meetings of heads with employees in departments are held. Taking into consideration the size of the collective, there is a possibility that the problem in communicating and expressing one's opinion is related only to one service and not the entire organization, and further analysis is necessary in order to determine what the obstacles for individual employees to express their opinions are and why they think that their opinion is not taken into consideration when decisions are made.

The inclusion of health personnel in the planning and implementation of innovations in technological and other organizational changes in the institution is extremely important. As far as job satisfaction is concerned, informing the employees about upcoming changes is most useful in the earlier phases of change. Those healthcare workers who received information about organizational changes in the phase of planning of that change felt more respected, had a stronger collegial capital, were more satisfied with their influence in the workplace, and were more satisfied with their managers (11,12).

The analysis of results in the field of organizational climate showed, in the majority of respondents' answers, that a stimulating atmosphere prevails in the organization. Nevertheless, the results of self-assessment indicate that work is needed to increase trust among employees. This can be achieved by supporting each employee to develop professionally, while team spirit should be developed in each department, where common goals and interests would be the employees' main concern.

In order to improve the flow of information, it is necessary to influence the speed, completeness and clarity of the flow of information among employees, considering the great possibility of influence of communication on organizational behavior (13).

Globalization and progress in information technologies and communications pose challenges to traditional models of centralized management. The need for decentralization in managing healthcare services is evident, where the holacracy model is offered as a solution (14).

In the context of Covid-19 pandemic, the question arises about the benefits of autonomy in the management of health systems, which emphasizes the importance of decentralization in solving emergency situations. The advantages of applying holacracy in healthcare institutions are multiple. Holacracy enables distributed decision-making, allowing health workers at different levels to make timely decisions within their roles (14). This can improve the response to patients' needs and improve the overall healthcare. The flexibility and adaptability of holacracy can help health care institutions to adapt quickly to evolving situations, such as public health crises or changes in patients' demography. With clear roles and responsibilities, health care teams can facilitate communication, which leads to more efficient patient care. The emphasis of holacracy on constant improvement can contribute to the improvement of healthcare process (15). Circles in holacracy facilitate collaborative efforts in healthcare teams. The improved communication

nizaciji podsticajna. Medjutim, postoji nedostatak homogenosti u stavovima zaposlenih po pitanjima korišćenja njihovih sposobnosti do maksimuma, neophodnosti svakog koraka njihovog radnog procesa, postojanja mogućnosti da svi zaposleni utiču na odluke u ustanovi, postojanja poverenja jednih u druge, kao i po pitanjima informisanja zaposlenih od strane rukovodstva i komunikacije.

Neophodno je uvođenje participativnijeg pristupa u procesu donošenja odluka u ustanovi i implementacija mera usmerenih ka korišćenju sposobnosti zaposlenih do maksimuma, uključivanju svih zaposlenih u proces odlučivanja u ustanovi, jačanju međusobnog poverenja i razvoju timskog rada, informisanja zaposlenih od strane rukovodstva i komunikacije, kako bi se unapredila efikasnost ustanove i postiglo održivo poboljšanje organizacione klime i rada rukovodstava u ZARZ Pasterov zavod, Novi Sad.

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

## Reference


1. Ingþórsson ÁH, Alfirević N, Pavičić J, Vican D, editors. Educational Leadership in Policy: Challenges and Implementation Within Europe. Cham: Springer International Publishing; 2019. doi: 10.1007/978-3-319-99677-6
2. Ramadani V, Kjosev S, Sergi BS. Entrepreneurship Development in the Balkans: Perspective from Diverse Contexts. Emerald Publishing Limited; 2023.
3. McWilliams A, Williams C. MGMT. Cengage Learning; 2014.
4. Axelrod RH. Terms of Engagement: changing the way we change organizations. Berrett-Koehler Publishers; 2002.
5. Marić B, Bagarić I, Tot V. Axiological movements in management technologies of our organizations in the process of transition and globalization. Strategijski Menandžment. 2003;7(1–2):129–31.
6. Morgeson FP, Humphrey SE. The Work Design Questionnaire (WDQ): developing and validating a comprehensive measure for assessing job design and the nature of work. J Appl Psychol. 2006;91(6):1321–39. doi10.1037/0021-9010.91.6.1321.
7. Wang H, Tang C, Zhao S, Meng Q, Liu X. Job Satisfaction among health-care staff in township health centers in rural China: results from a Latent Class Analysis. Int J Environ Res Public Health. 2017;14(10):1101. doi:10.3390/ijerph14101101
8. Leiter MP, Maslach C. Six areas of worklife: a model of the organizational context of burnout. J Health Hum Serv Adm. 1999;21(4):472–89.
9. Portoghese I, Galletta M, Coppola RC, Finco G, Campagna M. Burnout and workload among health care workers: the moderating role of job control. Saf Health Work. 2014;5(3):152–7. doi:10.1016/j.shaw.2014.05.004.
10. Rostami F, Babaei-Pouya A, Teimori-Boghsani G, Jahangirimehr A, Mehri Z, Feiz-Arefi M. Mental workload and job satisfaction in healthcare workers: the moderating role of job control. Front Public Health. 2021;9:683388. doi: 10.3389/fpubh.2021.683388.
11. Turja T. Rather sooner than later: participatory change management associated with greater job satisfaction in healthcare. J Adv Nurs. 2022;78(3):e49–51. doi: 101111/jan.15133.
12. Jakobsen MD, Clausen T, Andersen LL. Can a participatory organizational intervention improve social capital and organizational readiness to change? Cluster randomized controlled trial at five Danish hospitals. J Adv Nurs. 2020;76(10):2685–95. doi: 10.1111/jan.14441.
13. Elving WJL. The role of communication in organisational change. Corporate Communications: An International Journal. 2005;10(2):129–38. doi: 10.1108/13563280510596943.
14. Krasulja N, Radojević I, Janjušić D, Holacracy-The new menagement system. I International Scientific Conference 2017;47(1):187-96
15. Weirauch L, Galliker S, Elfering A. Holacracy, a modern form of organizational governance predictors for person-organization-fit and job satisfaction. Front Psychol. 2023;13:1021545. doi: 10.3389/fpsyg.2022.1021545.
16. Saleh MO, Eshah NF, Rayan AH. Empowerment predicting nurses' work motivation and occupational mental health. SAGE Open Nurs. 2022;8:23779608221076812. doi: 10.1177/23779608221076811.
17. Donnelly AL, Ackerman L, Hall R, Choder B, DeWilde C, Ley J, et al. Hospital Considerations. In: Pet-Specific Care for the Veterinary Team [Internet]. John Wiley &Sons, Ltd; 2021.p. 477–541. doi:10.1002/9781119540687.ch7

and shared responsibilities can foster a culture of teamwork, which leads to better health outcomes of patients (16). The autonomy provided by holacracy can encourage healthcare professionals to explore innovative solutions to challenges related to patient care. This can result in the implementation of new and efficient health services.

In addition, the explicit definition of roles and responsibilities of holacracy ensures clear accountability, which is crucial for maintaining standards of patient safety, and therefore, it can help prevent errors and improve the quality of care (17). On the other hand, the transition to holacracy could be met with resistance by healthcare workers who are used to traditional hierarchical structures. Efficient strategies of managing changes are necessary to overcome this resistance, and the transition can be complex and may require significant time and resources for training and adaptation. If roles and responsibilities are not well defined or if there is a lack of communication, there is a risk of inconsistent patient care. Health care institutions must ensure that standards of patient care are maintained during the transition. Integrating holacracy into a health care institution may be challenging in coexistence with existing hierarchical structures. Balancing the new approach with traditional reporting lines requires careful consideration by management.

The limitations of the conducted study are that a small number of respondents, employees of the Pasteur Institute in Novi Sad, participated in the study.

## Conclusion

Based on the conducted research on the attitudes of the employees of the Pasteur Institute in Novi Sad towards the organization itself, organizational climate and management, it can be concluded that the majority of employees believe that their functions are clearly defined, their goals are concrete, the employees' responsibilities in the organization are precisely defined, as well as that the atmosphere in the organization is stimulating. However, there is a lack of homogeneity of employees' attitudes towards issues related to the use of their abilities to the maximum, necessity of each step of their work process, the existence of the possibility that all employees participate in decision-making processes in the institution, the existence of trust in each other, as well as towards issues related to information provided by the management and communication.

It is necessary to introduce a more participatory approach in the decision-making process within the institution and implement measures aimed at using employees' abilities to the maximum, involving all employees in the decision-making process in the institution, strengthening mutual trust and developing teamwork, informing the employees and improving communication, in order to improve the efficiency of the institution and achieve the sustainable improvement of organizational climate and managers' work in the Pasteur Institute in Novi Sad.

## Competing interests

The authors declared no competing interests.

## References


1. Ingþórsson ÁH, Alfirević N, Pavičić J, Vican D, editors. Educational Leadership in Policy: Challenges and Implementation Within Europe. Cham: Springer International Publishing; 2019. doi: 10.1007/978-3-319-99677-6
2. Ramadani V, Kjosev S, Sergi BS. Entrepreneurship Development in the Balkans: Perspective from Diverse Contexts. Emerald Publishing Limited; 2023.
3. McWilliams A, Williams C. MGMT. Cengage Learning; 2014.
4. Axelrod RH. Terms of Engagement: changing the way we change organizations. Berrett-Koehler Publishers; 2002.
5. Marić B, Bagarić I, Tot V. Axiological movements in management technologies of our organizations in the process of transition and globalization. Strategijski Menandžment. 2003;7(1–2):129–31.
6. Morgeson FP, Humphrey SE. The Work Design Questionnaire (WDQ): developing and validating a comprehensive measure for assessing job design and the nature of work. J Appl Psychol. 2006;91(6):1321–39. doi10.1037/0021-9010.91.6.1321.
7. Wang H, Tang C, Zhao S, Meng Q, Liu X. Job Satisfaction among health-care staff in township health centers in rural China: results from a Latent Class Analysis. Int J Environ Res Public Health. 2017;14(10):1101. doi:10.3390/ijerph14101101
8. Leiter MP, Maslach C. Six areas of worklife: a model of the organizational context of burnout. J Health Hum Serv Adm. 1999;21(4):472–89.
9. Portoghese I, Galletta M, Coppola RC, Finco G, Campagna M. Burnout and workload among health care workers: the moderating role of job control. Saf Health Work. 2014;5(3):152–7. doi:10.1016/j.shaw.2014.05.004.
10. Rostami F, Babaei-Pouya A, Teimori-Boghsani G, Jahangirimehr A, Mehri Z, Feiz-Arefi M. Mental workload and job satisfaction in healthcare workers: the moderating role of job control. Front Public Health. 2021;9:683388. doi: 10.3389/fpubh.2021.683388.

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11. Turja T. Rather sooner than later: participatory change management associated with greater job satisfaction in healthcare. J Adv Nurs. 2022;78(3):e49–51. doi: 101111/jan.15133.
12. Jakobsen MD, Clausen T, Andersen LL. Can a participatory organizational intervention improve social capital and organizational readiness to change? Cluster randomized controlled trial at five Danish hospitals. J Adv Nurs. 2020;76(10):2685–95. doi: 10.1111/jan.14441.
13. Elving WJL. The role of communication in organisational change. Corporate Communications: An International Journal. 2005;10(2):129–38. doi: 10.1108/13563280510596943.
14. Krasulja N, Radojević I, Janjušić D, Holacracy-The new menagement system. I International Scientific Conference 2017;47(1):187-96
15. Weirauch L, Galliker S, Elfering A. Holacracy, a modern form of organizational governance predictors for person-organization-fit and job satisfaction. Front Psychol. 2023;13:1021545. doi: 10.3389/fpsyg.2022.1021545.
16. Saleh MO, Eshah NF, Rayan AH. Empowerment predicting nurses' work motivation and occupational mental health. SAGE Open Nurs. 2022;8:23779608221076812. doi: 10.1177/23779608221076811.
17. Donnelly AL, Ackerman L, Hall R, Choder B, DeWilde C, Ley J, et al. Hospital Considerations. In: Pet-Specific Care for the Veterinary Team [Internet]. John Wiley &Sons, Ltd; 2021.p. 477–541. doi:10.1002/9781119540687.ch7



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# OTKRIVANJE PROGNOSTIČKE MOĆI RANE SIMPTOMATOLOGIJE UMERENO TEŠKIH DO TEŠKIH OBLIKA COVID-19 BOLESTI

**Branko Beronja[1], Olja Stevanović[2], Nataša Nikolić[1,2], Nevena Todorović[2], Ana Filipović[2], Jelena Simić[2], Tatjana Gazibara[1,3], Jelena Dotlić[1,4], Biljana Lukić[5], Aleksandra Karan[5], Ivana Milošević[1,2]**

[1] Medicinski fakultet, Univerzitet u Beogradu, Beograd, Republika Srbija
[2] Klinika za infektivne i tropske bolesti, Univerzitetski Klinički Centar Srbije, Beograd, Republika Srbija
[3] Institut za Epidemiologiju, Medicinski fakultet, Univerzitet u Beogradu, Beograd, Republika Srbija
[4] Klinika za ginekologiju i akušerstvo, Univerzitetski Klinički Centar Srbije, Beograd, Republika Srbija
[5] Opšta bolnica "Dr Radivoj Simonović", Sombor, Republika Srbija

[*] Korespondencija: prof. dr Ivana Milošević, Klinika za infektivne i tropske bolesti, Klinički Centar Srbije, Medicinski fakultet Univerziteta u Beogradu, Bulevar oslobođenja 16, 11000 Beogra, Srbija; e-mail: ivana.milosevic@med.bg.ac.rs

**SAŽETAK**

**Uvod/Cilj:** Nije u potpunosti jasno koji početni simptomi mogu biti prediktori loših ishoda COVID-19 bolesti. Cilj ove studije je bio da identifikuje početne simptome i znake COVID-19 bolesti povezane sa potrebom lečenja u jedinici intenzivne nege (JIN) i smrtnim ishodom.
**Metode:** Sprovedena je retrospektivna analiza pacijenata koji su hospitalizovani u dve zdravstvene ustanove (u Beogradu i Somboru) od marta 2021. do aprila 2022. godine. Podaci su prikupljeni iz elektronske medicinske dokumentacije. Glavni ishodi bili su lečenje i umiranje u JIN. Korišćen je Koksov proporcionalni regresioni model kako bi se identifikovali početni simptomi i znaci COVID-19 povezani sa lečenjem i umiranjem u JIN.
**Rezultati:** U ovom istraživanju učestvovalo je 457 pacijenata. Prosečna starost pacijenata iznosila je 63,77±13,75 godina. Najčešći početni simptomi i znaci COVID-19 bili su febrilnost (85,1%), kašalj (77,2%) i malaksalost (54,5%). Najređi početni simptomi bili su promuklost (2,8%), teškoće pri gutanju (2,8%) i svrab očiju (1,7%). Model korigovan na relevantne faktore pokazao je da su stariji uzrast i bol u grudima nezavisno povezani sa potrebom za lečenjem u JIN. Takođe, stariji urast, otežano disanje, glavobolja i dijareja, kao i odsustvo nazalne kongestije, bili su nezavisni prediktori smrtnog ishoda.
**Zaključak:** Rezultati ove studije ukazuju na važnost pažljivog praćenja i brze intervencije kod pacijenata koji se javljaju sa bolom u grudima, otežanim disanjem, glavoboljom, dijarejom, posebno ako se radi o starijim osobama.

**Ključne reči:** COVID-19, prognoza, jedinica intezivne nege, smrtni ishod, simptomi.

## Uvod

Iako većina ljudi koji se zaraze koronavirusnom bolešću 2019 (COVID-19) imaju blagu kliničku sliku, pojedini pacijenti, posebno oni koji već imaju hronične bolesti, mogu razviti teške komplikacije, kao što su respiratorna insuficijencija, aritmije, septički šok, bubrežnu insuficijenciju, kardiovaskularno oštećenje, ili disfunkcija jetre (1,2). Iako je nazofarinks primarno mesto ulaska prouzrokovača COVID-19, nedavna studija je pokazala da osobe koje su zaražene koronavirusom 2 izazivačem teškog akutnog respiratornog sindroma (SARS-CoV-2) retko imaju simptome u nivou gornjih disajnih puteva na samom početku kliničke faze bolesti (3). Najčešći početni simptomi COVID-19 podrazumevaju febrilnost, kašalj, mijalgiju ili umor, gubitak čula ukusa i mirisa (4,5), koji se javljaju prilikom infekcije svim varijantama SARS-CoV-2.

Međutim, teško je razlikovati koji od ovih simptoma bi mogao biti najjači prediktor loših ishoda COVID-19. Prethodno istraživanje je pokazalo da ljudi koji imaju otežano disanje i bol u grudima imaju veće šanse za razvoj teške forme infekcije

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# UNVEILING THE PROGNOSTIC POWER OF EARLY SYMPTOMOLOGY IN MODERATE TO SEVERE FORM OF COVID-19 DISEASE

**Branko Beronja[1], Olja Stevanović[2], Nataša Nikolić[1,2], Nevena Todorović[2], Ana Filipović[2], Jelena Simić[2], Tatjana Gazibara[1,3], Jelena Dotlić[1,4], Biljana Lukić[5], Aleksandra Karan[5], Ivana Milošević[1,2]**

[1] Faculty of Medicine, University of Belgrade, 11000 Belgrade, Republic of Serbia
[2] Clinic of Infectious and Tropical Diseases, University Clinical Centre of Serbia, 11000 Belgrade, Republic of Serbia
[3] Institute of Epidemiology, Faculty of Medicine, University of Belgrade, Belgrade, Republic of Serbia
[4] Clinic for Gynecology and Obstetrics, University Clinical Center of Serbia, 11000 Belgrade, Republic of Serbia
[5] General Hospital "Dr Radivoj Simonović" 25000 Sombor, Republic of Serbia

* Correspondence: Assoc. Prof. Ivana Milošević, MD, PhD; Clinic of Infectious and Tropical Diseases, Clinical Centre of Serbia, Facultyof Medicine University of Belgrade; e-mail: ivana.milosevic@med.bg.ac.rs

**SUMMARY**

**Introduction/Aim:** It is not entirely clear what initial symptoms could predict poorer COVID-19 outcomes. The purpose of this study was to identify the initial COVID-19 symptoms associated with the need for an intensive care unit (ICU) treatment and having fatal outcomes of COVID-19.
**Methods:** A retrospective analysis was conducted on patients who were hospitalized in two health care facilities (in Belgrade and Sombor) from March 2021 to April 2022. Data were collected from the electronic medical records. The main outcomes were treatment in the ICU and ICU mortality. The Cox proportional hazard model was used to identify the initial COVID-19 symptoms associated with the ICU treatment and mortality.
**Results:** This research included 457 patients. The average age of patients was 63.77±13.75 years. The most common initial symptoms of COVID-19 were fever (85.1%), cough (77.2%), and fatigue (54.5%). The least common initial symptoms were hoarseness (2.8%), difficulty swallowing (2.8%), and eye itching (1.7%). The adjusted model showed that being older and having chest pain were independently associated with needing the ICU treatment. Furthermore, being older, having shortness of breath, headache and diarrhea, but absence of nasal congestion, were independently associated with poorer survival.
**Conclusion:** The results of this study emphasize the importance of vigilant monitoring and swift intervention in patients presenting with chest pain, shortness of breath, headache, and diarrhea, particularly among older people.

**Keywords:** COVID-19, prognosis, intensive care unit, fatal outcome, symptoms.

## Introduction

Even though most people who catch coronavirus disease 2019 (COVID-19) have mild illness, certain individuals, particularly those who have preexisting chronic health conditions, may develop severe complications, such as such as respiratory failure, arrhythmias, septic shock, renal failure, cardiovascular damage, or liver dysfunction (1, 2). Although the nasopharynx is the primary portal of entry for causative agent of COVID-19, a recent study has shown that individuals who are infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seldom present upper respiratory symptoms at the very beginning of the clinical phase of the disease (3). Most common initial symptoms of COVID-19 include fever, cough, myalgia or fatigue, loss of sense of taste and smell (4, 5), and they are consistent across all variants of the SARS-CoV-2.

However, it might be difficult to distinguish which of those symptoms could be the strongest predictor of poorer COVID-19 outcomes. Previous research found that people who present

COVID-19, jer ovi simptomi odgovaraju početnoj manifestaciji pneumonije (5). Početni simptomi COVID-19 mogu varirati u zavisnosti od vremena posmatranja što može dovesti do širokog spektra heterogenih nalaza (6). Ova varijabilnost je značajna kako bi se definisali ključni početni simptomi povezani sa lošijim ishodima COVID-19 (6).

Imajući u vidu sve prethodno navedeno, cilj ove studije je bio da se utvrde početni simptomi i znaci COVID-19 bolesti koji su povezani sa potrebom za lečenjem u jedinici intenzivne nege (JIN) i fatalnim ishodima kod osoba sa umereno do teškom COVID-19 bolešću.

## Metod

Ova retrospektivna studija sprovedena je u dve zdravstvene ustanove: na Klinici za infektivne i tropske bolesti, Univerzitetskog Kliničkog Centra Srbije (UKCS) u Beogradu i u Opštoj bolnici „Dr Radivoj Simonović“ u Somboru. Ovo istraživanje je obuhvatilo pacijenate koji su primljeni na bolničko lečenje između 1. marta 2021. i 7. aprila 2022. Da bi bili uključeni u studiju, pacijenti su morali da ispune sledeće kriterijume: 1) potvrđena infekcija SARS-CoV-2 metodom kvantitative polimerazne lančane reakcije (RT-PCR) ili antigenskim testom, 2) uzrast od 18 i više godina, 3) postojanje umerene do teške kliničke slike bolesti COVID-19, 4) postojanje detaljne evidenciju početnih simptoma u istoriji bolesti koja je dokumentovana prilikom prijema na bolničko lečenje, 5) imaju detaljnu evidenciju ishoda bolesti COVID-19 (prijem u JIN, smrtni ishod ili vreme otpusta).

Umereno teška klinička slika karakteriše se teškom hipoksijom koja zahteva: primenu kiseoničke terapije, prisustvom povišene telesne temperature, pojavom višestrukih opacifikacija na rendgenskom snimku pluća ili specifičnim promenama na plućima koje su uočljive na skeneru grudnog koša, kao i znacima citokinske oluje koja dovodi do pogoršanja opšteg stanja pacijenta uz nagli porast vrednosti bilo CRP, fibrinogena, D-dimera ili IL-6 (2). Teška klinička slika podrazumeva dalje napredovanje citokinske oluje koja dovodi do nastanka akutnog respiratornog distres sindroma (2).

Određivanje veličine uzorka studije zasnivalo se na: 1) veličini populacije gradskog područja Beograda (procenjeno na oko 1,4 miliona stanovnika) i veličini populacije Zapadnobačkog okruga (procenjeno na oko 0,18 miliona stanovnika); 2) očekivanoj prevalenciji COVID-19 pozitivnih osoba kojima je potrebno bolničko lečenje (9% prema literaturi (7)), 3) intervalu poverenja od 95% i 4) verovatnoći alfa greške od 5%. Primenom ovih parametara, minimalna izračunata veličina uzorka je bila 126 (https://www.calculator.net/sample-size-calculator.html).

Ovo istraživanje je sprovedeno u skladu sa odredbama Helsinške deklaracije. Studiju je odobrio etički odbor UKCS (odobrenje br. 82/3-2023) i etički odbor Opšte bolnice „Dr Radivoj Simonović“ u Somboru (odobrenje br. 23-2171/2023-2).

Demografski i klinički podaci su prikupljeni iz elektronske medicinske dokumentacije putem zdravstvenog informacionog sistema Heliant Health iz obe zdravstvene institucije. Demografski podaci uključivali su: pol, uzrast, glavne tegobe i fizikalni nalaz na prijemu, početne simptome bolesti COVID-19, kao i vakcinalni status protiv SARS-CoV-2. Početni simptomi COVID-19 infekcije koji su razmatrani u studiji bili su febrilnost, malaksalost, otežano disanje (dispneju), artalgiju, bol u grudima, gubitak apetita, glavobolju, dijareju, anosmiju, kvantitativne poremećaje svesti, povraćanje, bol u leđima, kvantitativne poremećaje svesti, nazalnu kongestiju, promuklost, svrab oka i otežano gutanje. Kvantitativni poremećaji svesti odnosili su se na smanjenje nivoa svesti kada je osoba budna, ali ima smanjenu reaktivnost na draži. S druge strane, kvalitativni poremećaji svesti uključivali su promene u stanju svesti, koje utiču na sadržaj tako i na jasnoću svesti (kao što su zbunjenost, uznemirenost i nemir).

Pacijenti su bili podeljeni u dve grupe u zavisnosti od toga da li su bili lečeni u JIN-e. U okviru podgrupe pacijenata lečenih u JIN-e, dalja klasifikacija je izvršena na osnovu ishoda lečenja, pri čemu su podeljeni dodatno i na pacijente koji su preživeli i na one koji nisu preživeli do kraja hospitalizacije. Ove podgrupe su označene kao: 2a) preživeli iz JIN-e i 2b) pacijenti iz JIN-e koji nisu preživeli.

Statističke analize su sprovedene korišćenjem IBM SPSS verzije 17 (IBM Corp). Vrednost verovatnoće p manja od 0,05 je smatrana statistički značajnom. Deskriptivne karakteristike su prikazane korišćenjem srednjih vrednosti i standardnih devijacija za kontinualne varijable, dok su frekvencije i procenti korišćeni za kategoričke vaijable.

Normalnost raspodele kontinualnih varijabli je procenjena pomoću Kolmogorov-Smirnov testa. Za proceni razlike normalno raspoređenih kon-

with shortness of breath and chest pain have higher chances of developing severe COVID-19 because these symptoms correspond to the initial presentation of pneumonia (5). The initial symptoms of COVID-19 may vary depending on the time of observation, and therefore generate a wide array of heterogeneous findings (6). This variability is relevant in efforts to define key symptoms associated with poorer COVID-19 outcomes (6).

Bearing in mind all mentioned above, the purpose of this study was to identify the initial COVID-19 symptoms associated with the need for the intensive care unit (ICU) treatment and fatal outcomes of COVID-19.

## Methods

This retrospective study was conducted at two healthcare facilities: the Clinic for Infectious and Tropical Diseases, University Clinical Center of Serbia (UCCS) in Belgrade and the General Hospital "Dr Radivoj Simonovic" situated in Sombor. This research included patients admitted to hospital between March 1, 2021, and April 7, 2022. To be eligible for study participation, the patients had to meet the following criteria: 1) confirmed SARS-CoV-2 infection by real-time reverse-transcription polymerase chain reaction (RT-PCR) or antigen testing, 2) being 18 years of age or older, 3) exhibit moderate to severe clinical forms of COVID-19 disease, 4) have a detailed record of the initial symptoms in their medical history upon hospital admission 5) have a detailed record of COVID-19 disease outcomes (ICU admission, vital status during hospital stay or time of discharge).

A moderately severe clinical presentation is characterized by severe hypoxia requiring: oxygen therapy, elevated body temperature, presence of multiple opacities on chest X-ray or specific lung changes visible on chest CT scan, signs of cytokine storm leading to worsening of patient's general health status with a sudden increase in either C-reactive protein (CRP), fibrinogen, D-dimer, or interleukin 6 (IL-6) levels (2). A severe clinical presentation includes further progression of the cytokine storm and possible acute respiratory distress syndrome (2).

The calculation of the sample size was based on 1) the size population of the Belgrade metropolitan area (approximately 1.4 million inhabitants) and the population of the West Bačka District (estimated at around 0.18 million inhabitants); 2) the prevalence of people severe COVID-19 who require hospitalization (9% as per literature (7));3) a 95% confidence interval, and 4) an alpha error of 5%. Using these parameters, the minimum sample size was 126 participants (https://www.calculator.net/sample-size-calculator.html).

This study was conducted in line with the Helsinki Declaration. Ethical approval was granted by both the Ethics Committee of UCCS (approval no. 82/3-2023) and the Ethics Committee of the "Dr. Radivoj Simonovic" General Hospital in Sombor (approval no. 23-2171/2023-2).

Demographic and clinical data were collected from electronic medical records using the Heliant Health information system from both health care institutions. The demographic data included: gender, age, chief complaints and physical findings upon admission as the initial COVID-19 symptoms and SARS-CoV-2 vaccination status. The initial symptoms of COVID-19 infection considered in the study were fatigue, shortness of breath, arthralgia, chest pain, loss of appetite, headache, diarrhea, anosmia, qualitative disturbance of consciousness, vomiting, back pain, quantitative disturbance of consciousness, nasal congestion, hoarseness, itching of the eye, and difficulty swallowing. Quantitative disturbances of consciousness referred to a decrease in consciousness levels when a person is awake, but has a diminished responsiveness. On the other hand, qualitative disturbances of consciousness involve changes in the state of consciousness, affecting both the content and clarity of consciousness (such as confusion, agitation and restlessness).

Patients were divided into two groups based on whether they received the ICU treatment or not. Within the subgroup of patients treated in the ICU, a further classification was performed based on the treatment outcome, distinguishing between patients who survived the ICU treatment and those who did not. These subgroups were labeled as: 2a) ICU survivors and 2b) ICU non-survivors.

Statistical analyses were conducted using the IBM SPSS version 17 (IBM Corp). A p-value of less than 0.05 was considered statistically significant. Descriptive characteristics were reported using means and standard deviations for continuous variables, while frequencies and percentages were used for categorical variables.

The normality of distribution of parametric variables was assessed by the Kolmogorov-Smirnov

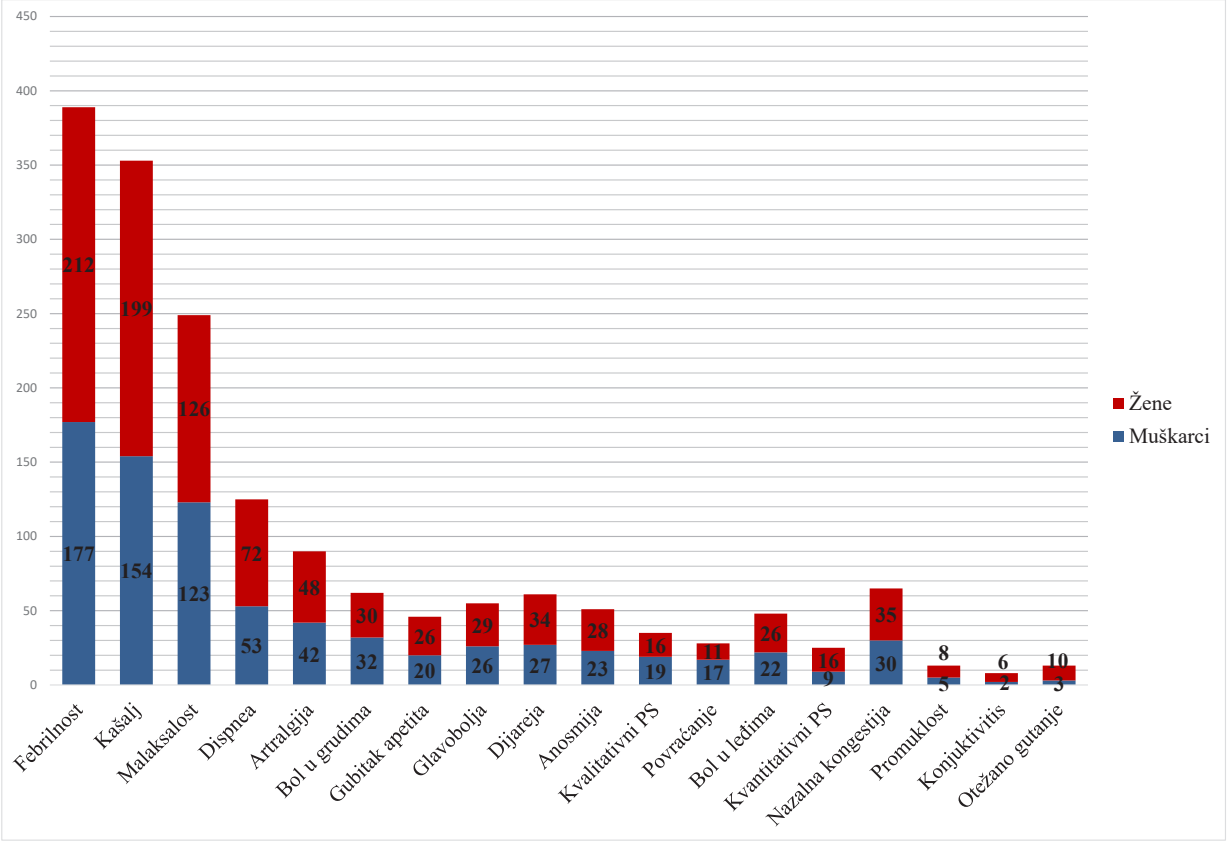
tinuiranih varijabli je korišćen t-test za dva nezavisna uzorka, dok je za kontinuirane varijable koje nisu imale normalnu raspodelu korišćen dvostrani Man-Vitnijev test. Procena razlike za kategoričke varijable je izvršena uz pomoć Fišerovog testa tačne verovatnoće i hi-kvadrat testom.

Koksov proporcijalni prediktivni model je korišćen za procenu faktora povezanih sa potrebom za lečenjem u JIN-u i smrtnim ishodom. Dimenzija vremena je obuhvatila dane od pojave prvih simptoma do analiziranih ishoda (lečenje u intenzivnoj nezi, smrt ili otpust iz bolnice). Najpre su analizirane sve demografske i kliničke varijable u univarijantnom modelu. Nakon testiranja nekoliko različitih pristupa multivarijantnom modelu, utvrđeno je da je optimalni multivarijantni model bio standardni opšti model u kojem su sve demografske i kliničke karakteristike analizirane zajedno.

## Rezultati

U studiju je uključeno 457 pacijenata. U uzorku je bilo nešto više žena u odnosu na muškarce (260; 56,9%). Prosečna starost ispitanika bila je 63,77±13,75 godine. Većina pacijenata nije bila vakcinisana (332; 74,6%). Najčešći početni simptomi su bili febrilnost (85,1%), kašalj (77,2%) i malaksalost (54,5%). Nešto ređi simptomi uključivali su otežano disanje (27,4%), artalgiju (19,7%), nazalnu kongestiju (14,2%), bol u grudima (13,6%) i dijareju (13,3%). Glavobolja (12,0%), gubitak apetita (12,0%), anosmija (11,1%) i bol u leđima (10,.5%) je navelo malo pacijenata. Najređi početni simptomi bili su kvalitativni (7,6%) i kvantitativni (5,4%) poremećaji svesti, povraćanje (6,1%), promuklost (2,8%), otežano gutanje (2,8%) i svrab oka (1,7%). Distribucija simptoma prema polu prikazana je na slici 1. U proseku, pacijenti su primljeni u bolnicu 5,2±1,9 dana od pojave simptoma. Takođe, srednje vreme od pojave simptoma do smrti bilo je 9,2±2,5 dana.

Pacijenti koji su lečeni u JIN-e češće su bili stariji (p=0,001) i češće nisu bili vakcinisani (p=0,005), češće su prijavljivali otežano disanje (p=0,018), bol u grudima (p=0,001) i anosmiju (p=0,019) kao početne simptome COVID-19, za razliku od pacijenata koji nisu bili lečeni u JIN-e. Ipak, značajne razlike u distribuciji ostalih početnih simptoma infekcije SARS-CoV-2 nisu zabeležene (Tabela 1).




Legenda: PS - poremećaj svesti

**Grafikon 1.** Broj ispitanika sa početnim simptomima infekcije uzrokovane virusom SARS-CoV2 u trenutku prijema u bolnicu

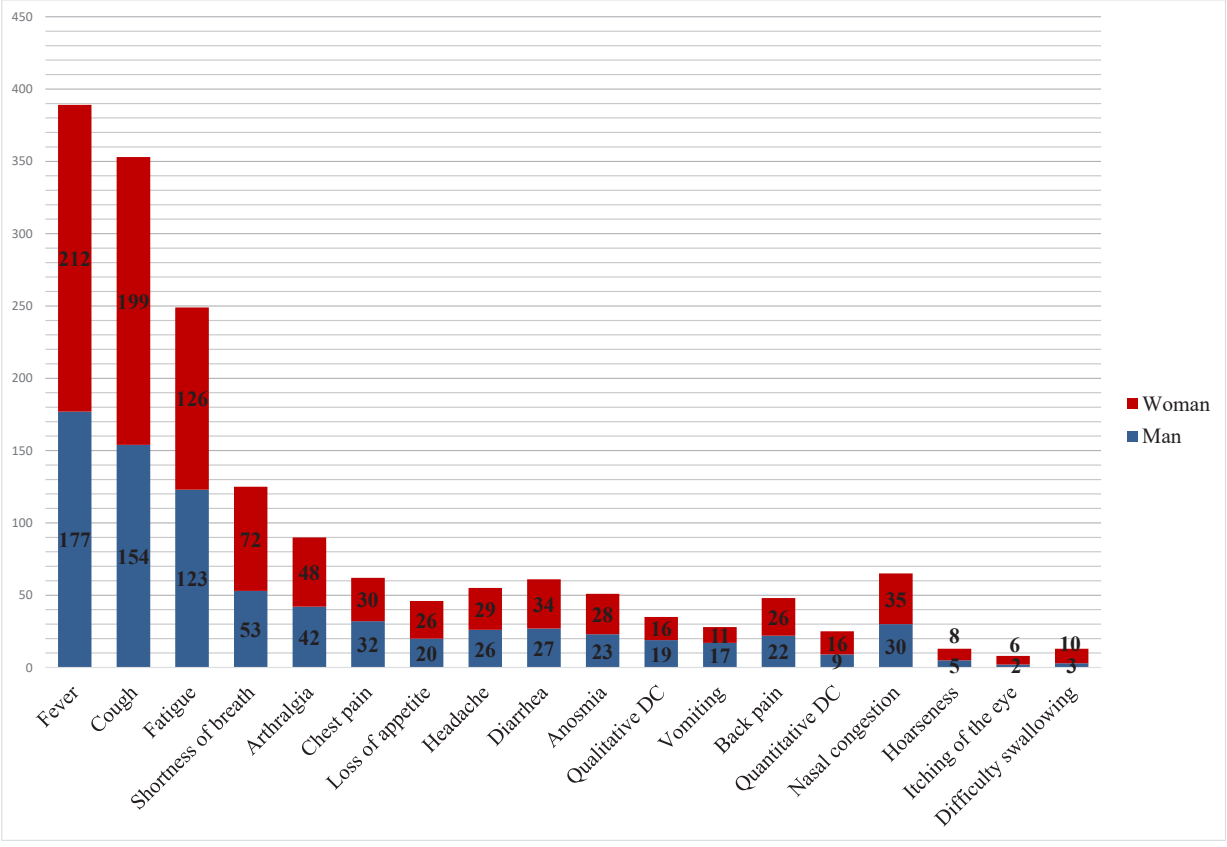
test. For normally distributed continuous variables, differences were assessed by the independent samples t-test, whereas non-normally distributed variables were analyzed using the nonparametric two-tailed Mann-Whitney test. Differences in categorical variables were evaluated using the Fisher's exact test and the Chi-square test.

The Cox proportional hazard model was applied to identify factors associated with the need for ICU treatment and ICU mortality. The timeline included days from the first symptom onset until the observed outcomes (ICU treatment, death or hospital discharge). First, we tested all demographic and clinical parameters a univariate model. After testing several different approaches to a selective multivariate model, we determined that the optimum adjusted model was the overall model when all demographic and clinical characteristics (symptoms) were analyzed together.

## Results

A total of 457 patients were included in the study. There were slightly more women than men (260; 56.9%). The average age of the study patients was 63.77±13.75 years. Most patients were not vaccinated (332;72.6%). The most frequent initial symptoms of COVID-19 were fever (85.1%), cough (77.2%), and fatigue (54.5%). Slightly less common symptoms included dyspnea (27.4%), arthralgia (19.7%), nasal congestion (14.2%), chest pain (13.6%) and diarrhea (13.3%). Headache (12.0%), loss of appetite (12.0%), anosmia (11.1%), and back pain (10.5%) were reported by few patients. The least frequent symptoms were qualitative (7.6%) and quantitative (5.4%) disturbances of consciousness, vomiting (6.1%), hoarseness (2.8%), swallowing difficulty (2.8%), and eye itching (1.7%). Distribution of symptoms according to gender is presented in Figure 1. On average, patients were admitted to hospital 5.2±1.9 days since the onset of symptoms. Also, mean time from the onset of symptoms until death was 9.2±2.5 days.

Patients treated in the ICU were older (p=0.001) and more often unvaccinated (p=0.005) compared to patients not needing the ICU treatment. Patients undergoing the ICU treatment more commonly reported shortness of breath (p=0.018), chest pain




Legend: DC - disturbance of consciousness

**Figure 1.** Number of patients with initial symptoms of SARS-CoV-2 infection upon hospital admission

**Tabela 1.** Demografske i kliničke karakteristike ispitanika u odnosu na potrebu za nastavkom lečenja u jedinici intenzivne nege

| Varijable | Potreba za nastavkom lečenja u JIN | | p vrednost |
|---|---|---|---|
| | Ne N=332 n (%) | Da N=125 n (%) | |
| **Pol** | | | |
| **Muški** | 145 (43,7) | 52 (41,6) | 0,223* |
| **Ženski** | 187 (56,3) | 73 (58,4) | |
| **Uzrast, medijana (IKO)** | 61,0 (19,7) | 74,0 (17,5) | **0,001†** |
| **COVID-19 vakcinacija** | | | |
| **Da** | 96 (28,9) | 20 (16,0) | **0,005*** |
| **Ne** | 236 (71,7) | 105 (84,0) | |
| **Febrilnost** | 284 (85,5) | 105 (84,0) | 0,840* |
| **Kašalj** | 259 (78,0) | 94 (75,2) | 0,643* |
| **Malaksalost** | 167 (50,3) | 66 (52,8) | 0,554* |
| **Dispneja** | 53 (42,4) | 72 (57,6) | **0,018*** |
| **Artalgija** | 63 (19,0) | 27 (21,6) | 0,529* |
| **Bol u grudima** | 25 (7,5) | 37 (29,6) | **0,001*** |
| **Gubitak apetita** | 33 (9,9) | 13 (10,4) | 0,884* |
| **Glavobolja** | 42 (12,7) | 13 (10,4) | 0,510* |
| **Dijareja** | 45 (13,6) | 16 (12,8) | 0,833* |
| **Anosmija** | 30 (9,0) | 21 (16,8) | **0,019*** |
| **Kvalitativni poremećaj svesti** | 26 (7,8) | 9 (7,2) | 0,821* |
| **Povraćanje** | 23 (6,9) | 5 (4,0) | 0,245* |
| **Bol u leđima** | 33 (9,9) | 15 (12,0) | 0,522* |
| **Kvantitativni poremećaj sveti** | 15 (4,5) | 10 (8,0) | 0,145* |
| **Nazalna kongestija** | 45 (13,6) | 20 (16,0) | 0,505* |
| **Promuklost** | 9 (2,7) | 3 (2,4) | 0,487* |
| **Konjunktivitis** | 7 (2,1) | 1 (0,8) | 0,456* |
| **Otežano gutanje** | 9 (2,7) | 4 (3,2) | 0,779* |

JIN-jedinica intenzivne nege; IKO - interkvartilni opseg;*prema Hi kvadrat testu ili Fišerovom testu tačne verovatnoće, † Man Vitnijev test; Podebljane vrednosti su statistički značajne

Pacijenti koji su preminuli u JIN-e češće su prijavljivali otežano disanje (p=0,001), dijareju (p=0,010) i anosmiju (p=0,001) u poređenju sa preživelim pacijentima u JIN-e. Pacijenti koji su se oporavili češće su imali febrilnost (p=0,005) i nazalnu kongestiju kao početne simptome COVID-19 u poređenju sa pacijentima koji su preminuli u JIN-e. Ostale razlike u distribuciji početnih simptoma nisu bile značajne (Tabela 2).

Tokom bolničkog lečenja 125 (27,3%) pacijenata sa COVID-19-om prevedeno je u JIN, dok je preostalih 332 (72,7%) pacijenata zbrinuto na opštim odeljenjima. Utvrđeno je da su stariji uzrast i bol u grudima kao početni simptom COVID-19 bili značajno povezani sa potrebom za lečenjem u JIN-e, prema rezultatu univarijantne analize. U multivarijantnoj analizi, stariji uzrast i bol u grudima, kao početni simptom COVID-19, ostali su značajno nezavisno povezani sa potrebom za lečenjem u JIN-e (Tabela 3).

Od 125 pacijenata koji su imali potrebu za nastavkom lečenja u JIN-e, 64 je umrlo, što je predstavlja letalitet u JIN-u od 51,2%. Na osnovu univarijantnog Koksovog proporcionalnog prediktivnog modela, stariji uzrast, dispneja, anosmija, kao i odsustvo temperature i nazalne kongestije, bili su značajno povezani sa smrtnošću u JIN-e. U multivarijantnom Koksovom proporcionalnom modelu,

**Table 1.** Demographic and clinical characteristics of the subjects in relation to the need for continued treatment in the intensive care unit

| Variable | Need for treatment in ICU | | p value |
|---|---|---|---|
| | No N=332 n (85.6%) | Yes N=125 n (27.3%) | |
| **Gender** | | | |
| **Male** | 145 (43.7) | 52 (41.6) | 0.223* |
| **Female** | 187 (56.3) | 73 (58.4) | |
| **Age, median** | 61.0 (19.7) | 74.0 (17.5) | **0.001†** |
| **COVID-19 vaccination** | | | |
| **Yes** | 96 (28.9) | 20 (16.0) | **0.005*** |
| **No** | 236 (71.7) | 105 (84.0) | |
| **Fever** | 284 (85.5) | 105 (84.0) | 0.840* |
| **Cough** | 259 (78.0) | 94 (75.2) | 0.643* |
| **Fatigue** | 167 (50.3) | 66 (52.8) | 0.554* |
| **Shortness of breath** | 53 (42.4) | 72 (57.6) | **0.018*** |
| **Arthralgia** | 63 (19.0) | 27 (21.6) | 0.529* |
| **Chest pain** | 25 (7.5) | 37 (29.6) | **0.001*** |
| **Loss of appetite** | 33 (9.9) | 13 (10.4) | 0.884* |
| **Headache** | 42 (12.7) | 13 (10.4) | 0.510* |
| **Diarrhea** | 45 (13.6) | 16 (12.8) | 0.833* |
| **Anosmia** | 30 (9.0) | 21 (16.8) | **0.019*** |
| **Qualitative disturbance of consciousness** | 26 (7.8) | 9 (7.2) | 0.821* |
| **Vomiting** | 23 (6.9) | 5 (4.0) | 0.245* |
| **Back pain** | 33 (9.9) | 15 (12.0) | 0.522* |
| **Quantitative disturbance of consciousness** | 15 (4.5) | 10 (8.0) | 0.145* |
| **Nasal congestion** | 45 (13.6) | 20 (16.0) | 0.505* |
| **Hoarseness** | 9 (2.7) | 3 (2.4) | 0.487* |
| **Itching of the eye** | 7 (2.1) | 1 (0.8) | 0.456* |
| **Difficulty swallowing** | 9 (2.7) | 4 (3.2) | 0.779* |

ICU-intensive care unit; IQR - interquartile range; *by Chi square test or Fisher's exact test, † Mann Whitney test; Bolded values denote statistical significance.

(p=0.001), and anosmia (p=0.019) as the initial COVID-19 symptoms, unlike patients who were not in need of the ICU. However, differences in the distribution of other initial symptoms of SARS-CoV-2 infection were not observed (Table 1).

Patients who died in the ICU more often reported shortness of breath (p=0.001), diarrhea (p=0.010), anosmia (p=0.001), and nasal congestion (p=0.011) compared to the surviving patients. Patients who recovered more often had fever (p=0.005) as the initial COVID-19 symptom compared to patients who died. Other differences in the distribution of initial symptoms were not recorded (Table 2).

During hospital stay, 125 (27.3%) COVID-19-infected patients were transferred to the ICU, while the remaining 332 (72.7%) patients were treated on the floor. It was found that being older and having chest pain as the initial COVID-19 symptoms were univariately associated with needing the ICU care. In the multivariate analysis, being older and having chest pain as the initial COVID-19 symptoms remained independently associated with needing the intensive care (Table 3).

Of 125 patients requiring ICU treatment, a total of 64 deaths occurred, resulting in an ICU case-fatality rate of 51.2%. Based on the univariate Cox

**Tabela 2.** Demografske i kliničke karakteristike ispitanika u odnosu na smrtni ishod u jedinici intenzivne nege

| Varijable | Smrtni ishod u JIN | | p vrednost |
|---|---|---|---|
| | Ne N=61 n (%) | Da N=64 n (%) | |
| **Pol** | | | |
| **Muški** | 27 (44,3) | 25 (39,1) | 0,555* |
| **Ženski** | 34 (55,7) | 39 (60,9) | |
| **Uzrast, medijana (IKO)** | 74,0 (16,5) | 73,5 (18,7) | 0,919† |
| **COVID-19 vakcinacija** | | | |
| **Da** | 12 (19,7) | 8 (12,5) | 0,274* |
| **Ne** | 49 (80,3) | 56 (87,5) | |
| **Febrilnost** | 57 (93,4) | 48 (75,0) | **0,005*** |
| **Kašalj** | 45 (73,8) | 49 (76,6) | 0,718* |
| **Malaksalost** | 27 (44,3) | 39 (60,9) | 0,062* |
| **Dispneja** | 23 (37,7) | 49 (76,6) | **0,001*** |
| **Artalgija** | 16 (26,2) | 11 (17,2) | 0,219* |
| **Bol u grudima** | 18 (29,5) | 19 (29,7) | 0,982* |
| **Gubitak apetita** | 7 (11,5) | 6 (9,4) | 0,701* |
| **Glavobolja** | 4 (6,6) | 9 (14,1) | 0,169* |
| **Dijareja** | 3 (4,9) | 13 (20,3) | **0,010*** |
| **Anosmija** | 2 (3,3) | 19 (29,7) | **0,001*** |
| **Kvalitativni poremećaj svesti** | 3 (4,9) | 6 (9,4) | 0,335* |
| **Povraćanje** | 1 (1,6) | 4 (6,3) | 0,189* |
| **Bol u leđima** | 9 (14,8) | 6 (9,4) | 0,355* |
| **Kvantitativni poremećaj sveti** | 3 (4,9) | 7 (10,9) | 0,215* |
| **Nazalna kongestija** | 15 (24,6) | 5 (7,8) | **0,011*** |
| **Promuklost** | 2 (3,3) | 1 (1,6) | 0,487* |
| **Konjunktivitis** | 0 (0,0) | 1 (1,6) | 0,327* |
| **Otežano gutanje** | 2 (3,3) | 2 (3,1) | 0,961* |

JIN-jedinica intenzivne nege; IKO - interkvartilni opseg; *prema $\chi 2$ testu ili Fišerovom testu tačne verovatnoće, † Man Vitnijev test; Podebljane vrednosti su statistički značajne

stariji uzrast, otežano disanje, glavobolja i dijareja, ali i odsustvo nazalne kongestije, kao početni simptomi COVID-19, bili su značajno nezavisno povezani sa smrtnim ishodom u JIN-e (Tabela 4).

## Diskusija

Ova studija je zabeležila da su dominantni početni simptomi i znaci COVID-19 kod pacijenata iz ove studijske populacije bili febrilnost, kašalj i umor. Na osnovu multivarijantnih modela, nezavisni prediktori potrebe za lečenjem u JIN-u bili su stariji uzrast i prisustvo bola u grudima. Dodatno, nezavisni prediktori fatalnog ishoda bili su stariji uzrast, otežano disanje, glavobolja, dijareja, ali i odsustvo nazale kongestije kao početni simptomi i znaci COVID-19. Iako su febrilnost, kašalj i umor česti, nisu bili povezani sa potrebom za lečenjem u JIN-u niti sa smrtnim ishodom usled bolesti COVID-19. Stoga, ova studija ističe specifične simptome i znake na početku COVID-19 koji mogu biti ključni za prognozu COVID-19 prilikom prijema u bolnicu.

U našoj studiji primećeno je da je stariji uzrast bio jedini zajednički prediktor potrebe za lečenjem u JIN-e i smrtnog ishoda usled COVID-19 u JIN-e. Stariji uzrast je očigledan i očekivan faktor udružen sa lošim ishodima COVID-19, zbog smanjene funkcionalne rezerve organa i višeg opšteg rizika od smrti. U studijama koje su ispitivale izolovani efekat uzrasta na ishode COVID-19, zabeležen je do porast rizika za bolničko lečenje za 3,4% i

**Table 2.** Demographic and clinical characteristics of subjects in relation to death in the intensive care unit

| Variable | Fatal outcome in ICU | | p value |
|---|---|---|---|
| | No N=61 n (%) | Yes N=64 n (%) | |
| **Gender** | | | |
| **Male** | 27 (44.3) | 25 (39.1) | 0.555* |
| **Female** | 34 (55.7) | 39 (60.9) | |
| **Age, median (IQR)** | 74.0 (16.5) | 73.5 (18.7) | 0.919† |
| **COVID-19 vaccination** | | | |
| **Yes** | 12 (19.7) | 8 (12.5) | 0.274* |
| **No** | 49 (80.3) | 56 (87.5) | |
| **Fever** | 57 (93.4) | 48 (75.0) | **0.005*** |
| **Cough** | 45 (73.8) | 49 (76.6) | 0.718* |
| **Fatigue** | 27 (44.3) | 39 (60.9) | 0.062* |
| **Shortness of breath** | 23 (37.7) | 49 (76.6) | **0.001*** |
| **Arthralgia** | 16 (26.2) | 11 (17.2) | 0.219* |
| **Chest pain** | 18 (29.5) | 19 (29.7) | 0.982* |
| **Loss of appetite** | 7 (11.5) | 6 (9.4) | 0.701* |
| **Headache** | 4 (6.6) | 9 (14.1) | 0.169* |
| **Diarrhea** | 3 (4.9) | 13 (20.3) | **0.010*** |
| **Anosmia** | 2 (3.3) | 19 (29.7) | **0.001*** |
| **Qualitative disturbance of consciousness** | 3 (4.9) | 6 (9.4) | 0.335* |
| **Vomiting** | 1 (1.6) | 4 (6.3) | 0.189* |
| **Back pain** | 9 (14.8) | 6 (9.4) | 0.355* |
| **Quantitative disturbance of consciousness** | 3 (4.9) | 7 (10.9) | 0.215* |
| **Nasal congestion** | 15 (24.6) | 5 (7.8) | **0.011*** |
| **Hoarseness** | 2 (3.3) | 1 (1.6) | 0.487* |
| **Itching of the eye** | 0 (0.0) | 1 (1.6) | 0.327* |
| **Difficulty swallowing** | 2 (3.3) | 2 (3.1) | 0.961* |

ICU-intensive care unit; IQR - interquartile range; *by Chi square test or Fisher's exact test, † Mann Whitney test; Bolded values denote statistical significance.

proportional hazard model, being older, having shortness of breath and anosmia, but absence of fever and nasal congestion were associated with the ICU mortality. In the multivariate Cox hazard model, being older, having shortness of breath, headache and diarrhea, but absence of nasal congestion as the initial symptoms of COVID-19 were independently associated with the ICU mortality in this population (Table 4).

## Discussion

This study reports that predominant initial symptoms of COVID-19 in our patients were fever, cough, and fatigue. Based on the multivariate models, the independent predictors of needing the ICU treatment were older age and having chest pain. Furthermore, the independent predictors of having fatal COVID-19 outcome were being older, having shortness of breath, headache, diarrhea, but no nasal congestion, as the initial symptoms of COVID-19. Despite being common, neither fever, nor cough nor fatigue was associated with receiving the ICU treatment and poor COVID-19 outcomes. Therefore, this study highlights specific symptoms at the beginning of clinically manifested COVID-19, which may be crucial for COVID-19 prognosis upon hospital admission.

**Tabela 3.** Rezultati univarijatnog i multivarijatnog Koksovog proporcionalnog prediktivnog modela: faktori povezani sa nastavkom lečenja u jedinici intenzivne nege

| | Univarijantni model* | | | Multivarijantni model* | | |
|---|---|---|---|---|---|---|
| **Varijable** | **HR** | **95% CI** | **p** | **HR** | **95% CI** | **p** |
| **Muški pol** | 0,79 | 0,55-1,14 | 0,206 | 0,75 | 0,51-1,11 | 0,153 |
| **Stariji uzrast** | 1,03 | 1,02-1,05 | **0,001** | 1,03 | 1,02- 1,05 | **0,001** |
| **COVID-19 vakcinacija** | 0,68 | 0,42-1,10 | 0,119 | 0,74 | 0,45-1,23 | 0,251 |
| **Febrilnost** | 0,91 | 0,56-1,47 | 0,702 | 0,89 | 0,53-1,50 | 0,668 |
| **Kašalj** | 1,01 | 0,67-1,52 | 0,959 | 0,95 | 0,62-1,47 | 0,843 |
| **Malaksalost** | 1,02 | 0,72-1,45 | 0,910 | 1,03 | 0,71-1,51 | 0,875 |
| **Dispneja** | 1,31 | 0,92-1,88 | 0,134 | 1,39 | 0,95-2,04 | 0,093 |
| **Artalgija** | 1,08 | 0,71-1,66 | 0,714 | 1,20 | 0,77-1,88 | 0,409 |
| **Bol u grudima** | 1,66 | 1,11-2,47 | **0,013** | 1,62 | 1,04-2,53 | **0,032** |
| **Gubitak apetita** | 1,06 | 0,59-1,88 | 0,851 | 1,24 | 0,67-2,30 | 0,487 |
| **Glavobolja** | 1,11 | 0,62-1,97 | 0,731 | 1,63 | 0,87-3,04 | 0,124 |
| **Dijareja** | 1,01 | 0,59-1,71 | 0,980 | 1,27 | 0,73-2,21 | 0,395 |
| **Anosmija** | 1,08 | 0,66-1,75 | 0,768 | 0,70 | 0,39-1,23 | 0,213 |
| **Kvalitativni poremećaj svesti** | 0,83 | 0,42-1,63 | 0,583 | 0,98 | 0,48-2,00 | 0,965 |
| **Povraćanje** | 0,51 | 0,21-1,25 | 0,145 | 0,60 | 0,24-1,52 | 0,280 |
| **Bol u leđima** | 0,89 | 0,52-1,54 | 0,685 | 0,8 | 0,50-1,55 | 0,649 |
| **Kvantitativni poremećaj sveti** | 0,15 | 0,81-2,45 | 0,192 | 1,65 | 0,79-3,42 | 0,182 |
| **Nazalna kongestija** | 0,97 | 0,59-1,60 | 0,974 | 1,08 | 0,64-1,81 | 0,766 |
| **Promuklost** | 0,66 | 0,21-2,08 | 0,480 | 0,39 | 0,11-1,30 | 0,124 |
| **Konjunktivitis** | 0,44 | 0,06-3,19 | 0,420 | 0,29 | 0,04-2,19 | 0,232 |
| **Otežano gutanje** | 1,38 | 0,51-3,74 | 0,528 | 1,38 | 0,49-3,91 | 0,546 |

JIN – jedinica intenzivne nege; HR-hazard ratio; CI-interval poverenja; Podebljane vrednosti su statistički značajne.

porast rizika za smrtni ishod u bolnici za 5,7% za svaku stariju godinu uzrasta (8, 9). Međutim, nema dokaza o postojanju praga starosti posle kojeg rizik za težu formu bolesti raste, pa je efekat starosti utvrđen kao linearan (9). U studiji koja je ispitivala prediktore respiratorne insuficijencije, primećeno je da je uzrast preko 60 godina značajan faktor povezan sa pojavom respiratorne insuficijencije i potrebom za mehaničkom ventilacijom (10). Stoga su naši rezultati u skladu sa prethodnim studijama.

Bol u grudima kao početni simptom je bio značajan prediktor nastavka lečenja u JIN-e u ovoj studijskoj grupi. Osnovni mehanizmi bola u grudima kao početnog simptoma u bolesti COVID-19 se mogu objasniti na nekoliko načina. Direktan uticaj virusa na tkiva pluća, koji rezultira inflamacijom i naknadnom aktivacijom nociceptivnih receptora u pleuri ili zidu grudnog koša, može dovesti do percepcije bola (11). Pored toga, neregulisani imunski odgovor izazvan SARS-CoV-2 karakteriše intenzivno oslobađanje proinflamatornih citokina kao što su IL-6 i faktor nekroze tumora alfa (TNF-α). Ovi medijatori doprinose patogenezi bola u grudima (12). Nadalje, potencijalni razvoj komplikacija povezanih sa bolešću COVID-19, poput pneumonije i akutnog respiratornog distres sindroma, može dodatno pogoršati neprijatne senzacije u nivou pluća i povećati nivo subjektivnog osećaja bola u grudnom košu (13).

Otežano disanje na početku bolesti COVID-19 kod pacijenata sa umerenom do teškom kliničkom slikom je zapažen kao prediktor fatalne forme COVID-19. Klinička slika dispneje, , kao rani simptom infekcije COVID-19 može se pripisati složenoj reakciji patofizioloških mehanizama koji uključuju virusom izazvanu bolest pluća, inflamatorne odgo-

**Table 3.** Univariate and multivariate Cox proportional predictive model results: factors associated with continuation of treatment in the intensive care unit

| | Univariate model | | | Multivariate model | | |
|---|---|---|---|---|---|---|
| **Variable** | **HR** | **95% CI** | **p** | **HR** | **95% CI** | **p** |
| **Male gender** | 0.79 | 0.55-1.14 | 0.206 | 0.75 | 0.51-1.11 | 0.153 |
| **Older age** | 1.03 | 1.02-1.05 | **0.001** | 1.03 | 1.02- 1.05 | **0.001** |
| **COVID-19 vaccination** | 0.68 | 0.42-1.10 | 0.119 | 0.74 | 0.45-1.23 | 0.251 |
| **Fever** | 0.91 | 0.56-1.47 | 0.702 | 0.89 | 0.53-1.50 | 0.668 |
| **Cough** | 1.01 | 0.67-1.52 | 0.959 | 0.95 | 0.62-1.47 | 0.843 |
| **Fatigue** | 1.02 | 0.72-1.45 | 0.910 | 1.03 | 0.71-1.51 | 0.875 |
| **Shortness of breath** | 1.31 | 0.92-1.88 | 0.134 | 1.39 | 0.95-2.04 | 0.093 |
| **Arthralgia** | 1.08 | 0.71-1.66 | 0.714 | 1.20 | 0.77-1.88 | 0.409 |
| **Chest pain** | 1.66 | 1.11-2.47 | **0.013** | 1.62 | 1.04-2.53 | **0.032** |
| **Loss of appetite** | 1.06 | 0.59-1.88 | 0.851 | 1.24 | 0.67-2.30 | 0.487 |
| **Headache** | 1.11 | 0.62-1.97 | 0.731 | 1.63 | 0.87-3.04 | 0.124 |
| **Diarrhea** | 1.01 | 0.59-1.71 | 0.980 | 1.27 | 0.73-2.21 | 0.395 |
| **Anosmia** | 1.08 | 0.66-1.75 | 0.768 | 0.70 | 0.39-1.23 | 0.213 |
| **Qualitative disturbance of consciousness** | 0.83 | 0.42-1.63 | 0.583 | 0.98 | 0.48-2.00 | 0.965 |
| **Vomiting** | 0.51 | 0.21-1.25 | 0.145 | 0.60 | 0.24-1.52 | 0.280 |
| **Back pain** | 0.89 | 0.52-1.54 | 0.685 | 0.8 | 0.50-1.55 | 0.649 |
| **Quantitative disturbance of consciousness** | 0.15 | 0.81-2.45 | 0.192 | 1.65 | 0.79-3.42 | 0.182 |
| **Nasal congestion** | 0.97 | 0.59-1.60 | 0.974 | 1.08 | 0.64-1.81 | 0.766 |
| **Hoarseness** | 0.66 | 0.21-2.08 | 0.480 | 0.39 | 0.11-1.30 | 0.124 |
| **Itching of the eye** | 0.44 | 0.06-3.19 | 0.420 | 0.29 | 0.04-2.19 | 0.232 |
| **Difficulty swallowing** | 1.38 | 0.51-3.74 | 0.528 | 1.38 | 0.49-3.91 | 0.546 |

HR-hazard ratio; CI-confidence interval; Bolded values are statistically significant, DC - disturbance of consciousness.

In our study, it was observed that older age was the only common predictor of both needing the ICU treatment and of fatal COVID-19 outcomes. Age is an obvious and expected contributor to poorer COVID-19 outcomes, due to the reduced organ reserve and higher risk of mortality in general. In studies examining the isolated effect of age on COVID-19 outcomes, there was a 3.4% increase in risk for hospital treatment and 5.7% increase in risk of hospital mortality per each year of age (8, 9). Furthermore, there was no evidence of an age threshold at which the risk of disease severity increases, because the effect of age on poorer COVID-19 outcomes was identified as linear (9). In a study focusing on predictors of respiratory failure, it was observed that age above 60 years is a contributor to respiratory failure and needing mechanical ventilation (10). Thus, our results are in line with previous studies.

Chest pain emerged as an initial symptom predictive of needing the ICU treatment in this study. The underlying mechanisms of chest pain as an initial symptom in COVID-19 infection can be explained through several pathways. The direct viral impact on lung tissues resulting in the inflammation and subsequent activation of nociceptive receptors in the pleura or chest wall can lead to a subjective perception of pain (11). Additionally, the dysregulated immune response in COVID-19 includes an abundant release of pro-inflammatory cytokines, such as the IL-6 and tumor necrosis factor-alpha (TNF-α). These mediators have been found to facilitate the onset of chest pain (12). Furthermore, potential development of COVID-19-related complications, such as pneumonia and acute respiratory distress

**Tabela 4.** Rezultati univarijantnog i multivarijantnog Koksovog proporcionalnog prediktivnog modela: faktori povezani sa smrtnim ishodom u jedinici intenzivne nege

| | Univarijantni model* | | | Multivarijantni model* | | |
|---|---|---|---|---|---|---|
| **Varijable** | **HR** | **95% CI** | **p** | **HR** | **95% CI** | **p** |
| **Muški pol** | 0,14 | 0,41-1,14 | 0,145 | 0,78 | 0,44-1,37 | 0,385 |
| **Godine** | 1,03 | 1,01-1,05 | **0,004** | 1,04 | 1,01-1,06 | **0,001** |
| **COVID-19 vakcinacija** | 0,52 | 0,25-1,09 | 0,084 | 0,62 | 0,28-1,34 | 0,228 |
| **Febrilnost** | 0,53 | 0,30-0,93 | **0,027** | 0,70 | 0,35-1,36 | 0,292 |
| **Kašalj** | 1,07 | 0,59-1,91 | 0,830 | 1,03 | 0,54-1,94 | 0,935 |
| **Malaksalost** | 1,39 | 0,84-2,32 | 0,199 | 1,19 | 0,67-2,10 | 0,541 |
| **Dispneja** | 3,10 | 1,73-5,57 | **0,001** | 3,02 | 1,62-5,62 | **0,001** |
| **Artalgija** | 0,82 | 0,43-1,57 | 0,549 | 0,99 | 0,50-1,96 | 0,980 |
| **Bol u grudima** | 1,59 | 0,91-2,78 | 0,130 | 1,53 | 0,78-2,96 | 0,208 |
| **Gubitak apetita** | 0,95 | 0,41-2,21 | 0,907 | 1,40 | 0,56-3,45 | 0,470 |
| **Glavobolja** | 1,67 | 0,81-3,33 | 0,174 | 2,51 | 1,10-5,66 | **0,027** |
| **Dijareja** | 1,76 | 0,95-3,24 | 0,072 | 2,43 | 1,21-4,83 | **0,012** |
| **Anosmija** | 2,27 | 1,28-3,88 | **0,005** | 1,35 | 0,67-2,71 | 0,393 |
| **Kvalitativni poremećaj svesti** | 1,11 | 0,48-2,58 | 0,807 | 1,20 | 0,48-3,01 | 0,692 |
| **Povraćanje** | 0,81 | 0,30-2,26 | 0,697 | 0,93 | 0,31-2,78 | 0,901 |
| **Bol u leđima** | 0,67 | 0,29-1,56 | 0,353 | 0,78 | 0,32-1,89 | 0,583 |
| **Kvantitativni poremećaj sveti** | 2,16 | 0,98-4,78 | 0,056 | 1,18 | 0,41-3,31 | 0,757 |
| **Nazalna kongestija** | 0,35 | 0,13-0,97 | **0,045** | 0,32 | 0,10-0,93 | **0,037** |
| **Promuklost** | 0,39 | 0,05-2,83 | 0,622 | 0,28 | 0,03-2,16 | 0,221 |
| **Konjunktivitis** | 0,95 | 0,13-6,89 | 0,961 | 0,52 | 0,06-4,19 | 0,547 |
| **Otežano gutanje** | 1,33 | 0,32-4,46 | 0,692 | 1,29 | 0,28-5,92 | 0,739 |

JIN – jedinica intenzivne nege; HR-hazard ratio; CI-interval poverenja; Podebljane vrednosti su statistički značajne

vore i disregulaciju sistema renin-angiotenzin-aldosteron (14-16). SARS-CoV-2 izaziva kaskadu inflamatornih procesa preko receptora angiotenzin-konvertujućeg enzima 2 (ACE2) eksprimiranih pretežno u respiratornom epitelu (15). To dovodi do aktivacije imunih ćelija, kao što su makrofagi i limfociti (15). Aktivacija puteva koagulacije i formiranje mikrotromba u plućnoj vaskulaturnoj mreži dalje doprinosi narušavanju razmene gasova i nastanku respiratornog distresa u teškim slučajevima infekcije (16). Multifaktorska priroda otežanog disanja kod COVID-19 naglašava složenu interakciju između patogeneze virusa, imunoloških odgovora i kardiovaskularne dinamike (15).

Refleks kašlja kod COVID-19 oboljenja je prvenstveno odgovor na iritaciju respiratorne sluzokože zbog inflamatornog odgovora koji je virus izazvao, što dovodi do povećane proizvodnje sluzi i hiperreaktivnosti disajnih puteva (16). Štaviše, neurogena inflamacija povezana sa aktivacijom senzornih nerava u epitelu disajnih puteva može doprineti upornom kašlju koji je primećen kod nekih pacijenata (15). Svi ovi faktori, dakle, mogu predisponirati osobu za razvoj sistemskih efekata zapaljenja, posledično, respiratorne insuficijencije.

U ovoj studiji zabeleženo je da je glavobolja kao početni simptom povezana sa smrtnim ishodom COVID-19 bolesti. Naši nalazi su u suprotnosti sa prethodno objavljenom meta-analizom koja je sugerisala da pacijenti koji prijavljuju glavobolju kao početni simptom COVID-19 imaju veće šanse za preživljavanje u poređenju sa osobama koje nemaju glavobolju (17). Postoje oprečni rezultati o vezi između glavobolje i nivoa proinflamatornih citokina. Naime, nivoi IL-6 su viši kod osoba koje prijavljuju glavobolju kao početni simptom COVID-

**Table 4.** Univariate and multivariate Cox proportional predictive model results: factors associated with fatal outcome in the intensive care unit

| | Univariate model | | | Multivariate model | | |
|---|---|---|---|---|---|---|
| **Variable** | **HR** | **95% CI** | **p** | **HR** | **95% CI** | **p** |
| **Male gander** | 0.14 | 0.41-1.14 | 0.145 | 0.78 | 0.44-1.37 | 0.385 |
| **Age** | 1.03 | 1.01-1.05 | **0.004** | 1.04 | 1.01-1.06 | **0.001** |
| **COVID-19 vaccination** | 0.52 | 0.25-1.09 | 0.084 | 0.62 | 0.28-1.34 | 0.228 |
| **Fever** | 0.53 | 0.30-0.93 | **0.027** | 0.70 | 0.35-1.36 | 0.292 |
| **Cough** | 1.07 | 0.59-1.91 | 0.830 | 1.03 | 0.54-1.94 | 0.935 |
| **Fatigue** | 1.39 | 0.84-2.32 | 0.199 | 1.19 | 0.67-2.10 | 0.541 |
| **Shortness of breath** | 3.10 | 1.73-5.57 | **0.001** | 3.02 | 1.62-5.62 | **0.001** |
| **Arthralgia** | 0.82 | 0.43-1.57 | 0.549 | 0.99 | 0.50-1.96 | 0.980 |
| **Chest pain** | 1.59 | 0.91-2.78 | 0.130 | 1.53 | 0.78-2.96 | 0.208 |
| **Loss of appetite** | 0.95 | 0.41-2.21 | 0.907 | 1.40 | 0.56-3.45 | 0.470 |
| **Headache** | 1.67 | 0.81-3.33 | 0.174 | 2.51 | 1.10-5.66 | **0.027** |
| **Diarrhea** | 1.76 | 0.95-3.24 | 0.072 | 2.43 | 1.21-4.83 | **0.012** |
| **Anosmia** | 2.27 | 1.28-3.88 | **0.005** | 1.35 | 0.67-2.71 | 0.393 |
| **Qualitative disturbance of consciousness** | 1.11 | 0.48-2.58 | 0.807 | 1.20 | 0.48-3.01 | 0.692 |
| **Vomiting** | 0.81 | 0.30-2.26 | 0.697 | 0.93 | 0.31-2.78 | 0.901 |
| **Back pain** | 0.67 | 0.29-1.56 | 0.353 | 0.78 | 0.32-1.89 | 0.583 |
| **Quantitative disturbance of consciousness** | 2.16 | 0.98-4.78 | 0.056 | 1.18 | 0.41-3.31 | 0.757 |
| **Nasal congestion** | 0.35 | 0.13-0.97 | **0.045** | 0.32 | 0.10-0.93 | **0.037** |
| **Hoarseness** | 0.39 | 0.05-2.83 | 0.622 | 0.28 | 0.03-2.16 | 0.221 |
| **Itching of the eye** | 0.95 | 0.13-6.89 | 0.961 | 0.52 | 0.06-4.19 | 0.547 |
| **Difficulty swallowing** | 1.33 | 0.32-4.46 | 0.692 | 1.29 | 0.28-5.92 | 0.739 |

HR-hazard ratio; CI-confidence interval; Bolded values are statistically significant.

syndrome, can further exacerbate chest discomfort and increase the level of subjective pain (13).

Shortness of breath, as an initial symptom of COVID-19 in patients with moderate to severe clinical form, has been identified as the predictor of fatal COVID-19. The onset of dyspnea, commonly known as shortness of breath, as an early symptom of COVID-19, can be attributed to a complex interplay of pathophysiological mechanisms involving viral-induced lung injury, inflammatory responses, and dysregulation of the renin-angiotensin-aldosterone system (RAAS) (14-16). The SARS-CoV-2 induces a cascade of inflammatory processes through angiotensin-converting enzyme 2 (ACE2) receptors expressed predominantly in the respiratory epithelium (15). This leads to the activation of immune cells, such as macrophages and lymphocytes (15). The activation of coagulation pathways and the formation of microthrombi within the pulmonary vasculature further contribute to the impairment of gas exchange and the onset of respiratory distress in severe cases of the infection (16). The multifactorial nature of dyspnea in COVID-19 suggests that there is interplay between viral pathogenesis, immunological responses, and cardiovascular dynamics (15).

The cough reflex in COVID-19 is primarily a result of irritation of the respiratory mucosa due to the inflammatory response to SARS-CoV-2 (16). Hence, there is an increased mucus production and airway hyperresponsiveness (16). Furthermore, the neurogenic inflammation associated with the activation of sensory nerves in the respiratory epithelium could contribute to the persistent cough observed in some patients (15). All these factors can, therefore, predispose an individual to

19, ali nema daljih nepovoljnih efekata u kasnijim fazama infekcije (18). Druga studija je zabeležila da su nivoi IL-6 viši kod osoba sa glavoboljom tokom COVID-19, ali da kasnije vrednosti IL-6 dostižu plato koji odsustvuje kod onih pacijenata koji ne prijavljuju glavobolju (19). Studije koje su ispitivale pacijente koji su prethodno imali glavobolje takođe beleže nešto više stope preživljavanja u poređenju sa opštom populacijom obolelom od COVID-19 bolesti, što se pripisuje modifikovanoj funkciji sistema renin-angiotenzin-aldosteron tokom lečenja glavobolje i ranijom suplementacijom vitaminom D (20, 21). Ova razlika u našim rezulatatima i podacima iz literature ukazuje na potrebu za daljim istraživanjima o uticaju glavobolje kao početnog simptoma COVID-19 na ishode bolesti.

U našoj studiji, dijareja kao početni simptom infekcije je bila povezana sa smrtnim ishodom COVID-19 infekcije. Prethodna studija je pokazala da je potrebno duže vreme za prijem u bolnicu kad pacijenti sa COVID-19 oboljenjem a koji imaju gastrointestinalne smetnje u poređenju sa onima bez njih (22). Ovo se pripisuje odsustvu tipičnih respiratornih simptoma u početku, što usporava pravovremenu dijagnozu i lečenje (22). Noviji podaci sugerišu da je dijareja povezana sa težim oblicima COVID-19 i ukazuju na to da bi njeno prisustvo moglo biti pouzdaniji indikator razvoja teškog oblika COVID-19 (23). U drugim studijama, dijareja je bila povezana sa težom formom bolesti COVID-19 (24). Međutim, postoje podaci o inicijalnoj manifestaciji COVID-19 infekcije sa dijarejom i glavoboljom istovremeno, gde je ovaj način početka infekcije bio povezan sa boljim preživljavanjem pacijenata (25). Zbog razlika u rezultatima, potrebna su dalja istraživanja kako bi se bolje razumeli ovi simptomi i njihova veza sa lakom do teškom formom COVID-19 bolesti praćenom dijarejom.

U ovoj studiji, odsustvo nazalne kongestije bilo je povezano sa smrtnim ishodom COVID-19. Slične studije su zabeležile da odsustvo nazalne kongestije, u kombinaciji sa anosmijom, može biti povezan sa ozbiljnijim ispoljavanjem COVID-19 (26, 27). Međutim, nedostaju detaljni patofiziološki mehanizmi koji objašnjavaju ovaj nalaz. U ovoj studiji, sistemski simptomi, poput glavobolje, dijareje i otežanog disanja, bili su udruženi sa lošim ishodom COVID-19 bolesti. Iako se COVID-19 klasifikuje kao respiratorna infekcija, koja se prenosi kapljičnim putem, nema sumnje da se radi o sistemskoj infekciji koja zahvata praktično sve sisteme organa. Iz tog razloga, potrebna je pažljiva evaluacija pacijenata primljenih u bolnicu u vezi sa njihovim simptomima kako bi se precizno predvideo dalje lečenje u JIN-e i ishod lečenja.

Ograničenja ove studije odnose se na činjenicu da je analiza sprovedena u dve medicinske ustanove. Zato potencijalna pristrasnosti izbora u selekciji ispitanika može onemogućiti generalizaciju rezultata ove studije na celokupnu populaciju obolelih od infekcije COVID-19. Dodatno, ova studija nije istraživala uticaj pojedinačnih varijanti SARS-CoV-2, iako mogu postojati razlike u njihovim ishodima. Budući da su uzeti u obzir samo simptomi i znaci, a ne i drugi relevantni podaci, poput laboratorijskih parametara, moguće je da postoji i rezidualna pristrasnost usled pridruženosti (konfaunding).

## Zaključak

Rezultati ove studije ističu važnost pažljivog praćenja i brze intervencije kod pacijenata koji imaju bol u grudima, otežano disanje, glavobolju i dijareju, posebno kod starijih osoba. Dalja istraživanja sa različitim kohortama pacijenata i dužim periodom praćenja su neophodna kako bi se potvrdili ovi prediktori. Razumevanje početnih simptoma COVID-19 i njihove povezanosti sa lošim ishodima infekcije mogu pomoći u definisanju odgovarajućih pristupa lečenju sa ciljem optimizacije ishoda COVID-19.

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

## Reference


1. Almaghaslah D, Kandasamy G, Almanasef M, Vasudevan R, Chandramohan S. Review on the coronavirus disease (COVID-19) pandemic: Its outbreak and current status. Int J Clin Pract. 2020;74(11):e13637. doi: 10.1111/ijcp.13637.
2. Yi Y, Lagniton PNP, Ye S, Li E, Xu RH. COVID-19:what has been learned and to be learned about the novel coronavirus disease. Int J Biol Sci. 2020;16:1753-1766. doi: 10.7150/ijbs.45134
3. Hoque MN, Sarkar MMH, Rahman MS, Akter S, Banu TA, Goswami B, et al. SARS-CoV2 infection reduces human nasopharyngeal commensal microbiome with inclusion of pathobionts. Sci Rep. 2021;11(1):24042. doi: 10.1038/s41598-021-03245-4
4. Nakayama T, Lee IT, Jiang S, Matter MS, Yan CH, Overdevest JB, et al. Determinants of SARS-CoV-2 entry and replication in airway mucosal tissue and susceptibility in smokers. Cell Rep Med. 2021;2(10):100421. doi:10.1016/j.xcrm.2021.100421

detrimental systemic effects of the inflammation and, subsequently, respiratory failure.

In this study, we observed that headache as the initial symptom is associated with fatal outcomes of COVID-19. Our findings contradict the previously published meta-analysis which suggested that patients reporting headache atthe onset of COVID-19 have higher chances of survival compared to those people without headache (17). There are inconsistent findings regarding the association between headache and proinflammatory cytokine levels. Specifically, IL-6 levels are higher in individuals reporting headache at the onset of COVID-19, but they do not sustain further detrimental effects in later stages of the infection (18). Another study found that IL-6 levels are elevated in individuals with headache during COVID-19, but later, IL-6 values reach a plateau, which is absent in those patients not reporting headache (19). Studies focusing on patients with pre-existing headaches also reported slightly higher survival rates compared to the general population with COVID-19. This is attributed to a modified RAAS system function during headache treatment and earlier vitamin D supplementation (20, 21). This discrepancy with our findings underscores the necessity for more research focusing on the impact of headache as an initial symptom of COVID-19 on disease outcomes.

In our study, diarrhea as an initial symptom of the infection was associated with fatal COVID-19 outcomes. A previous study reported that patients with gastrointestinal disturbances took longer time to be admitted to hospital compared to those without them (22). This was attributed to the absence of typical respiratory symptoms initially, thus delaying timely diagnosis and treatment (22). Emerging data suggest that diarrhea is linked to severe forms of COVID-19 and indicate that it could serve as a reliable indicator of risk of developing severe COVID-19 form (23). In other studies, diarrhea has been associated with an increase in severity of COVID-19-related pathology (24). However, there are data on the simultaneous initial presentation of COVID-19 infection with diarrhea and headache, where this combination of symptoms is associated with better survival (25). Due to disparities in results, further research is needed to better understand these characteristics and their association with severe COVID-19 accompanied by diarrhea.

In the present study, the absence of nasal congestion was associated with poor COVID-19 outcome. Related studies have identified the absence of nasal congestion, combined with anosmia, may potentially be associated with a more severe presentation of COVID-19 (26, 27). However, detailed pathophysiological mechanisms explaining this finding are lacking. In this set of patients, systemic symptoms, such as headache, gastrointestinal presentation and shortness of breath were the key symptoms at the onset of COVID-19 predictive of poorer infection outcomes. While COVID-19 is classified as a respiratory infection, transmitted via droplet spread, there is no doubt that it is a systemic infection which affects virtually all organ systems. For this reason, careful assessment of patients admitted to hospital is needed with regards to their symptoms to accurately predict further ICU treatment and outcomes.

Limitations of this study are related to the notion that this analysis was conducted at two medical centers. This potential selection bias may restrict generalization of study findings to the entire population who were affected by COVID-19. Additionally, this study did not investigate the impact of individual SARS-CoV-2 variants, as there may be differences in outcomes. Because only symptoms were taken into account and not other relevant data, such as serum parameters, this analysis is open to potential unobserved confounding.

## Conclusion

The results of this study emphasize the importance of vigilant monitoring and swift intervention in patients presenting with chest pain, shortness of breath, headache, and diarrhea, particularly among older people. Further research with diverse patient cohorts and an extended follow-up period is essential to validate these findings. Understanding initial COVID-19 symptoms and their association with poor infection outcomes can help to design tailored approaches to treatment with the goal to optimize COVID-19 outcomes.

## Competing interests

The authors declared no competing interests.

5. Meyerowitz EA, Richterman A, Gandhi RT, Sax PE. Transmission of SARS-CoV-2: A Review of Viral, Host, and Environmental Factors. Ann Intern Med. 2021;174(1):69-79. doi: 10.7326/M20-5008
6. Alimohamadi Y, Sepandi M, Taghdir M, Hosamirudsari H. Determine the most common clinical symptoms in COVID-19 patients: a systematic review and meta-analysis. J Prev Med Hyg. 2020;61(3):E304-E312. doi:10.15167/2421-4248/jpmh2020.61.3.1530
7. Menachemi N, Dixon BE, Wools-Kaloustian KK, Yiannoutsos CT, Halverson PK. How Many SARS-CoV-2-Infected People Require Hospitalization? Using Random Sample Testing to Better Inform Preparedness Efforts. J Public Health ManagPract. 2020;27(3):246-250. doi: 10.1097/PHH.0000000000001331
8. Romero Starke K, Reissig D, Petereit-Haack G, Schmauder S, Nienhaus A, Seidler A. The isolated effect of age on the risk of COVID-19 severe outcomes: a systematic review with meta-analysis. BMJ Glob Health. 2021;6(12):e006434. doi: 10.1136/bmjgh-2021-006434.
9. Liu Y, Mao B, Liang S, Yang JW, Lu HW, Chai YH, et al. Association between age and clinical characteristics and outcomes of COVID-19. Eur Respir J. 2020:55(5):2001112. doi: 10.1183/13993003.01112-2020.
10. Singhal S, Kumar P, Singh S, Saha S, Dey AB. Clinical features and outcomes of COVID-19 in older adults: a systematic review and meta-analysis. BMC Geriatr. 2021:9;21(1):321. doi: 10.1186/s12877-021-02261-3.
11. Borges do Nascimento IJ, Cacic N, Abdulazeem HM, von Groote TC, Jayarajah U, Weerasekara I, et al. Novel Coronavirus Infection (COVID-19) in Humans: A Scoping Review and Meta-Analysis. J Clin Med. 2020;9(4):941. doi: 10.3390/jcm9040941.
12. Conti P, Ronconi G, Caraffa A, Gallenga CE, Ross R, Frydas I, et al. Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies. J Biol Regul Homeost Agents. 2020;34(2):327-331. doi: 10.23812/CONTI-E.
13. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-513. doi: 10.1016/S0140-6736(20)30211-7.
14. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020;395(10234):1417-1418. doi: 10.1016/S0140-6736(20)30937-5.
15. Magro C, Mulvey JJ, Berlin D, Nuovo G, Salvatore S, Harp J, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. Transl Res. 2020;220:1-13. doi: 10.1016/j.trsl.2020.04.007.
16. Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD. Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Covid-19. N Engl J Med. 2020;382(17):1653-1659. doi: 10.1016/j.trsl.2020.04.007.
17. Gallardo VJ, Shapiro RE, Caronna E, Pozo-Rosich P. The relationship of headache as a symptom to COVID-19 survival: A systematic review and meta-analysis of survival of 43,169 inpatients with COVID-19. Headache. 2022;62(8):1019-1028. doi: 10.1111/head.14376.
18. Zhang X, Tan Y, Ling Y, Lu G, Liu F, Yi Z et al. Viral and host factors related to the clinical outcome of COVID-19. Nature. 2020;583(7816):437-440. doi: 10.1038/s41586-020-2355-0.
19. Bolay H, Karadas Ö, Oztürk B, Sonkaya R, Tasdelen B, Bulut TDS, et al. HMGB1, NLRP3, IL-6 and ACE2 levels are elevated in COVID-19 with headache: a window to the infection-related headache mechanism. J Headache Pain. 2021;22(1):94. doi: 10.1186/s10194-021-01306-7.
20. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020;181(2):271-280.e8. doi: 10.1016/j.cell.2020.02.052.
21. Nowaczewska M, Wiciński M, Osiński S, Kaźmierczak H. The Role of Vitamin D in Primary Headache-from Potential Mechanism to Treatment. Nutrients. 2020;12(1):243. doi: 10.3390/nu12010243.
22. Tian S, Chang Z, Wang Y, Wu M, Zhang W, Zhou G, et al. Clinical Characteristics and Reasons for Differences in Duration From Symptom Onset to Release From Quarantine Among Patients With COVID-19 in Liaocheng, China. Front Med (Lausanne). 2020;7:210. doi: 10.3389/fmed.2020.00210.
23. Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, et al. Clinical Characteristics of COVID-19 Patients With Digestive Symptoms in Hubei, China: A Descriptive, Cross-Sectional, Multicenter Study. Am J Gastroenterol. 2020;115(5):766-773. doi: 10.14309/ajg.0000000000000620.
24. Dhakal S, Charoen P, Pan-Ngum W, Luvira V, Sivakorn C, Hanboonkunupakarn B, et al. Severity of COVID-19 in Patients with Diarrhoea: A Systematic Review and Meta-Analysis. Trop Med Infect Dis. 2023;8(2):84. doi: 10.3390/tropicalmed8020084.
25. Fernández-de-Las-Peñas C, Martín-Guerrero J, Navarro-Pardo E, Torres-Macho J, Canto-Diez MG, Pellicer-Valero O. Gastrointestinal symptoms at the acute COVID-19 phase are risk factors for developing gastrointestinal post-COVID symptoms: a multicenter study. Intern Emerg Med. 202;17(2):583-586. doi: 10.1007/s11739-021-02850-5.
26. Salmon Ceron D, Bartier S, Hautefort C, Nguyen Y, Nevoux J, Hamel AL, et al. Self-reported loss of smell without nasal obstruction to identify COVID-19. The multicenter Coranosmia cohort study. J Infect. 2020;81(4):614-620. doi: 10.1016/j.jinf.2020.07.005.
27. Moein ST, Hashemian SM, Mansourafshar B, Khorram-Tousi A, Tabarsi P, Doty RL. Smell dysfunction: a biomarker for COVID-19. Int Forum Allergy Rhinol. 2020;10(8):944-950. doi: 10.1002/alr.22587.

## References


1. Almaghaslah D, Kandasamy G, Almanasef M, Vasudevan R, Chandramohan S. Review on the coronavirus disease (COVID-19) pandemic: Its outbreak and current status. Int J Clin Pract. 2020;74(11):e13637. doi: 10.1111/ijcp.13637.
2. Yi Y, Lagniton PNP, Ye S, Li E, Xu RH. COVID-19:what has been learned and to be learned about the novel coronavirus disease. Int J Biol Sci. 2020;16:1753-1766. doi: 10.7150/ijbs.45134
3. Hoque MN, Sarkar MMH, Rahman MS, Akter S, Banu TA, Goswami B, et al. SARS-CoV2 infection reduces human nasopharyngeal commensal microbiome with inclusion of pathobionts. Sci Rep. 2021;11(1):24042. doi: 10.1038/s41598-021-03245-4
4. Nakayama T, Lee IT, Jiang S, Matter MS, Yan CH, Overdevest JB, et al. Determinants of SARS-CoV-2 entry and replication in airway mucosal tissue and susceptibility in smokers. Cell Rep Med. 2021;2(10):100421. doi:10.1016/j.xcrm.2021.100421
5. Meyerowitz EA, Richterman A, Gandhi RT, Sax PE. Transmission of SARS-CoV-2: A Review of Viral, Host, and Environmental Factors. Ann Intern Med. 2021;174(1):69-79. doi: 10.7326/M20-5008
6. Alimohamadi Y, Sepandi M, Taghdir M, Hosamirudsari H. Determine the most common clinical symptoms in COVID-19 patients: a systematic review and meta-analysis. J Prev Med Hyg. 2020;61(3):E304-E312. doi:10.15167/2421-4248/jpmh2020.61.3.1530
7. Menachemi N, Dixon BE, Wools-Kaloustian KK, Yiannoutsos CT, Halverson PK. How Many SARS-CoV-2-Infected People Require Hospitalization? Using Random Sample Testing to Better Inform Preparedness Efforts. J Public Health ManagPract. 2020;27(3):246-250. doi: 10.1097/PHH.0000000000001331
8. Romero Starke K, Reissig D, Petereit-Haack G, Schmauder S, Nienhaus A, Seidler A. The isolated effect of age on the risk of COVID-19 severe outcomes: a systematic review with meta-analysis. BMJ Glob Health. 2021;6(12):e006434. doi: 10.1136/bmjgh-2021-006434.
9. Liu Y, Mao B, Liang S, Yang JW, Lu HW, Chai YH, et al. Association between age and clinical characteristics and outcomes of COVID-19. Eur Respir J. 2020:55(5):2001112. doi: 10.1183/13993003.01112-2020.
10. Singhal S, Kumar P, Singh S, Saha S, Dey AB. Clinical features and outcomes of COVID-19 in older adults: a systematic review and meta-analysis. BMC Geriatr. 2021:9;21(1):321. doi: 10.1186/s12877-021-02261-3.
11. Borges do Nascimento IJ, Cacic N, Abdulazeem HM, von Groote TC, Jayarajah U, Weerasekara I, et al. Novel Coronavirus Infection (COVID-19) in Humans: A Scoping Review and Meta-Analysis. J Clin Med. 2020;9(4):941. doi: 10.3390/jcm9040941.
12. Conti P, Ronconi G, Caraffa A, Gallenga CE, Ross R, Frydas I, et al. Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies. J Biol Regul Homeost Agents. 2020;34(2):327-331. doi: 10.23812/CONTI-E.
13. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-513. doi: 10.1016/S0140-6736(20)30211-7.
14. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020;395(10234):1417-1418. doi: 10.1016/S0140-6736(20)30937-5.
15. Magro C, Mulvey JJ, Berlin D, Nuovo G, Salvatore S, Harp J, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. Transl Res. 2020;220:1-13. doi: 10.1016/j.trsl.2020.04.007.
16. Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD. Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Covid-19. N Engl J Med. 2020;382(17):1653-1659. doi: 10.1016/j.trsl.2020.04.007.
17. Gallardo VJ, Shapiro RE, Caronna E, Pozo-Rosich P. The relationship of headache as a symptom to COVID-19 survival: A systematic review and meta-analysis of survival of 43,169 inpatients with COVID-19. Headache. 2022;62(8):1019-1028. doi: 10.1111/head.14376.
18. Zhang X, Tan Y, Ling Y, Lu G, Liu F, Yi Z et al. Viral and host factors related to the clinical outcome of COVID-19. Nature. 2020;583(7816):437-440. doi: 10.1038/s41586-020-2355-0.
19. Bolay H, Karadas Ö, Oztürk B, Sonkaya R, Tasdelen B, Bulut TDS, et al. HMGB1, NLRP3, IL-6 and ACE2 levels are elevated in COVID-19 with headache: a window to the infection-related headache mechanism. J Headache Pain. 2021;22(1):94. doi: 10.1186/s10194-021-01306-7.
20. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020;181(2):271-280.e8. doi: 10.1016/j.cell.2020.02.052.
21. Nowaczewska M, Wiciński M, Osiński S, Kaźmierczak H. The Role of Vitamin D in Primary Headache-from Potential Mechanism to Treatment. Nutrients. 2020;12(1):243. doi: 10.3390/nu12010243.
22. Tian S, Chang Z, Wang Y, Wu M, Zhang W, Zhou G, et al. Clinical Characteristics and Reasons for Differences in Duration From Symptom Onset to Release From Quarantine Among Patients With COVID-19 in Liaocheng, China. Front Med (Lausanne). 2020;7:210. doi: 10.3389/fmed.2020.00210.
23. Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, et al. Clinical Characteristics of COVID-19 Patients With Digestive Symptoms in Hubei, China: A Descriptive, Cross-Sectional, Multicenter Study. Am J Gastroenterol. 2020;115(5):766-773. doi: 10.14309/ajg.0000000000000620.
24. Dhakal S, Charoen P, Pan-Ngum W, Luvira V, Sivakorn C, Hanboonkunupakarn B, et al. Severity of COVID-19 in Patients with Diarrhoea: A Systematic Review and Meta-Analysis. Trop Med Infect Dis. 2023;8(2):84. doi: 10.3390/tropicalmed8020084.

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25. Fernández-de-Las-Peñas C, Martín-Guerrero J, Navarro-Pardo E, Torres-Macho J, Canto-Diez MG, Pellicer-Valero O. Gastrointestinal symptoms at the acute COVID-19 phase are risk factors for developing gastrointestinal post-COVID symptoms: a multicenter study. Intern Emerg Med. 202;17(2):583-586. doi: 10.1007/s11739-021-02850-5.
26. Salmon Ceron D, Bartier S, Hautefort C, Nguyen Y, Nevoux J, Hamel AL, et al. Self-reported loss of smell without nasal obstruction to identify COVID-19. The multicenter Coranosmia cohort study. J Infect. 2020;81(4):614-620. doi: 10.1016/j.jinf.2020.07.005.
27. Moein ST, Hashemian SM, Mansourafshar B, Khorram-Tousi A, Tabarsi P, Doty RL. Smell dysfunction: a biomarker for COVID-19. Int Forum Allergy Rhinol. 2020;10(8):944-950. doi: 10.1002/alr.22587.



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# MAMOGRAFIJA SA INTRAVENSKOM PRIMENOM KONTRASTNOG SREDSTVA KAO NOVI STANDARD BRIGE O ZDRAVLJU DOJKE

**Kristina Stevanović[1], Bojana Maričić[2], Jovana Radovanović[3]**

[1] Dom zdravlja „Dr Milutin Ivković“, Beograd, Republika Srbija
[2] Urgentni centar Univerzitetskog Kliničkog centra Srbije, Republika Srbija
[3] Fakultet medicinskih nauka, Univerzitet Kragujevac, Kragujevac, Republika Srbija

[*] Korespondencija: Kristina Stevanović, Dom zdravlja „Dr Milutin Ivković“, Kneza Danila 16, Beograd, Republika Srbija; e-mail: kristinamladenovic89@gmail.com

**SAŽETAK**

Kontrastna mamografija (KM) (eng. *Contrast-enhanced mammography* - CEM) postaje sve više prisutna metoda u dijagnostici karcinoma dojke tokom poslednjih nekoliko decenija, a posebno tokom poslednjih nekoliko godina. Sve je više dokaza o visokoj dijagnostičkoj efektivnosti i senzitivnosti KM u otkrivanju karcinoma dojke. Takođe, nova istraživanja pokazuju sličnost u efektivnosti i senzitivnosti KM u poređenju sa magnetnom rezonancom (MR), uz manje slučajeva lažno pozitivnih rezultata. Kako se primena KM sve više širi, od potencijalne njene primene u skriningu kod žena sa gustim tkivom dojke do određivanja stadijuma maligniteta dojke, sve je više neophodna dobra upućenost u ovu metodu i njenu implementaciju. Ovim preglednim radom biće sagledan značaj KM kako za skrining, tako i za dijagnostičku proceduru, sa posebnim akcentom na sagledavanje njenih prednosti i nedostataka u odnosu na ultrazvuk, standardnu mamografiju i MR.

**Ključne reči:** kontrastna mamografija, skrining, karcinom dojke

## Uvod

Kontrastna mamografija (KM) (eng. *Contrast-enhanced mammography* - CEM) definiše se kao mamografija koja se realizuje intravenskom primenom kontrastnog sredstva. Stoga se ova tehnika danas smatra novom, jer koristi jodirane kontrastne materijale za vizualizaciju neovaskularnosti dojke na identičan način kao magnetna rezonanca (MR) (1). U okviru procesa angiogeneze obrazuju se krvni sudovi koji se veoma dobro ispunjavaju kontrastom (2), te stoga omogućavaju dobro kontrastno propuštanje kroz samo tkivo tumora, što dalje omogućava dobijanje kvalitetne dijagnostičke slike (3). Zahvaljujući prethodno opisanom procesu, KM omogućava da se postojanje malignih nodusa vizualizuje, čak i pri značajno velikoj gustini tkiva dojke, koje inače u standardnoj mamografiji predstavlja značajnu dijagnostičku poteškoću. Slično je i sa potencijalnim suspektnim lezijama, koje se upravo zbog gustine parenhima preklapaju sa tkivom dojke i predstavljaju izazov za dijagnostiku na standardnim mamografskim snimcima. Princip rada KM zasnovan je na aplikaciji intravenskog kontrastnog sredstva, pomoću kog se omogućava njegova akumulacija iz abnormalnih, propusnih krvnih sudova u potencijalno prisutno tumorsko tkivo dojke (4), što se jasno vizualizuje na dobijenom snimku visokog kvaliteta. U literaturi se KM naziva i kontrastno poboljšanom spektralnom mamografijom i kontrastno poboljšanom digitalnom mamografijom i kontrastno poboljšanom dualnom mamografijom. Bez obzira na naziv, reč je o savremenoj dijagnostičkoj tehnici koja obezbeđuje individualni pristup svakom pacijentu, omogućavajući da se tretman „prilagodi“ njihovim potrebama.

Prema dostupnim epidemiološkim podacima, karcinom dojke jedan je od najučestalijih karcinoma širom sveta, posebno ako se razmatraju oba pola (3). Studija *Sung*-a i saradnika iz 2020. godine pokazala je značajan porast broja novoobolelih od karcinoma dojke u odnosu na, do sada vodeći, kar-

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# CONTRAST-ENHANCED MAMMOGRAPHY AS THE NEW STANDARD IN BREAST HEALTH CARE

**Kristina Stevanović[1], Bojana Maričić[2], Jovana Radovanović[3]**

[1] Health Center „Dr Milutin Ivković“, Belgrade, Republic of Serbia
[2] Emergency Center, University Clinical Center of Serbia, Republic of Serbia
[3] Faculty of Medicine, University of Kragujevac, Kragujevac, Republic of Serbia

* Correspondence: Kristina Stevanović, Healh Center „Dr Milutin Ivković“, Kneza Danila St 16, 11000 Belgrade, Republic of Serbia; e-mail: kristinamladenovic89@gmail.com

**SUMMARY**

Contrast-enhanced mammography (CEM) has become a ubiquitous method in breast diagnostics over the last few decades, especially in recent years. There is an increasing body of strong evidence regarding the high diagnostic efficiency and sensitivity of CEM in detecting breast cancer. There is more and more evidence about the high diagnostic effectiveness and sensitivity of CEM in detecting breast cancer. Also, new research has shown similarity in the efficiency and sensitivity of CEM compared to magnetic resonance, with fewer cases of false positive results. As the application of CEM expands from potential use in screening for women with dense breast tissue to the staging of known breast malignancy, it becomes increasingly important to become well-versed in this method and its implementation. This review article will perceive the importance of CEM both for screening and in the diagnostic procedure, with a special emphasis placed on the advantages and disadvantages compared to ultrasound, standard mammography and MRI.

**Keywords:** contrast-enhanced mammography, screening, breast cancer

## Introduction

Contrast-enhanced mammography (CEM) is defined as mammography, which is realized with the intravenous administration of a contrast agent. Therefore, this technique is deemed to be new today because it uses iodinated contrast materials for the visualization of breast neovascularization identically as magnetic resonance (MR) (1). Within the process of angiogenesis, blood vessels, which are filled well with contrast, are formed (2), and therefore, they allow good contrast transmission through the tumor tissue itself, which further enables a high-quality diagnostic image to be obtained (3). Thanks to the previously described process, CEM allows the visualization of present malignant nodes, even with a significantly high density of breast tissue, which otherwise represents a significant diagnostic problem in standard mammography. Similar is the case with potentially suspicious lesions, which overlap with the breast tissue due to the density of parenchyma, and therefore, they are challenging for diagnosing on standard mammographic images. The working principle of CEM is based on the application of an intravenous contrast agent, which enables its accumulation from abnormal, permeable blood vessels into the potentially present tumor tissue of the breast (4), which is clearly visualized on the obtained high-quality image. In the literature, CEM is called contrast-enhanced spectral mammography and contrast-enhanced dual mammography. Regardless of the name, it is a modern diagnostic technique, which enables an individual approach to each patient, allowing the treatment to be “adapted” to their needs.

According to the available epidemiological data, breast cancer is one of the most common cancers worldwide, especially if both sexes are taken into consideration (3). A study by Sung et al. from 2020 showed a significant increase in the number of new cases of breast cancer in comparison to lung

cinom pluća (4). Bez obzira na izuzetno intenzivan i značajan napredak tehnologije, dijagnostika karcinoma dojke i dalje je veoma kompleksna i nosi sa sobom veliki broj nedoumica, te zahteva kontinuirano unapređenje, razvoj i težnju ka novim dijagnostičkim tehnikama koje će omogućiti brže i efektivnije otkrivanje maligniteta u što ranijem stadijumu bolesti (2,5,6). Čak i u dobu savremene terapije, otkrivanje maligniteta dojke u ranim stadijumima ključno je za bolji ishod lećenja (7). Dijagnostičke metode za pregled dojke evoluiraju, a njihova snaga i slabosti kontinuirano se procenjuju kako bi se formulisale preporuke i smernice koje su korisne za kliničku praksu.

Ovim preglednim radom biće sagledan značaj KM kako za skrining, tako i za dijagnostičku proceduru, sa posebnim akcentom na sagledavanje njenih prednosti i nedostataka u odnosu na ultrazvuk, standardnu mamografiju i MR.

## Metod

U ovom preglednom radu pretraženo je nekoliko elektronskih baza podataka: *Google Scholar* napredne pretrage, Konzorcijuma biblioteka Srbije za objedinjenu nabavku – KoBSON i platforma *PubMed*. U cilju pretraživanja literature korišćene su sledeće ključne reči: mamografija, kontrastna mamografija i karcinom dojke. Ovim preglednim radom obuhvaćene su radovi koji su publikovani u periodu 2014-2024. godine na srpskom ili engleskom jeziku, a koji su obrađivali navedenu tematiku.

## Osnove kontrastne mamografije

KM tehnika je počela da se razvija postepeno i polako, počevši od 1985. godine kada je prvobitno nazvana digitalna subtrakcijska angiografija dojke. Prvobitno ova tehnika je razvijana kao neinvanzivna dijagnostička metoda za indentifikaciju tumora dojke koji je do tada najčešće bio dijagnostikovan biopsijom ili hirurškim zahvatima. Inicijalna KM tehnika izvodila se pomoću katetera koji je morao biti plasiran u regiju gornje šuplje vene kroz koji se aplikovao kontrast koji je omogućavao višeslojnu ekspoziciju i prikaz krvnih sudova unutar dojke. Opisana tehnika imala je niz nedostataka i zahtevala je prekontrastno, potom i kontrastno snimanje, zatim i kompresiju dojke, što je iniciralo dodatna tehnološka rešenja, kako bi ova tenhnika bila primenjivana na efikasniji način koji bi bio bolje kontrolisan od prvobitnog i koji bi značajno kraće trajao.

KM tehnika koja koristi dualnu energiju (engl. *dual energy*) pravi razliku u apsorpciji rendgenskih zraka između tkiva dojke i joda kada se koriste spektri niske i visoke energije. Ova tehnika je prvobitno opisana tokom 2003. godine, kao alternativna tehnika subtrakciji (6). Pregledi KM sastoje se od uparenih slika niske i visoke energije dobijenih korišćenjem rendgenskih energija ispod i iznad ivice kontrasta. Iz ovih uparenih ekspozicija dobijenih pod istom kompresijom, generiše se rekonstruisana slika koristeći postupak naknadne obrade koji izoluje samo koncentraciju joda. Pre nego što se izvrši snimanje, neophodno je aplikovati nejonski kontrastni agens sa niskom osmolskom vrednošću, još u periodu dok je dojka van kompresije, kako bi se omogućio najveći protok krvi. Koncentracija joda varira od 300 mg/mL do 370 mg/mL (8). Iako standardizovani parametri snimanja za KM još uvek nisu konstituisani, generalno je prihvaćeno da se daje volumen od 1,5 ml/kg telesne mase (maksimalno 150 ml) brzinom od 2-3 ml/s, po mogućstvu korišćenjem automatskih injektora (9). Oko 2-3 minuta nakon ubrizgavanja kontrasta, dobijaju se uparene slike niske i visoke energije dojke, koja je pod kompresijom, u dve standardne projekcije - kraniokaudalne i mediolateralne kose. Dodatne projekcije mogu se dobiti unutar 10 minuta od aplikacije kontrasta. Rekombinovane slike za svaku dobijenu projekciju generišu se nakon obrade.

Ipak i pored svih prednosti treba naglasiti da KM ne prikazuje kinetiku i dinamiku kontrastnog pojačanja. Međutim, nekoliko publikovanih radova koji su ispitivali odloženu akviziciju dobijenu 6 do 8 minuta nakon ubrizgavanja kontrasta pokazali su poboljšanje specifičnosti KM sa 83% na 89% kod žena koje su bile podvrgnute KM radi procene odgovora na neoadjuvantnu hemioterapiju (10) i sa 80% na 92% kod žena sa denznim dojkama i suspektnim tumorskim promenama (11).

## Dijagnostičke mogućnosti KM

Kao što je u samom uvodu pomenuto tehnika kontrastno pojačane mamografije se vremenom menjala, razvijala i unapređivala. Inicijalno ova tehnika snimanja prikazana je 1985. godine uz digitalnu subtrakcionu angiografiju dojke, u kojoj je bilo dominanto dobijanje prekontrastne slike, ali i slike uz kompresiju dojke nakon čega se pristupalo intravenskoj aplikaciji kontrasta (12,13). Naime,

cancer, which had a leading position until then (4). Regardless of the extremely intensive and significant progress of technology, the diagnostics of breast cancer is still very complex and carries with it a large number of doubts. Therefore, it demands continuous improvement, development and striving for new diagnostic techniques, which will enable faster and more effective detection of breast malignancy at the earliest possible stage (2,5,6). Even in the age of modern therapy, detection of breast malignancy at early stages is crucial for a better treatment outcome (7). Diagnostic methods for breast examination are evolving, while their strengths and weaknesses are continually being evaluated in order to formulate recommendations and guidelines that are useful for clinical practice.

The significance of CEM for screening, as well as for diagnostic procedures will be considered in this review article, while special emphasis will be placed on realizing its advantages and disadvantages in comparison to ultrasound, standard mammography and MR.

## Methods

In this review article, a few electronic databases were searched: Google Scholar advanced search, the Consortium of Serbian Libraries for Unified Procurement (Serbian: KoBSON) and the PubMed platform. The following key words were used in the literature search: mammography, contrast mammography and breast cancer. This review articles includes works published in the period 2014-2024 in the Serbian or English language, which analyzed the above mentioned topic.

## Basics of contrast mammography

The CEM technique has developed gradually and slowly since 1985 when it was originally called digital subtraction breast angiography. Originally, this technique was developed as a non-invasive diagnostic method for the identification of breast tumors, which had been diagnosed by biopsy or surgical procedures until then. The initial CEM technique was carried out using a catheter that had to be placed in the region of the superior vena cava, through which contrast was administered, which allowed the multi-layered exposure and display of blood vessels inside the breast. The described technique had a number of disadvantages and it required pre-contrast, and then contrast imaging, then breast compression, which initiated additional technological solutions, so that this technique could be applied in a more efficient way, which had to be better controlled than the original one and which would be significantly shorter.

The CEM technique, which uses dual energy, makes difference in the absorption of X-rays between breast tissue and iodine, when the spectra of low and high energy are used. This technique was originally described in 2003 as an alternative technique to subtraction (6). The CEM examination consists of paired images of low and high energy obtained with the help of X-ray energies below and above the level of contrast. From these paired exposures obtained under the same compression, a reconstructed image is generated using the procedure of post-processing which isolates only the iodine concentration. Before the imaging is performed, it is necessary to apply a non-ionic contrast agent with a low osmolality value, when the breast is not under compression, in order to allow the greatest blood flow. The concentration of iodine varies from 300 mg/ml to 370 mg/ml (8). Although standardized imaging parameters for CEM have not been established yet, it has generally be accepted that a volume of 1.5 ml/kg of body mass (maximum 150 ml) is administered at a rate of 2-3 ml/s, preferably using automatic injectors (9). About 2-3 minutes after contrast injection, paired images of low and high energy of breast under compression is obtained in two standard projections – craniocaudal and mediolateral oblique viiews. Additional projections can be obtained within 10 minutes from contrast administration. Recombined images for each resulting projection are generated after processing.

Despite all the advantages, it should be pointed out that CEM does not show the kinetics and dynamics of contrast enhancement. However, a few published papers, which examined delayed acquisition 6 to 8 minutes after contrast was injected, showed the improvement of the specificity of CEM from 83% to 89% in women who underwent CEM on order to assess the response to neoadjuvant chemotherapy (10) and in 80% to 92% of women with dense breasts and suspicious tumor changes (11).

ova procedura pored toga što je bila veoma invanzivna i neprijatna, davala je suboptimalne rezultate, te njena primena nije značajno zaživela.

Nešto kasnije KM se počela razvijati uz korišćenje temporalne tehnike tokom koje je dojka takođe bila izložena kopresiji, rađena su predkontrastna snimanja i aplikovan je intravenski kontrast nakon čega je u vremenskom intervalu od 5 do 7 minuta rađeno višestruko snimanje. U odnosnu na prethodno opisanu, inicijalnu mamografiju, ova verzija je bila unapređena u segmentu što se predkontrastna slika oduzima od postkontrastne slike, pri čemu dolazi do vizuelizacije kontrastne apsorpcije. Ova tehnika pokazala se izuzetno efikasnom i uspešnom za postavljenje dijagnoze maligniteta dojke (14), ali i pored toga pokazala je niz nedostataka poput pojave artefakata zbog pomeranja pacijenta, izuzetno dugački vremenski interval akvizicije, tako da tokom jednog pregleda može biti pregledana samo jedna dojka. Svaki dodatni pogled na ipsilateralnu ili kontralateralnu dojku zahteva dodatnu dozu kontrasta. Na kraju, dojka je pod kompresijom tokom unošenja kontrasta, što može ograničiti protok krvi i rezultirati suboptimalnim poboljšanjem tkiva.

Tehnika KM koja koristi dualnu energiju razvijena je tokom 2003. godine sa ciljem da bude alternativa temporalnoj tehnici. Suština korišćenja dualne energije u ovoj tehnici je da se maksimizira iskoristivost kontrasta u smislu da se iskoriti njegova mogućnost različitog stepena apsorpcije od strane tkiva dojke i joda. Ova metoda je bila veoma prihvaćena posebno iz perspektive iskoristljivosti već postojeće opreme. Naime, kako bi se izvela ova tehnika snimanja pored standardne opreme za mamografiju bila je neophodna samo sofverski nadograditi postojeći sistem i dodatak bakarne filtracije. Ovako dopunjen standardno opremeljen uređaj omogućavao je tzv. „*dual-energy*" slikanje. Naime, ova tehnika zahtevala je da se pre nego što se izvrši akvizicija slikanja izvrši i intravenska aplikacija kontrasnog sredstva koji ima nisku osmolarnost. U ovom slučaju aplikacija kontrasnog sredstva vršena je pomoću injektora, a preporučena doza kontrasnog sredstva bila je od 1,5 ml/kg do maksimalno 150 ml/kg, obično u koncentraciji 300–370 mg joda/ml, brzinom od 3 ml/s (15). Takođe, kao i prethodna tehnika i ova tehnika zahtevala je kompresiju dojke, s tim što je u ovom slučaju kompresiju dojke bilo potrebno izvršiti tek oko dva minuta pre nego što će se izvršiti kompletna aplikacija kontrasnog sredstva. Na prethodno opisan način, a zahvaljujući delovanju kompresije i kontrasta omogućeno je dobijanje uparene slike niske i visoke energije u standardnim kraniokaudalnim i mediolateralnim projekcijama. KM koristi fotoelektrični efekat joda koji omogućava isticanje oblasti apsorpcije kontrasta. Sam fotoelektrični efekat zavisi od energije rendgenskog zraka i ivice materijala. Slike koje dolaze iz polja niske energije, dobijaju se ispod K nivoa joda na kVp vrednosti 28–33 i prikazuju samo tkivo dojke, dok se slike visoke energije dobijaju iznad K nivoa joda na kVp vrednosti 45–49 i prikazuju apsorpciju joda u tkivo dojke, ali nisu zahvalne za tumačenje. Nakon obrade, kreiraju se rekonstruisane slike koje naglašavaju oblasti u kojima je došlo do apsorpcije joda, odnosno naglašavaju se tzv. zone „pojačanja", dok je signal koji dolazi iz pozadinskog tkiva potisnut. Zahvaljujući ovakvoj apsorpciji joda omogućena je vizuelizacija vaskularnosti tumora dojke. Nakon aplikacije kontrasnog sredstva najefektivnije snimanje obavlja se u vremenskom intervalu od 2 do 8 minuta (16). Ovaj vremenski raspon idealan je za snimanje jer postoje dokazi da se sam kontrast zadržava svega do 10 minuta, te dodatna snimanja zahtevaju dodatne aplikacije kontrasta (17). Takođe je važno napomenuti da nije nužno da se mamografske slike dobijaju u određenom redosledu.

Pregled KM obuhvata slike niske energije i rekonstruisane slike. To znači da nalaz može biti vidljiv samo na slikama niske energije, samo na rekonstruisanim slikama, ili na obema. Slike niske energije su slične slikama dobijenim standardnom digitalnom mamografijom i tumače se na isti način koristeći leksikon mamograma definisan u atlasu Američkog koledža radiologa za izveštavanje i sistem podataka o dojkama (BI-RADS) (engl. *College of Radiology Breast Imaging Reporting and Data System*-BI-RADS) iz 2013. godine (12). Rekonstruisane slike se tumače kako bi se identifikovalo svako abnormalno pojačanje koje može ili ne mora imati korelaciju na slikama niske energije. Nedavno objavljen dodatak BI-RADS atlasu iz 2013. godine dopunjuje smernice za tumačenje slika KM. U KM leksikonu su uvedena dva nova termina BI-RADS-a koja podrazumevaju i izraženu asimetriju i uočljivost lezije. Izražena asimetrija je nalaz koji je moguće uočiti u jednom pogledu, ili samo pomoću rekonstruisanih slika i/ili na obema rekonstruisanim i slikama niske energije. Uočlji-

## Diagnostic possibilities of CEM

As it was mentioned at the very beginning, the technique of contrast-enhanced mammography has changed, developed and improved over time. Initially, this imaging technique was demonstrated in 1985 with digital subtraction breast angiography, in which pre-contrast images were dominant, as well as images with breast compression, after which intravenous contrast was administered (12,13). Namely, this procedure, in addition to being very invasive and unpleasant, gave suboptimal results, and therefore, its application did not proceed significantly.

A little later, CEM began to develop with the use of temporal technique, during which the breast was also exposed to compression, pre-contrast imaging was performed and intravenous contrast was applied, after which multiple imaging was done in a time interval of 5 to 7 minutes. In relation to the previously described, initial mammography, this version was improved in the segment where the pre-contrast image is subtracted from the post-contrast image, whereby contrast absorption is visualized. This technique proved to be very efficient and successful for the diagnosis of breast malignancy (14), but also it showed a number of disadvantages such as the appearance of artifacts due to the movement of patients, and a long interval of acquisition, so that only one breast can be examined during one examination. Each additional view of the ipsilateral or contralateral breast requires an additional dose of contrast. Finally, the breast is under compression during contrast administration, which can limit blood flow and result in suboptimal tissue enhancement.

The CEM technique that uses dual energy was developed in 2003 with the aim of being an alternative to the temporal technique. The essence of using dual energy in this technique is to maximize the use of contrast in the sense of exploiting its possibility of different degrees of absorption by breast tissue and iodine. This method was very well accepted, especially from the perspective of the utilization of already existing equipment. Namely, in order to carry out this imaging technique, in addition to the standard equipment for mammography, it was only necessary to upgrade the software of the existing system and add copper filtration. The standard device, which was additionally equipped in this way, enabled the so-called "dual-energy" imaging. Namely, this technique required the intravenous application of a contrast agent which has low osmolarity before the acquisition of imaging is performed. In this case, the application of the contrast agent was performed using an injector, while the recommended dose of the contrast agent was from 1.5 ml/kg to a maximum of 150 ml, usually in a concentration of 300-370 mg of iodine/ml at a speed of 3 ml/s (15). Also, like the previous, this technique demanded breast compression, but in this case breast compression needed to be performed about two minutes before the complete application of the contrast medium would be completed. In the previously described way, and thanks to the effect of compression and contrast, it is possible to obtain the paired image of low and high energy in standard craniocaudal and mediolateral projections. CEM uses the photoelectric effect of iodine, which makes it possible to highlight the areas of contrast absorption. The photoelectric effect itself depends on the energy of X-ray beam and the edge of the material. Images that come from the field of low energy are obtained below the K level of iodine at kVp values of 28-33 and show only the breast tissue, while high-energy images are obtained above the iodine K level at kVp values of 45-49 and show the absorption of iodine into the breast tissue, but they are not convenient for interpretation. After processing, the reconstructed images are created and they emphasize the areas where iodine had been absorbed, that is, they highlight the so-called zones of "amplification", while the signal, which is coming from the background tissue, is suppressed. Thanks to this absorption of iodine, the visualization of the vascularity of breast tumor is possible. After the application of the contrast agent, the most effective imaging is carried out in a time interval of 2 to 8 minutes (16). This time interval is ideal for imaging because there is evidence that the contrast itself is retained only up to 10 minutes, and therefore, additional imaging requires additional contrast applications (17). Also, it is important to note that mammographic images are not necessarily obtained in a specific order.

The CEM examination includes low-energy images and reconstructed images. This means that findings may only be visible only on low-energy images, only on reconstructed images, or on both images. Low-energy images are similar to images obtained with the help of standard digital mammography and they are interpreted

vost lezije odnosi se na stepen intenziteta lezije u odnosu na pozadinsko parenhimsko pojačanje (BPE). Ovaj KM BI-RADS leksikon obezbeđuje standardizaciju izveštavanja i doslednost, što je ključno za sprovođenje KM.

## Uloga KM u ranom otkrivanju tumora

Žene koje imaju povećan rizik od razvoja maligniteta dojke imaju korist bilo od ultrazvuka ili MR. MR je najosetljiviji skrining alat, ali se trenutno preporučuje samo ženama koje imaju visok (više od 20%) rizik od razvoja raka dojke zbog visokih troškova i ograničene dostupnosti. Žene koje imaju umeren (15–20%) rizik tokom života, a uključuju žene sa porodičnom istorijom maligniteta dojke, ličnom istorijom maligniteta dojke, prethodno potvrđenim biopsijskim visokorizičnim lezijama i gustim tkivom dojke, imaju opciju da se podvrgnu dopunskom skriningu ultrazvukom, što može otkriti karcinom koji nije vidljiv na mamografiji.

Sve više podataka ukazuje da KM kao skrining test žena sa povećanim rizikom od maligniteta dojke doprinosi boljem ranom otkrivanju poremećaja zdravlja u poređenju sa digitalnom mamografijom i/ili mamografijom i ultrazvukom zajedno (19,20). Pojedini autori ističu da se dijagnostička efektivnost KM značajno približila onoj kod MR (21). Naime, 2017. godine *Jochelson* i grupa autora publikovali su prvu prospektivnu studiju koja se bavila komparativnim poređenjem KM i MR kao skrining testova za karcinom dojke (22). U pomenutoj studiji bilo je uključeno 307 žena kojima je indentifikovan umeren do visok rizik od maligniteta dojke tokom života, a koje su podvrgnute KM i MR, nakon čega su praćene tokom 24 meseca. U periodu od prve etape skrininga, koja je trajala 12 meseci, dijagnostikovana su tri invanzivna karcinoma dojke, od kojih su dva indentifikovana na obe dijagnostičke procedure, a jedan duktalni karcinom in situ je viđen samo na MR. Dakle, prema opisanoj studiji u prvoj etapi istraživanja ni jedan karcinom nije bio indentifikovan samo pomoću KM. U zaključku pomenute studije, autori su naveli da je specifičnost ispitivanih dijagnostičkih procedura u celokupnom istraživanju bila indentična (oko 94%) (22). Godinu dana kasnije, *Klang* i grupa autora publikovali su studiju u kojoj su napravili komparativno poređenje između efektivnosti KM i ultrazvuka u cilju skrininga maligniteta dojke (23). Oni su izneli da je KM pokazala veću senzitivnost (97,3%) i specifičnost (40,0%), u poređenju sa ultrazvukom (91,9% i 8,0% ) (23). U okviru pomenute studije otkriveno je ukupno 37 karcinoma dojke, a autori su zaključili da ni jedan od otkrivenih karcinoma KM nije čak ni delovao benigno, dok su na ultrazvuku čak tri pokazivala benigni karakter. Kao najupečatljiviji zaključak opisane studije je da zapravo ultrazvučni skrining nakon adekvatnog pregleda KM može da rezultira samo nepotrebno indikovanim biopsijama. Značajno je spomenuti da je u maloj grupi od 132 žene sa povećanim rizikom od maligniteta dojke zbog lične istorije lobularne neoplazije, KM kao skrining test pokazao senzitivnost od 100% u otkrivanju 6 karcinoma koji su svi bili skriveni na standardnoj digitalnoj mamografiji (21). Specifičnost skrining testa je bila 88%.

Pored potencijalne ekonomske isplativosti i dostupnosti u odnosu na MR, KM ima druge prednosti u skriningu. Ženama sa povećanim rizikom od maligniteta dojke koje se ne mogu podvrgavati MR zbog klaustrofobije, metalnih implanta ili alergija na kontrast na bazi gadolinijuma može se bezbedno uraditi KM. Ako im se pruži izbor, većina pacijentkinja preferira KM umesto MR (24).

## Budućnost kontrastne mamografije

U budućnosti, KM zauzima značajnu ulogu u dijagnostici maligniteta dojke sa očekivanim napretkom u nekoliko ključnih aspekata. Prvo, očekuje se dalji tehnički razvoj KM tehnologije, uključujući poboljšanje algoritma za obradu slika, povećanje rezolucije i smanjenje doze zračenja. Ovi napreci doprinose većoj tačnosti dijagnostike i poboljšavaju iskustvo pacijenata. Širenje indikacija predstavlja drugi ključni aspekt. Očekuje se da će KM proširiti svoju primenu na različite vrste patoloških promena i specifične grupe pacijenata, uz prilagođene protokole za skrining kod određenih populacija. Ovo bi omogućilo širu primenu KM u kliničkoj praksi. Edukacija i implementacija igraće ključnu ulogu u široj upotrebi KM. Potrebno je osigurati da zdravstveni radnici, uključujući radiologe, tehničare i medicinsko osoblje, budu dobro obučeni za interpretaciju slika KM i postupke u slučaju reakcija na kontrast.

Ukoliko bi se KM koristila kao alternativa za MR, dijagnostičke prakse koje se značajno oslanjaju na prihode od MR mogle bi se suočiti sa značajnim finansijskim padom. U tom kontekstu

in the same way using the mammogram lexicon which was defined in the Atlas of the American College of Radiology Breast Imaging Reporting and Data System BI-RADS in 2013 (12). The reconstructed images are interpreted in order to identify any abnormal enhancement that may or does not have to correlate with the low-energy images. A recently published supplement to the BI-RADS atlas from 2013 adds guidelines for the interpretation of CEM images. In the CEM lexicon, two new BI-RADS terms have been introduced, and they imply the pronounced asymmetry and conspicuity of the lesion. The pronounced asymmetry is a finding that can be seen at a glance, or only with the help of reconstructed images and/or on both reconstructed images and low-energy images. The conspicuity of the lesion refers to the degree of intensity of the lesion in relation to the background parenchymal enhancement (BPE). This CEM BI-RADS lexicon ensures the standardization of reporting and consistency, which is important for the CEM procedure.

## The role of CEM in the early detection of tumors

Women who are at increased risk of developing breast malignancy benefit from either ultrasound or MRI. MRI is the most sensitive screening test, which is currently recommended only to women who have a high (more than 20%) risk of developing breast cancer due to high costs and limited availability. Women who have a moderate risk (15-20%) during lifetime, including women with a family history of breast malignancy, a personal history of breast malignancy, high-risk lesions and dense breast tissue that was previously confirmed by biopsy, have the option to undergo additional ultrasound screening, which can detect cancer that is not visible on mammography.

More and more data indicate that CEM as a screening test for women at an increased risk of breast malignancy contributes to the early detection of health disorders in comparison to digital mammography and/or mammography and ultrasound together (19,20). Some authors point out that the diagnostic effectiveness of CEM has significantly approached the effectiveness of MRI (21). Namely, in 2017, Johelson et al. published the first prospective study, which compared CEM and MRI as screening tests for breast cancer (22). In the above mentioned study, 307 women, who were identified as having a moderate to high risk of breast malignancy during their lifetime, and who underwent CEM and MRI, were included, after which they were followed for 24 months. In the period of the first stage of screening, which lasted 12 months, three invasive breast cancers were diagnosed, two of which were identified on both diagnostic procedures, while one ductal carcinoma in situ was seen only on MRI. Therefore, according to the described study, during the first stage, there were no cancer cases that were identified only using CEM. In the conclusion of the above mentioned study, the authors stated that the specificity of the examined diagnostic procedures in the whole research was identical (92%) (22). A year later, Klang et al. published a study, in which they made a comparative analysis between the effectiveness of CEM and ultrasound aimed at screening breast malignancy (23). They reported that CEM showed higher sensitivity (97.3%) and specificity (40.0%) in comparison to ultrasound (91.0% and 8%) (23). Within the above mentioned study, a total of 37 breast cancers were detected, and the authors concluded that none of the CEM cancers appeared benign, while on ultrasound, even three showed a benign character. The most striking conclusion of the described study is that the ultrasound screening after an adequate CEM examination can only result in unnecessarily indicated biopsies. It is important to mention that in a small group of 132 women with an increased risk of breast malignancy due to a personal history of lobular neoplasia, CEM as a screening test showed a sensitivity of 100% in detecting 6 cancer cases that were all hidden on standard digital mammography (21). The specificity of the screening test was 88%.

In addition to the potential economic cost-effectiveness and availability in comparison to MRI, CEM has other advantages in screening. Women at an increased risk of breast malignancy who cannot undergo MRI due to claustrophobia, metal implants or allergies to gadolinium-based contrast can safely undergo CEM. If they are offered choice, most patients prefer CEM to MRI (24).

## The future of CEM

In the future, CEM will have a significant role in the diagnostics of breast malignancy with

troškovna efikasnost predstavlja bitan faktor, a ako KM ostane ekonomičnija opcija u poređenju s drugim dijagnostičkim metodama, to će povećati njenu prihvatljivost u zdravstvenim sistemima. Sa druge strane, KM bi potencijalno mogla omogućiti ekonomičnu dopunsku dijagnostičku opciju za podgrupe žena kojima je trenutno MR finansijski nepristupačan ili je iz nekog razloga kontraindikovan, kao što su žene sa srednjim rizikom od maligniteta dojke, čime bi se potencijalno povećao obim skrininga i dijagnostike, a smanjili potencijalno dodatni troškovi. Takođe, važno je u ovom segmentu napomenuti da je KM i značajno brža metoda sa aspekta izvođenja i tumačenja, kao i da ima niže troškove nabavke i održavanja opreme u poređenju sa MR.

Dalja istraživanja i klinički radovi biće ključni za potvrdu dugoročne efektivnosti KM, identifikaciju novih indikacija i usavršavanje protokola primene. Povezivanje s tehnologijama veštačke inteligencije takođe ima potencijal da unapredi interpretaciju slika KM i ubrza proceduru izvođenja. U suštini, budućnost KM obećava dalji napredak u otkrivanju maligniteta dojke, nudeći napredne metode sa sve većim fokusom na preciznost, tačnost, dostupnost i udobnost pacijenata.

## Zaključak

Očekivanja u vezi s globalnim prihvatanjem KM kao standarda u otkrivanju maligniteta dojke zavise od više ključnih faktora. Najpre, dalja klinička ispitivanja su ključni koraci kako bi se potvrdila njegova efektivnost na široj populaciji. Ako KM pokaže doslednu dijagnostičku preciznost i tačnost, kao i prednosti u poređenju sa dosadašnjim metodama, to će snažno podržati njegovo globalno prihvatanje. Pored toga, edukacija i osposobljavanje zdravstvenih radnika igraju ključnu ulogu u uspešnom uvođenju KM. Ekonomska održivost takođe će biti presudna, te ako KM pruži visoku dijagnostičku efektivnost uz prihvatljive troškove, olakšaće se njegova integracija u zdravstvene sisteme širom sveta. Regulativni okviri takođe predstavljaju neizostavnu kariku, pružajući jasne smernice i standarde za sigurnost i efikasnost KM. Informisanost pacijenata i edukativne kampanje su od suštinske važnosti.. Konačno, globalno prihvatanje zahtevaće saradnju između različitih zdravstvenih sistema, uključujući javne i privatne ustanove. Ukoliko KM ispuni očekivanja u ovim ključnim oblastima, postoji potencijal da postane globalni standard za rano otkrivanje raka dojke. Međutim, dinamika i brzina prihvatanja zavisiće od napretka u istraživanjima, obrazovanju, ekonomskoj opravdanosti i saradnji između različitih aktera u oblasti zdravstvene nege

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

## Reference


1. Patel BK, Lobbes MBI, Lewin J. Contrast Enhanced Spectral Mammography: A Review.Semin Ultrasound CT MR 2018;39(1):70–79. doi.org/10.1053/j.sult.2017.08.005
2. Funke M. Diagnostic Imaging of Breast Cancer: An Update. Radiologe. 2016;56:921–938. doi: 10.1007/s00117-016-0134-6
3. Luczynska E, Piegza T, Szpor J, Heinze S, Popiela T, Kargol J, et al. Contrast-Enhanced Mammography (CEM) Capability to Distinguish Molecular Breast Cancer Subtypes. Biomedicines. 2022;10(10):2384. doi: 10.3390/biomedicines10102384
4. Sung H, Ferlay J, Siegel R.L, Laversanne M, Soerjomataram I, Jemal A, et al.. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J. Clin. 2021;71:209–249. doi: 10.3322/caac.21660
5. Grigoryants NF, Sass S, Alexander J. Novel Technologies in Breast Imaging: A Scoping Review. Cureus. 2023;15(8):e44061. doi: 10.7759/cureus.44061
6. Steyerova P, Burgetova A. Current imaging techniques and impact on diagnosis and survival —a narrative review. Annals of Breast Sur. 2022; 6: 25. doi: 10.21037/abs-21-2
7. Dibden A, Offman J, Duffy SW, Gabe R. Worldwide Review and Meta-Analysis of Cohort Studies Measuring the Effect of Mammography Screening Programmes on Incidence-Based Breast Cancer Mortality. Cancers (Basel). 2020; 12(4):976. doi: 10.3390/cancers12040976
8. Coffey K, Jochelson M. Contrast-enhanced mammography in breast cancer screening. European Journal of Radiology. 2022; 156: 110513. doi.org/10.1016/j.ejrad.2022.110513
9. Yang M.L, Bhimani C, Roth, R. et al. Contrast enhanced mammography: focus on frequently encountered benign and malignant diagnoses. Cancer Imaging. 2023; 10: 23. doi.org/10.1186/s40644-023-00526-1
10. Bernardi D, Vatteroni G, Acquaviva A, Valentini M, Sabatino V, Bolengo I. et al. Contrast-enhanced mammography versus MRI in the evaluation of neoadjuvant therapy response in patients with breast cancer: a prospective study. American Journal of Roentgenology, 219(6), 884-894. doi.org/10.2214/AJR.22.27756
11. Ainakulova AS, Zholdybay ZZ, Kaidarova D R, Inozemtceva NI, Gabdullina MO, Zhakenova ZK, et al. Contrast-enhanced spectral mammography without and with a delayed image for diagnosing malignancy among mass lesions in dense breast. Contemporary Oncology/Współczesna Onkologia. 2021; 25(1): 17-22. doi.org/10.5114/wo.2021.105030

expected advances in several key aspects. First, further technical development of CEM technology is expected, including the improvement of the algorithm for image processing, increase in resolution and decrease in radiation dose. These advances contribute to greater diagnostic accuracy and improve the patients' experience. The expansion of indications is another key aspect. CEM is expected to expand its application to different types of pathological changes and specific groups of patients, with adapted screening protocols in specific populations. This would enable a wider application of CEM in clinical practice. Education and implementation will play a key role in the wider use of CEM. It is necessary to ensure that healthcare professionals, including radiologists, technicians and medical staff are well trained in the interpretation of CEM images and procedures in case of contrast reactions.

If CEM were used as an alternative for MRI, diagnostic practices, which rely significantly on revenues gained from MRI, could face a significant financial decline. In that context, cost effectiveness is an important factor, and if CEM remains a more economical option compared to other diagnostic methods, it will increase its acceptability in healthcare systems. On the other hand, CEM could potentially provide a cost-effective additional diagnostic option for subgroups of women, for whom MRI is currently financially not accessible or contraindicated for some reason, such as women with an intermediate risk of breast malignancy, thus potentially increasing the scope of screening and diagnostics, and reducing additional costs. Also, it is important to note in this segment that CEM is a significantly faster method in terms of its execution and interpretation, as well as that it has lower costs in terms of purchase and maintenance of equipment in comparison to MRI.

Further research and clinical studies will be crucial to confirm the long-term effectiveness of CEM, identify new indications and improve the application protocols. Connecting with artificial intelligence technologies also has the potential to improve the interpretation of CEM images and accelerate the procedure. In essence, the future of CEM promises further advances in the detecting of breast malignancy, offering advanced methods with an increasing focus on precision, accuracy, availability and patients' comfort.

## Conclusion

Expectations related to the global acceptance of CEM as a standard in the detection of breast malignancy depend on several key factors. First, further clinical trials are key steps to confirm the efficiency in the wider population. If CEM demonstrates consistent diagnostic precision and accuracy, as well as advantages compared to current methods, its global acceptance will strongly be supported. In addition, education and training of health workers play a key role in the successful introduction of CEM. Economic sustainability will also be crucial, and therefore, if CEM shows high diagnostic effectiveness with acceptable costs, its integration into health systems around the world will be facilitated. Regulatory frameworks are also an indispensable link, providing clear guidelines and standards for the safety and effectiveness of CEM. Patients' awareness and educational campaigns are essential. Finally, global acceptance will require the cooperation between different healthcare systems, including public and private institutions. If CEM fulfills expectations in these key areas, it has the potential to become the global standard for the early detection of breast cancer. However, dynamics and speed of acceptance will depend on the progress in research, education, economic justification and cooperation between different actors in the field of healthcare.

## Competing interests

The authors declared no competing interests.

## References


1. Patel BK, Lobbes MBI, Lewin J. Contrast Enhanced Spectral Mammography: A Review.Semin Ultrasound CT MR 2018;39(1):70–79. doi.org/10.1053/j.sult.2017.08.005
2. Funke M. Diagnostic Imaging of Breast Cancer: An Update. Radiologe. 2016;56:921–938. doi: 10.1007/s00117-016-0134-6
3. Luczynska E, Piegza T, Szpor J, Heinze S, Popiela T, Kargol J, et al. Contrast-Enhanced Mammography (CEM) Capability to Distinguish Molecular Breast Cancer Subtypes. Biomedicines. 2022;10(10):2384. doi: 10.3390/biomedicines10102384
4. Sung H, Ferlay J, Siegel R.L, Laversanne M, Soerjomataram I, Jemal A, et al.. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J. Clin. 2021;71:209–249. doi: 10.3322/caac.21660
5. Grigoryants NF, Sass S, Alexander J. Novel Technologies in Breast Imaging: A Scoping Review. Cureus. 2023;15(8):e44061. doi: 10.7759/cureus.44061

12. Ackerman LV, Watt AC, Shetty P, Flynn MJ, Burke M, Kambouris A, et al. Breast lesions examined by digital angiography. Work in progress. Radiology 1985;155:65–8. doi.org/10.1097/00004424-198708000-00017
13. Jong RA, Yaffe MJ, Skarpathiotakis M, Shumak RS, Danjoux NM, Gunesekara A,et al. Contrast-enhanced digital mammography: initial clinical experience. Radiology 2003;228:842–50. doi.org/10.1148/radiol.2283020961
14. Diekmann F, Freyer M, Diekmann S, Fallenberg EM, Fischer T, Bick U, et al. Evaluation of contrast-enhanced digital mammography. Eur J Radiol. 2011; 78:112–21. doi.org/10.1016/j.ejrad.2009.10.002
15. Zanardo M, Cozzi A, Trimboli RM, Labaj O, Monti CB, Schiaffino S, et al.. Technique, protocols and adverse reactions for contrast-enhanced spectral mammography (CESM): a systematic review. Insights Imaging 2019; 10: 76. doi.org/10.1186/s13244
16. Neeter L. M, Raat H. P. J, Alcantara R, Robbe Q, Smidt M. L, Wildberger J. E. et al. Contrast-enhanced mammography: what the radiologist needs to know. BJR| Open. 2021; 3(1), 20210034.doi.org/10.1259/bjro.20210034
17. Jochelson MS, Lobbes MBI. Contrast-Enhanced mammography: state of the art. Radiology 2021; 299: 36–48. doi: https://doi.org/10.1148/radiol.2021201948
18. Sickles EA, D'Orsi C, Bassett L, Appleton C, Berg W, Burnside E. "Acr bi-rads® mammography." ACR BI-RADS® atlas, breast imaging reporting and data system 5 (2013): 2013.
19. Amir T, Hogan M , Jacobs S, Sevilimedu V, Sung J, Jochelson M. Comparison of False-Positive Versus True-Positive Findings on Contrast-Enhanced Digital Mammography. American Journal of Roentgenology. 2021; 218 (5):24. https://doi.org/10.2214/AJR.21.26847
20. James J. Contrast-enhanced spectral mammography (CESM)-guided breast biopsy as an alternative to MRI-guided biopsy. Br J Radiol. 2022;95(1132):20211287. doi: 10.1259/bjr.20211287
21. Hogan MP, Amir T, Sevilimedu V, Sung J, Morris EA, Jochelson MS. Contrast-Enhanced Digital Mammography Screening for Intermediate-Risk Women With a History of Lobular Neoplasia. AJR Am J Roentgenol. 2021;216(6):1486-1491. doi: 10.2214/AJR.20.23480
22. Jochelson MS, Pinker K, Dershaw DD, Hughes M, Gibbons GF, Rahbar K. et al. Comparison of screening CEDM and MRI for women at increased risk for breast cancer:A pilot study.Eur J Radiol.2017;97:37-43. doi: 10.1016/j.ejrad.2017.10.001
23. Klang E, Krosser A, Amitai MM, Sorin V, Halshtok Neiman O, Shalmon A, et al. Utility of routine use of breast ultrasound following contrast-enhanced spectral mammography. Clin Radiol. 2018;73(10):908.e11-908.e16. doi: 10.1016/j.crad.2018.05.031
24. Phillips J, Miller MM, Mehta TS, Fein-Zachary V, Nathanson A, Hori W. et al. Contrast-enhanced spectral mammography (CESM) versus MRI in the high-risk screening setting: patient preferences and attitudes. Clin Imaging. 2017;42:193-197. doi: 10.1016/j.clinimag.2016.12.011



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6. Steyerova P, Burgetova A. Current imaging techniques and impact on diagnosis and survival —a narrative review. Annals of Breast Sur. 2022; 6: 25. doi: 10.21037/abs-21-2
7. Dibden A, Offman J, Duffy SW, Gabe R. Worldwide Review and Meta-Analysis of Cohort Studies Measuring the Effect of Mammography Screening Programmes on Incidence-Based Breast Cancer Mortality. Cancers (Basel). 2020; 12(4):976. doi: 10.3390/cancers12040976
8. Coffey K, Jochelson M. Contrast-enhanced mammography in breast cancer screening. European Journal of Radiology. 2022; 156: 110513. doi.org/10.1016/j.ejrad.2022.110513
9. Yang M.L, Bhimani C, Roth, R. et al. Contrast enhanced mammography: focus on frequently encountered benign and malignant diagnoses. Cancer Imaging. 2023; 10: 23. doi.org/10.1186/s40644-023-00526-1
10. Bernardi D, Vatteroni G, Acquaviva A, Valentini M, Sabatino V, Bolengo I. et al. Contrast-enhanced mammography versus MRI in the evaluation of neoadjuvant therapy response in patients with breast cancer: a prospective study. American Journal of Roentgenology, 219(6), 884-894. doi.org/10.2214/AJR.22.27756
11. Ainakulova AS, Zholdybay ZZ, Kaidarova D R, Inozemtceva NI, Gabdullina MO, Zhakenova ZK, et al. Contrast-enhanced spectral mammography without and with a delayed image for diagnosing malignancy among mass lesions in dense breast. Contemporary Oncology/Współczesna Onkologia. 2021; 25(1): 17-22. doi.org/10.5114/wo.2021.105030
12. Ackerman LV, Watt AC, Shetty P, Flynn MJ, Burke M, Kambouris A, et al. Breast lesions examined by digital angiography. Work in progress. Radiology 1985;155:65–8. doi.org/10.1097/00004424-198708000-00017
13. Jong RA, Yaffe MJ, Skarpathiotakis M, Shumak RS, Danjoux NM, Gunesekara A,et al. Contrast-enhanced digital mammography: initial clinical experience. Radiology 2003;228:842–50. doi.org/10.1148/radiol.2283020961
14. Diekmann F, Freyer M, Diekmann S, Fallenberg EM, Fischer T, Bick U, et al. Evaluation of contrast-enhanced digital mammography. Eur J Radiol. 2011; 78:112–21. doi.org/10.1016/j.ejrad.2009.10.002
15. Zanardo M, Cozzi A, Trimboli RM, Labaj O, Monti CB, Schiaffino S, et al.. Technique, protocols and adverse reactions for contrast-enhanced spectral mammography (CESM): a systematic review. Insights Imaging 2019; 10: 76. doi.org/10.1186/s13244
16. Neeter L. M, Raat H. P. J, Alcantara R, Robbe Q, Smidt M. L, Wildberger J. E. et al. Contrast-enhanced mammography: what the radiologist needs to know. BJR| Open. 2021; 3(1), 20210034.doi.org/10.1259/bjro.20210034
17. Jochelson MS, Lobbes MBI. Contrast-Enhanced mammography: state of the art. Radiology 2021; 299: 36–48. doi: https://doi.org/10.1148/radiol.2021201948
18. Sickles EA, D'Orsi C, Bassett L, Appleton C, Berg W, Burnside E. "Acr bi-rads® mammography." ACR BI-RADS® atlas, breast imaging reporting and data system 5 (2013): 2013.
19. Amir T, Hogan M , Jacobs S, Sevilimedu V, Sung J, Jochelson M. Comparison of False-Positive Versus True-Positive Findings on Contrast-Enhanced Digital Mammography. American Journal of Roentgenology. 2021; 218 (5):24. https://doi.org/10.2214/AJR.21.26847
20. James J. Contrast-enhanced spectral mammography (CESM)-guided breast biopsy as an alternative to MRI-guided biopsy. Br J Radiol. 2022;95(1132):20211287. doi: 10.1259/bjr.20211287
21. Hogan MP, Amir T, Sevilimedu V, Sung J, Morris EA, Jochelson MS. Contrast-Enhanced Digital Mammography Screening for Intermediate-Risk Women With a History of Lobular Neoplasia. AJR Am J Roentgenol. 2021;216(6):1486-1491. doi: 10.2214/AJR.20.23480
22. Jochelson MS, Pinker K, Dershaw DD, Hughes M, Gibbons GF, Rahbar K. et al. Comparison of screening CEDM and MRI for women at increased risk for breast cancer:A pilot study.Eur J Radiol.2017;97:37-43. doi: 10.1016/j.ejrad.2017.10.001
23. Klang E, Krosser A, Amitai MM, Sorin V, Halshtok Neiman O, Shalmon A, et al. Utility of routine use of breast ultrasound following contrast-enhanced spectral mammography. Clin Radiol. 2018;73(10):908.e11-908.e16. doi: 10.1016/j.crad.2018.05.031
24. Phillips J, Miller MM, Mehta TS, Fein-Zachary V, Nathanson A, Hori W. et al. Contrast-enhanced spectral mammography (CESM) versus MRI in the high-risk screening setting: patient preferences and attitudes. Clin Imaging. 2017;42:193-197. doi: 10.1016/j.clinimag.2016.12.011




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# INSTRUMENTI PROCENE ZDRAVSTVENE PISMENOSTI ADOLESCENATA

**Katarina Pavić[1], Dragana Simin[2]**

[1] Odsek za medicinske i poslovno-tehnološke studije, Akademija strukovnih studija Šabac, Šabac, Republika Srbija
[2] Katedra za zdravstvenu negu, Medicinski fakultet Novi Sad, Univerzitet u Novom Sadu, Novi Sad, Republika Srbija

[*] Korespondencija: Katarina Pavić, Odsek za medicinske i poslovno-tehnološke studije, Akademija strukovnih studija Šabac, Hajduk Veljkova 10, Šabac, Republika Srbija; e-mail: katarinapavic994@gmail.com

**SAŽETAK**

Zdravstvena pismenost označena je kao sposobnost pojedinca da primi, obradi i razume zdravstvene informacije. Adolescencija je ključni stadijum psiho-fizičkog razvoja, te bi unapređenje zdravstvene pismenosti mladih značajno doprinelo usvajanju zdravih navika i osnažilo ih da preuzmu kontrolu nad sopstvenim zdravljem. Cilj ovog preglednog rada je bio da prikaže instrumente procene zdravstvene pismenosti u adolescentskoj populaciji. Identifikovanje instrumenata za adolescentsku populaciju spovedeno je pretragom literature korišćenjem različitih baza podataka. Od 9 instrumenata, koji su poređeni u odnosu na domen merenja zdravstvene pismenosti i način prikupljanja podataka, šest (HLS-Child-Q15, HELiASeSS, HAS-A, HELMA, eHEALS, HLAT-8) procenjuju zdravstvenu pismenost u sva tri domena te mogu pružiti kompletniju sliku o nivou zdravstvene pismenosti adolescenata. Od ovih 6 instrumenata, HLS-Child-Q15 i HELMA su dostupni za preuzimanje što može da utiće na njihovu veću primenu u budućnosti za procenu zdravstvene pismenosti u adolescentskoj populaciji. U budućim istraživanjima trebalo bi još detaljnije analizirati instrumente za procenu zdravstvene pismenosti, a posebno njihovu validnost i pouzdanost.

**Ključne reči:** zdravstvena pismenost, adolescent, instrumenti procene zdravstvene pismenosti

## Uvod

Zdravstvena pismenost je sposobnost pojedinca da primi, obradi i razume zdravstvene informacije. Predstavlja značajnu determinantu javnog zdravlja, a označena je i kao globalni cilj za unapređenje promocije zdravlja (1). Prema Svetskoj zdravstvenoj organizaciji (SZO) zdravstvena pismenost podrazumeva kognitivne i socijalne veštine koje određuju motivaciju i sposobnost pojedinaca da pristupi, razume i koristi informacije na načine koji promovišu i održavaju dobro zdravlje. Termin zdravstvene pismenosti prvi put je opisan u tekstu *Health Education as Social Policy*, iz 1974. godine, čiji je autor bio profesor *Simonds* sa Univerziteta u Mičigenu (2).

U prethodne dve decenije pridavana je velika pažnja konceptu zdravstvene pismenosti, jer je utvrđeno da ima značajan doprinos održivosti sistema zdravstvene zaštite, pogotovo u vremenu kada su masovne nezarazne bolesti u porastu. Strategije za unapređenje javnog zdravlja u razvijenim zemljama ističu potrebu pojedinaca da preuzme brigu o sopstvenom zdravlju čime će doprineti efektivnijem korišćenju usluga zdravstvene zaštite i smanjenju troškova. Zbog shvatanja da donosi veliku korist za javno zdravlje, mnoge zemlje, kao što su SAD, Kanada, Australija su ga istakle kao prioritet u svojim zdravstvenim politikama (3).

Empirijska istraživanja pokazuju da je nizak nivo zdravstvene pismenosti povezan sa nizom štetnih ishoda po zdravlja (4), dok novija istraživanja kao posledice niske zdravstvene pismenosti navode neodazivanje na skrining preglede, otkrivanje oboljenja u kasnoj fazi, povećanu učestalost komplikacija i produženu hospitalizaciju kod hroničnih bolesnika (5).

Nacionalne studije u SAD-u, Kanadi i Kini, kao i Evropska uporedna analiza, pokazale su da je problem neadekvatne zdravstvene pismenosti stanovništva globalan. Samo 12% ispitivane populacije u SAD-u (6) i oko 8% u Kini imalo je adekvatan

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# INSTRUMENTS FOR THE ASSESSMENT OF HEALTH LITERACY IN ADOLESCENTS

**Katarina Pavić[1], Dragana Simin[2]**

[1] Department for Medical, Business and Technological Studies, Academy of Vocational Studies Šabac, Šabac, Republic of Serbia
[2] Department of Healthcare, Faculty of Medicine, University of Novi Sad, Novi Sad, Republic of Serbia

[*] Correspondence: Katarina Pavić, Department for Medical, Business and Technological Studies, Academy of Vocational Studies Šabac, Hajduk Veljko's street 10, Šabac, Republic of Serbia; e-mail: katarinapavic994@gmail.com

**SUMMARY**

Health literacy is defined as an individual's ability to receive, process and understand health information. Adolescence is a key stage of psycho-physical development, and therefore, improving the health literacy of young people would significantly contribute to the adoption of healthy habits and empower them to take control of their own health. The aim of this review article was to present instruments for assessing health literacy in the adolescent population. The identification of instruments for the adolescent population was carried out through a literature search using different databases. Of 9 instruments, which were compared in relation to the domain of measuring health literacy and the method of data collection, six (HLS-Child-Q15, HELiASeSS, HAS-A, HELMA, eHEALS, HLAT-8) assess health literacy in all three domains, and therefore, they can offer a more complete picture of the level of health literacy in adolescents. Of these 6 instruments, HLS-Child-Q15 and HELMA are available for downloading which can influence the greater implementation in the future for the assessment of health literacy in adolescents.

**Keywords:** health literacy; adolescents; health literacy assessment instruments

## Introduction

Health literacy is the ability of an individual to receive, process and understand health information. It represents a significant determinant of public health, and it has been designated as a global goal related to the improvement of health promotion (1). According to the World Health Organization (WHO), health literacy includes cognitive and social skills that determine the motivation and ability of individuals to access, understand and use information in ways that promote and maintain good health. The term health literacy was first described in the text Health Education as Social Policy in 1974 by Professor Simonds from the University of Michigan (2).

In the last two decades, much attention has been paid to the concept of health literacy due to its significant contribution to the sustainability of healthcare system, especially at the time when mass non-communicable diseases are on the rise. Strategies for the improvement of public health in developed countries emphasize the need of individuals to take care of their own health, thus contributing to more efficient use of healthcare services and cost reduction. Since it has been realized that it brings a great benefit to public health, many countries such as the USA, Canada, Australia have given priority to it in their health policies (3).

Empirical studies have shown that a low level of health literacy is associated with a number of harmful health outcomes (4), while it has been indicated in recent studies that the consequences of low health literacy include not going to screening examinations, detection of diseases at a late stage, increased frequency of complications and prolonged hospitalization in chronic patients (5).

National studies in the USA, Canada and China, as well as the European comparative analysis have shown that the problem of inadequate health literacy of the population is global. Only 12% of the

nivo zdravstvene pismenosti (7). U kanadskoj studiji pronađeno je da oko 60% ispitanika ima neadekvatan nivo zdravstvene pismenosti (8), a u Evropi je taj procenat 47,6% (9).

Rešavanje problema neadekvatne zdravstvene pismenosti postalo je prioritet u mnogim zemljama, jer se to smatra najekonomičnijom i najefikasnijom merom za poboljšanje zdravlja celokupnog stanovništva. Poseban akcenat se stavlja na unapređenje zdravstvene pismenosti dece i adolescenata. Istraživanja pokazuju da 34% adolescenata u SAD i 67,6% u Australiji ima niske nivoe zdravstvene pismenosti (10,11). Adolescencija je ključni stadijum psiho-fizičkog razvoja, te bi unapređenje zdravstvene pismenosti mladih značajno doprinelo usvajanju zdravih navika i osnažilo ih da preuzmu kontrolu nad sopstvenim zdravljem (12).

Cilj ovog rada bio je da prikaže instrumente procene zdravstvene pismenosti u adolescentskoj populaciji.

## Metode

Pretraživanjem baza *PubMed* i *Google Scholar* pronađeno je mnoštovo radova na temu zdravstvene pismenosti, a za analizu definicija korišćeni su pregledni radovi koji su na engleskom jeziku i koji su najviše citirani.

## Definicije i koncepti zdravstvene pismenosti

Prema preglednim radovima *Sorensen*-a i saradnika (4) i *Liu*-a i saradnika (3) formirana je tabela definicija zdravstvene pismenosti (Tabela 1). SZO u svojoj definiciji (1) ističe značaj interakcije kognitivnih i socijalnih veština neophodnih za pristup, razumevanje i interpretaciju zdravstvenih informacija koje mogu doprineti dobrom zdravlju, a nasuprot tome, u definiciji Američke medicinske asocijacije akcenat je na sposobnosti razumevanja numeričkih zadataka i čitanja (13). Novije definicije naglašavaju važnost prevazilaženja individualnog pristupa i posmatraju zdravstvenu pismenost kao interakciju između zahteva zdravstvenih sistema i veština pojedinca. Prema *Nutbeam*-u (14) zdravstvena pismenost zavisi od ličnih, kognitivnih i socijalnih veština, a *Kwan* i saradnici (15) u svojoj definiciji ističu značaj interakcije veština i sposobnosti svih subjekata uključenih u proces donošenja odluka vezanih za zdravlje.

Različiti istraživači koji su se bavili zdravstvenom pismenošću shvataju je kao višedimenzionalan koncept. Većina konceptualnih modela prikazanih u literaturi razmatra ključne komponente zdravstvene pismenosti, individualne i sistemske faktore koji utiču na nivo zdravstvene pismenosti, kao i povezanost nivoa zdravstvene pismenosti sa ishodima po zdravlje (4). U dostupnoj literaturi se najčešće pominje *Nutbeam*-ov koncept po kome se razlikuju tri tipa zdravstvene pismenosti (14):

1. Funkcionalna, koja uključuje veštine čitanja i pisanja,
2. Interaktivna, odnosi se na naprednije kognitivne veštine i veštine pismenosti koje pojedincu omogućavaju da izdvoji informacije, primeni ih u različitim situacijama i bude sigurniji u komunikaciji sa zdravstvenim profesionalcima,

**Tabela 1.** Definicije zdravstvene pismenosti

| | |
|---|---|
| **Svetska zdravstvena organizacija (SZO, 1998)** | Skup kognitivnih i socijalnih veština i kapaciteta potrebnih za pristup, razumevanje i korišćenje informacija na način kojim se promoviše i štiti dobro zdravlje (1). |
| **Američka medicinska asocijacija (AMA, 1999)** | Skup veština neophodnih za funkcionisanje u zdravstvenom okruženju koje uključuju sposobnost izvođenja osnovnih numeričkih zadataka i čitanja (13). |
| ***Nutbeam* (2000)** | Lične, kognitivne i društvene veštine koje određuju sposobnost pojedinaca da dobiju pristup, razumeju i koriste informacije za promovisanje i održavanje dobrog zdravlja (14). |
| ***Kwan, et al.* (2006)** | Sposobnost pojedinca da traži, razume i koristi zdravstvene informacije u okviru zdravstvene zaštite (15). |
| ***Sorensen, et al.* (2012)** | Zdravstvena pismenost je povezana sa pismenošću i podrazumeva znanje pojedinca, motivaciju i sposobnosti da pristupi, razume, proceni i primeni informacije o zdravlju, kako bi u svakodnevnom životu prosuđivao i donosio odluke u vezi sa zdravljem, prevencijom bolesti i unapređivanjem zdravlja u cilju održavanja ili poboljšanja kvaliteta života tokom životnog veka (4). |

examined population in the USA (6) and around 8% in China had an adequate level of health literacy (7). In one Canadian study, it was found that about 60% of respondents had an inadequate level of health literacy (8), and in Europe that percentage was 47.6% (9).

Solving the problem of inadequate health literacy has become a priority in many countries, since it is considered to be the most economical and effective measure for improving the health of the whole population. Special emphasis has been placed on improving the health literacy of children and adolescents. Research has shown that 34% of adolescents in the USA and 67.6% in Australia have low levels of health literacy (10,11). Adolescence is a key stage of psycho-physical development, and improving the health literacy of young people would significantly contribute to the adoption of healthy habits and empower them to take control over their own health (12).

The aim of this study was to present the instruments for the assessment of health literacy in the adolescent population.

## Methods

By searching the databases PubMed and Google Scholar, a lot of papers examining the topic of health literacy have been found, while mostly cited review articles in the English language have been used.

## Definitions and concepts of health literacy

According to the review articles of Sorensen and associates (4), Liu and associates (3), the table of definitions of health literacy has been formed (Table 1). The World Health Organization in its definition (1) emphasizes the importance of the interaction of cognitive and social skills necessary for accessing, understanding and interpreting health information that can contribute to good health, and in contrast, in the definition of the American Medical Association, the emphasis is placed on the ability to understand numerical tasks and reading (13). Newer definitions emphasize the importance of going beyond the individual approach and perceive health literacy as an interaction between the demands of health systems and skills of an individual. According to Nutbeam (14), health literacy depends on personal, cognitive and social skills, while Kwan and associates (15) in their definition emphasize the importance of the interaction between skills and abilities of all subjects involved in the process of decision-making related to health.

Different researchers, who have dealt with health literacy, understand it as a multidimensional concept. Most of the conceptual models which are presented in the literature consider the key components of health literacy, individual and systematic factors that influence the level of health literacy, as well as the connection between the level of health literacy and health outcomes (4). In the available literature, Nutbeam's concept is most often mentioned, according to which three types of health literacy are distinguished (14):

1. Functional, which includes reading and writing skills,
2. Interactive, which refers to more advanced

**Table 1.** Definitions of health literacy

| | |
|---|---|
| **World Health Organization (WHO, 1998)** | The set of cognitive and social skills and capacities needed to access, understand and use information in a way that promotes and protects good health (1). |
| **American Medical Association (AMA, 1999)** | The set of skills necessary for functioning in a healthcare environment that include the ability to perform basic numerical tasks and reading (13). |
| **Nutbeam (2000)** | Personal, cognitive and social skills that determine the ability of individuals to access, understand and use information necessary for promoting and maintaining good health (14). |
| **Kwan, et al. (2006)** | The ability of an individual to search for, understand and use health information within healthcare (15). |
| **Sorensen, et al. (2012)** | Health literacy is related to literacy and includes the knowledge, motivation and ability of individuals to access, understand, evaluate and apply information about health, so that in everyday life they could judge and make decisions related to health, disease prevention and health promotion aimed at maintaining and improving the quality of life during lifetime (4). |

3. Kritička, odnosi se na najsloženije kognitivne veštine koje u interakciji sa socijalnim veštinama mogu da se koriste za kritičku analizu informacija i bolju kontrolu različitih situacija i životnih događaja.

Kako bi otklonili nedostatke različitih konceptualnih okvira zdravstvene pismenosti, *Sorensen* i saradnici (4) su konstruisali integrisani model zdravstvene pismenosti koji obuhvata glavne dimenzije postojećih konceptualnih modela. U centralnom delu modela prikazane su 4 dimenzije zdravstvene pismenosti: pristup informacijama o zdravlju, razumevanje informacija o zdravlju, interpretacija informacija o zdravlju i primena informacija o zdravlju (4).

## Zdravstvena pismenost adolescenata

Zdravstvena pismenost adolescenata ima specifičnosti u odnosu na zdravstvenu pismenost odraslih, jer je ovo ključni stadijum razvoja i razvijene veštine za unapređenje zdravlja mogu ostati tokom čitavog života (10). Od adolescenata se očekuje da razumeju sve složenije zdravstvene informacije, veliku količinu edukativnog materijala koji im pružaju zdravstveni radnici i obrazovni sistem, kao i da postanu odgovorni za svoje zdravlje (16).

Sistematska analiza potvrdila je pozitivnu korelaciju između viših nivoa zdravstvene pismenosti i boljih ishoda po zdravlje adolescenata (17), a studija preseka sprovedena među adolescentima u Kini o stavovima prema vakcinaciji protiv kovid-19 je pokazala da je neodlučnost o vakcinaciji povezana sa ograničenim nivoom zdravstvene pismenosti (18).

S obzirom da mladi provode veliki deo vremena u školskom okruženju, bilo bi značajno sprovoditi aktivnosti za unapređenje zdravstvene pismenosti kako učenika, kao i njihovih roditelja i profesora. Shodno tome, SZO se angažovala u brojnim akcijama za poboljšanje zdravlja kroz promovisanje i unapređenje zdravstvene pismenosti, a obrazovni sektor prepoznat je kao najvažnije okruženje za to (2).

## Instrumenti procene zdravstvene pismenosti adolescenata

Instrumenti procene zdravstvene pismenosti mogu biti opšti koji se primenjuju u opštoj populaciji, i specifični koji se primenjuju u određenoj starosnoj grupi, ili kod obolelih od određene bolesti. Pretragom baze instrumenata za procenu zdravstvene pismenosti (engl. *Health Literacy Tool Shed*) (19) i analizom preglednog rada *Guo*-a i saradnika (20) pronađeni su instrumenti validirani za adolescentsku populaciju. Ovi instrumenti se razlikuju po domenu merenja zdravstvene pismenosti, ali je najviše onih koji procenjuju zdravstvenu pismenost u sva tri domena: funkcionalna, interaktivna i kritička. Kriterijumi za uključivanje bili su: validirani instrument za procenu zdravstvene pismenosti u adolescentskoj populaciji u rasponu od 10 do 24 godine, rad dostupan u punom tekstu, i instrumenti koji procenjuju opštu zdravstvenu pismenost.

Najčešći instrumenti za procenu zdravstvene pismenosti koji su ispunili zadate kriterijume u pregledanoj literaturi su:

1. Kineska verzija kratke forme Testa za procenu funkcionalne zdravstvene pismenosti adolescenata (engl. *Chinese version of short-form Test of Functional Health Literacy in Adolescents* – c-sTOFHLAd) (21),
2. Instrument za brzu procenu pismenosti adolescenata u medicini – kratka forma (engl. *Rapid Estimate of Adolescent Literacy in Medicine Short Form* – REALM-TeenS) (22),
3. Instrument za merenje zdravstvene pismenosti adolescenata (engl. *Measurement of Health Literacy Among Adolescents Questionnaire* – MOHLAA-Q) (23),
4. Evropski upitnik za procenu zdravstvene pismenosti stanovništva (engl. *European Health Literacy Survey* – HLS.EU.Q) je validiran za decu (0-9 godina) i adolescente (10-17 godina) (24),
5. Instrument procene zdravstvene pismenosti učenika srednje škole (engl. *Instrument for the Health Literacy Assessment of Secondary School Students* – HELiASeSS) (25),
6. Skala za procenu zdravstvene pismenosti adolescenata (engl. *Health Literacy Assessment Scale for Adolescents* - HAS-A) (26),
7. Instrument za procenu zdravstvene pismenosti adolescenata (engl. *Health Literacy Measure for Adolescents* – HELMA) (27),
8. Instrument za procenu elektronske zdravstvene pismenosti (engl. eHealth Literacy Scale – eHEALS) (28),
9. Instrument za procenu zdravstvene pismenosti sa 8 stavki (engl. *Health Literacy Assessment Tool* – HLAT-8) (29).

Prikaz navedenih instrumenata prema načinu procene zdravstvene pismenosti, kao i druge značajne karakteristike istih, izvršen je u Tabeli 2.

cognitive and literacy skills that allow the individual to elicit information, apply it in different situations and be more confident while communicating with healthcare professionals,
3. Critical, which refers to the most complex cognitive skills that, in interaction with social skills, can be used for the critical analysis of information and better control of different situations and life events.

In order to overcome the shortcomings of different conceptual frameworks of health literacy, Sorensen et al. (4) constructed an integrated model of health literacy that includes the main dimensions of existing conceptual models. In the central part of the model, the following four dimensions of health literacy are presented: access to information about health, understanding of health related information, interpretation of information about health and application of information about health (4).

## Health literacy of adolescents

The health literacy of adolescents has specificities compared to the health literacy of adults, because this is a key stage of development and developed skills necessary for improving health can remain throughout life (10). Adolescents are expected to understand the increasingly complex health information, a large amount of educational materials provided by health workers and educational system, as well as to become responsible for their health (16).

A systematic analysis has confirmed a positive correlation between higher levels of health literacy and better outcomes related to adolescents' health (17), while a cross-sectional study, which was conducted among the adolescents in China about their attitudes to vaccination against Covid-19, showed that hesitancy to get vaccinated was associated with the limited level of health literacy (18).

Given that young people spend much time in the school environment, it would be important to implement activities for improving the health literacy of students, as well as their parents and professors. Therefore, the World Health Organization (WHO) has engaged in numerous actions for improving health through promoting and improving health literacy, while the educational sector has been recognized as the most important environment for this (2).

## Instruments for the assessment of health literacy

The instruments for the assessment of health literacy can be general, which are applied in the general population, and specific, which are applied in a certain age group, or in patients with a certain disease. By searching the Health Literacy Tool Shed (19) and analyzing the review article by Guo et al. (20), instruments validated for the adolescent population were found. These instruments differ according to the domain of measuring health literacy, but most of them evaluate health literacy in all three domains: functional, interactive and critical. Inclusion criteria were the following: validated instrument for the assessment of health literacy in the adolescent population from 10 to 24 years, a paper is available as a full text, and instruments that assess the general health literacy. The most common instruments for the assessment of health literacy that met the set criteria in the reviewed literature are the following:

1. Chinese version of short-form Test of Functional Health Literacy in Adolescents (c-sTOFHLAd) (21),
2. Rapid Estimate of Adolescent Literacy in Medicine Short Form (REALM-Teens) (22),
3. Measurement of Health Literacy Among Adolescents Questionnaire (MOHLAA) (23),
4. European Health Literacy Survey (HLS.EU.Q) was validated for children (0-9 years) and adolescents (10-17 years) (24),
5. Instrument for the Health Literacy Assessment of Secondary School Students (HELiASeSS) (25),
6. Health Literacy Assessment Scale for Adolescents (HAS-A) (26),
7. Health Literacy Measure for Adolescents (HELMA) (27),
8. eHealth Literacy Scale (eHEALS) (28),
9. Health Literacy Assessment Tool – HLAT-8 (29).

The presentation of the above mentioned instruments according to the method of assessment of health literacy, as well as other significant characteristics of those instruments are shown in Table 2.

Out of these 9 instruments for the assessment of health literacy in adolescents, 6 assess health literacy in all three domains (functional, interactive and critical), which speaks in favor of giving importance to empowering adolescents in health

**Tabela 2.** Pregled instrumenata za procenu zdravstvene pismenosti adolescenata prema tipu i načinu primene

| Autor | Naziv instrumenta | Tip merenja | Vreme potrebno za popunjavanje/ Broj pitanja | Populacija u kojoj su validirani | Jezik na kome je validiran |
|---|---|---|---|---|---|
| ***Chang, et al.* (2012)** | Kineska verzija kratke forme instrumenta za procenu funkcionalne zdravstvene pismenosti adolescenata (engl. *Chinese version of short-form Test of Functional Health Literacy in Adolescents* – c-sTOFHLAd) | Razumevanje pročitanog teksta | 11 minuta/ 36 stavki | Adolescenti 10-17 godina | Tajvanski |
| ***Manganello, et al.* (2017)** | Instrument za brzu procenu pismenosti adolescenata u medicini – kratka forma (engl. *Rapid Estimate of Adolescent Literacy in Medicine Short Form* – REALM-TeenS) | Test prepoznavanja i izgovaranja medicinskih reči, numeričke sposobnosti | 4 min/ 10 pitanja | Adolescenti 10-17 godina | Engleski |
| ***Domanska, et al.* (2020)** | Skala za merenje zdravstvene pismenosti adolescenata (engl. *Measurement of Health Literacy Among Adolescents Questionnaire* – MOHLAA-Q) | Razumevanje zdravstvenih informacija | Neograničeno vreme/ 29 pitanja | Adolescenti 14-17 godina | Nemački |
| ***Bollweg, et al.* (2020)** | Evropski upitnik za procenu zdravstvene pismenosti – verzija upitnika prilagođena uzrastu (engl. *Age Adapted Survey version of the European Health Literacy Questionnaire for fourth-graders* – HLS-Child-Q15) | Test razumevanja, primena zdravstvenih informacija, komunikacija: veština slušanja | 10 minuta/ 15 pitanja | Deca 0-9 godina Adolescenti 10-17 godina | Nemački |
| ***Bechraki, et al.* (2022)** | Instrument procene zdravstvene pismenosti učenika srednje škole (engl. *Instrument for the Health Literacy Assessment of Secondary School Students* – HELiASeSS) | Traženje, razumevanje, procena, zdravstvenih informacija; Komunikacijske veštine | Neograničeno vreme/ 37 pitanja | Adolescenti 10-17 godina | Grčki |
| ***Manganello* (2015)** | Skala za procenu zdravstvene pismenosti adolescenata (engl. *Health Literacy Assessment Scale for Adolescents* – HAS-A) | Traženje, razumevanje i obrada zdravstvenih informacija | Neograničeno vreme/ 15 pitanja | Adolescenti 10-17 godina | Engleski |
| ***Ghanbari, et al.* (2016)** | Instrument za procenu zdravstvene pismenosti adolescenata (engl. *Health Literacy Measure for Adolescents* – HELMA) | Razumevanje pročitanog teksta, komunikacijske i numeričke veštine, primena zdr. informacija | Neograničeno vreme/ 44 pitanja | Adolescenti 14-17 godina | Engleski |
| ***Norman and Skinner* (2006)** | Instrument za procenu elektronske zdravstvene pismenosti (engl. *eHealth Literacy Scale*-eHEALS) | Pristupanje, procena i primena zdravstvenih informacija | Neograničeno vreme/ 8 pitanja | Adolescenti 13-21 godina | Engleski |
| ***Abel, et al.* (2014)** | Instrument za procenu zdravstvene pismenosti sa 8 stavki (engl. *Health Literacy Assessment Tool* – HLAT-8) | Pronalaženje, razumevanje i primena zdravstvenih informacija | Neograničeno vreme/ 8 pitanja | Adolescenti 18-24 godine | Engleski |

Od 9 instrumenata za procenu zdravstvene pismenosti adolescenata, 6 procenjuje zdravstvenu pismenost u sva tri domena (funkcionalna, interaktivna i kritička), što govori u prilog davanju značaja osnaživanju adolescenata u promociji zdravlja. Poređenje instrumenata u odnosu na domen merenja zdravstvene pismenosti i način prikupljanja podataka (subjektivno procenjivanje vrši ispitanik samostalno – test samoprocene veština, dok je za objektivno procenjivanje potrebna asistencija edukovanog zdravstvenog profesionalca) prikazano je u Tabeli 3.

**Table 2.** Review of instruments for the assessment of health literacy in adolescents according to the type and method of application

| Author | Instrument's name | Type of measurement | Time needed to complete/ Number of questions | Population in which it was validated | Language in which it was validated |
|---|---|---|---|---|---|
| **Chang, et al. (2012)** | Chinese version of short-form Test of Functional Health Literacy in Adolescents (c-sTOFHLAd) | Reading comprehension | 11 minutes/ 36 items | Adolescents 10-17 years | Taiwanese |
| **Manganello, et al. (2017)** | Rapid Estimate of Adolescent Literacy in Medicine Short Form (REALM-TeenS) | Test of recognizing and understanding medical words, numerical abilities | 4 min/ 10 questions | Adolescents 10-17 years | English |
| **Domanska, et al. (2020)** | Measurement of Health Literacy Among Adolescents Questionnaire (MOHLAA-Q) | Understanding health related information | Time is not limited/ 29 questions | Adolescents 14-17 years | German |
| **Bollweg, et al. (2020)** | Age Adapted Survey version of the European Health Literacy Questionnaire for fourth-graders (HLS-Child-Q15) | Test of understanding, application of health information, communication: listening skill | 10 minutes/ 15 questions | Children 0-9 years Adolescents 10-17 years | German |
| **Bechraki, et al. (2022)** | Instrument for the Health Literacy Assessment of Secondary School Students (HELiASeSS) | Searching for, understanding, evaluating health information; communication skills | Time is not limited/ 37 questions | Adolescents 10-17 years | Greek |
| **Manganello (2015)** | Health Literacy Assessment Scale for Adolescents (HAS-A) | Searching for, understanding and analyzing health information | Time is not limited/ 15 questions | Adolescents 10-17 years | English |
| **Ghanbari, et al. (2016)** | Health Literacy Measure for Adolescents (HELMA) | Reading comprehension, communication and numerical skills, application of health information | Time is not limited/ 44 questions | Adolescents 14-17 years | English |
| **Norman and Skinner (2006)** | eHealth Literacy Scale (eHEALS) | Accessing, evaluating and applying health information | Time is not limited/ 8 questions | Adolescents 13-21 years | English |
| **Abel, et al. (2014)** | Health Literacy Assessment Tool (HLAT-8) | Finding, understanding and applying health information | Time is not limited/ 8 questions | Adolescents 18-24 years | English |

promotion. The comparison of instruments in relation to the domain of measuring health literacy and the method of collecting data (subjective assessment is performed by the respondent independently – self-assessment of skills, while objective assessment requires the assistance of educated health professional) was shown in Table 3.

By analyzing the identified instruments, it was observed that only the REALM-TeenS instrument requires the presence of an educated health worker who will carry out testing, while the other instruments of self-assessment of skills and levels of health literacy are realized by respondents, which indicates that the instruments of self-assessment are more often used in practice for the assessment of health literacy. Similar results were shown in the review article by Guo et al. (20), while the use of instruments of self-assessment is a cheaper and easier option for the collection of data, although it may have certain disadvantages. Namely, adolescents are still, to a great extent, dependent on their parents when it comes to making health-related decisions, so if they filled out the self-

**Tabela 3.** Poređenje instrumenata u odnosu na domen merenja zdravstvene pismenosti i način prikupljanja podataka

| Instrument | Funkcionalna | Interaktivna | Kritička | Numerička | Subjektivno/ Objektivno merenje |
|---|---|---|---|---|---|
| **C-sTOFHLAd** | + | - | - | + | S |
| **REALM-TeenS** | + | - | - | + | O |
| **MOHLAA-Q** | - | + | - | - | S |
| **HLS-Child-Q15** | + | + | + | - | S |
| **HELiASeSS** | + | + | + | - | S |
| **HAS-A** | + | + | + | - | S |
| **HELMA** | + | + | + | + | S |
| **eHEALS** | + | + | + | + | S |
| **HLAT-8** | + | + | + | - | S |

+ = DA; - = NE; S-subjektivno merenje; O-objektivno merenje

Analizom identifikovanih instrumenata, uočeno je da jedino REALM-TeenS instrument zahteva prisustvo edukovanog zdravstvenog radnika koji će sprovoditi testiranje, dok se ostali instrumenti samoprocene veština i nivoa zdravstvene pismenosti realizuju od strane ispitanika što ukazuje na to da se instrumenti samoprocene češće koriste u praksi za procenu zdravstvene pismenosti. Slične rezultate pokazao je i pregledni rad *Guo*-a i saradnika (20), a primena instrumenata samoprocene je jeftinija i lakša opcija prikupljanja podataka, ali može imati određene nedostatke. Naime, adolescenti još uvek u velikoj meri zavise od roditelja kada je donošenje odluka vezanih za zdravlje u pitanju, te ako bi sami popunjavali upitnike samoprocene moglo bi doći do pogrešnih rezultata. Zbog toga bi upitnici trebalo da budu razumljivi, kako bi adolescenti shvatili šta se od njih traži (30).

Instrumenti koji se fokusiraju samo na procenu veštine čitanja i prepoznavanja medicinskih reči, kao što su c-s-TOFHLA i MOHLAA-Q, ne procenjuju druge veštine zdravstvene pismenosti (numeričke sposobnosti, konceptualna znanja i dr.) koje su značajne za potpunije određivanje nivoa zdravstvene pismenosti (20).

Šest instrumenata (HLS-Child-Q15, HELiASeSS, HAS-A, HELMA, eHEALS, HLAT-8) procenjuju zdravstvenu pismenost u sva tri domena te mogu pružiti kompletniju sliku o nivou zdravstvene pismenosti adolescenata od prva tri instrumenta navedena u Tabeli 2 (C-sTOFHLAd, REALM-TeenS, MOHLAA-Q). Od pomenutih 6 instrumenata, HLS-Child-Q15 i HELMA su dostupni za preuzimanje te bi mogli biti primenjeni za buduća istraživanja zdravstvene pismenosti u adolescentskoj populaciji.

U budućim istraživanjima trebalo bi još detaljnije analizirati instrumente za procenu zdravstvene pismenosti adolescenata, a posebno njihovu validnost i pouzdanost.

## Zaključak

Od analiziranih instrumenata za procenu zdravstvene pismenosti adolescenata 6 procenjuje zdravstvenu pismenost u sva tri domena, te bi bili adekvatniji za primenu od instrumenata koji procenjuju samo određenu veštinu zdravstvene pismenosti. Neophodna su dalja istraživanja u ovoj oblasti, a posebno procena njihove validnosti i pouzdanosti.

## Konflikt interesa

Autori su izjavili da nema konflikta interesa.

## Reference


1. World Health Organization. Improving health literacy. 1998. [Internet]. [cited 09 August 2023] Available from: https://www.who.int/activities/improving-health-literacy
2. World Health Organization. Shanghai declaration on promoting health in the 2030 Agenda for Sustainable Development. Health Promot Int. 2017;32(1):7-8. doi:10.1093/heapro/daw103
3. Liu C, Wang D, Liu C, Jiang J, Wang X, Chen H, et al. What is the meaning of health literacy? A systematic review and qualitative synthesis. Fam Med Community Health. 2020;8(2). doi:10.1136/fmch-2020-000351

**Table 3.** Comparison of instruments according to the domain of measuring health literacy and the method of data collection

| Instrument | Functional | Interactive | Critical | Numerical | Subjective/ Objective measurement |
|---|---|---|---|---|---|
| **C-sTOFHLAd** | + | - | - | + | S |
| **REALM-TeenS** | + | - | - | + | O |
| **MOHLAA-Q** | - | + | - | - | S |
| **HLS-Child-Q15** | + | + | + | - | S |
| **HELiASeSS** | + | + | + | - | S |
| **HAS-A** | + | + | + | - | S |
| **HELMA** | + | + | + | + | S |
| **eHEALS** | + | + | + | + | S |
| **HLAT-8** | + | + | + | - | S |

+ = YES; - = NO; S-subjective measurement; O-objective measurement

assessment questionnaires on their own, the results could be wrong. Therefore, questionnaires should be comprehensible, so that adolescents would understand what they were asked (30).

Instruments that focus only on the assessment of reading skills and recognition of medical words, such as c-s-TOFHLA and MOHLAA-Q, do not evaluate other skills of health literacy (numerical abilities, conceptual knowledge, etc.) that are important for a more complete determination of the level of health literacy (20).

Six instruments (HLS-Child-Q15, HELiASeSS, HAS-A, HELMA, eHEALS, HLAT-8) assess health literacy in all three domains, and therefore, they can provide a more complete picture of the level of health literacy of adolescents than the first three instruments listed in Table 2 (C-sTOFHLAd, REALM-TeenS, MOHLAA-Q). Of the mentioned 6 instruments, HLS-Child-Q15 and HELMA are available for downloading and therefore, they could be applied in future research of health literacy in the adolescent population.

In future research, the instruments for the assessment of health literacy in adolescents should be analyzed in more detail, especially their validity and reliability.

## Conclusion

Of the analyzed instruments for the assessment of health literacy in adolescents, 6 assess health literacy in all three domains, and therefore, they would be more adequate for application than instruments that assess only a certain health literacy skill. Further research in this field is necessary, especially the assessment of their validity and reliability.

## Competing interests

The authors declared no competing interests.

## References


1. World Health Organization. Improving health literacy. 1998. [Internet]. [cited 09 August 2023] Available from: https://www.who.int/activities/improving-health-literacy
2. World Health Organization. Shanghai declaration on promoting health in the 2030 Agenda for Sustainable Development. Health Promot Int. 2017;32(1):7-8. doi:10.1093/heapro/daw103
3. Liu C, Wang D, Liu C, Jiang J, Wang X, Chen H, et al. What is the meaning of health literacy? A systematic review and qualitative synthesis. Fam Med Community Health. 2020;8(2). doi:10.1136/fmch-2020-000351
4. Sørensen K, Broucke SV, Fullam J, Doyle G, Pelikan J, Slonska Z, et al. Health literacy and public health: A systematic review and integration of definitions and models. BMC Public Health. 2012;12:80. doi:10.1186/1471-2458-12-80
5. Cajita MI, Cajita TR, Han HR. Health Literacy and Heart Failure: A Systematic Review. J Cardiovasc Nurs. 2016;31(2):121-30. doi:10.1097/JCN.0000000000000229
6. Mark K, Elizabeth G, Ying J, Paulsen K. The health literacy of America's adults: results from the 2003 National Assessment of adult literacy. Washington: National Center for education. Statistics. 2006;39(10):685–87.
7. Wang W, Zhang Y, Lin B, Mei Y, Ping Z, Zhang Z. The Urban-Rural Disparity in the Status and Risk Factors of Health Literacy: A Cross-Sectional Survey in Central China. Int J Environ Res Public Health. 2020;17(11):3848. doi:10.3390/ijerph17113848

4. Sørensen K, Broucke SV, Fullam J, Doyle G, Pelikan J, Slonska Z, et al. Health literacy and public health: A systematic review and integration of definitions and models. BMC Public Health. 2012;12:80. doi:10.1186/1471-2458-12-80
5. Cajita MI, Cajita TR, Han HR. Health Literacy and Heart Failure: A Systematic Review. J Cardiovasc Nurs. 2016;31(2):121-30. doi:10.1097/JCN.0000000000000229
6. Mark K, Elizabeth G, Ying J, Paulsen K. The health literacy of America's adults: results from the 2003 National Assessment of adult literacy. Washington: National Center for education. Statistics. 2006;39(10):685–87.
7. Wang W, Zhang Y, Lin B, Mei Y, Ping Z, Zhang Z. The Urban-Rural Disparity in the Status and Risk Factors of Health Literacy: A Cross-Sectional Survey in Central China. Int J Environ Res Public Health. 2020;17(11):3848. doi:10.3390/ijerph17113848
8. Visscher KL, Hutnik CM. Reprint of: health literacy in Canada and the ophthalmology patient. Can J Ophthalmol. 2015;50(1):40–6. doi:10.1016/j.jcjo.2015.04.008
9. Sørensen K, Pelikan JM, Röthlin F, Ganahl K, Slonska Z, Doyle G, et al. Health literacy in Europe: comparative results of the European health literacy survey (HLS-EU). Eur J Public Health. 2015;25(6):1053-8. doi:10.1093/eurpub/ckv043
10. Guo S. Understanding and Measuring Health Literacy among Secondary Students in Beijing and Melbourne [dissertation]. Melbourne: The University of Melbourne; 2018.
11. Australian Bureau of Statistics. 4233.0-Health Literacy, Australia, 2006. Canberra: Australian Bureau of Statistics; 2008 Jun 25 [cited 2014 Mar 23]; Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/4233.02006?OpenDocument.
12. Guo S, Yu X, Okan O. Moving health literacy research and practice towards a vision of equity, precision and transparency. Int J Environ Res Public Health. 2020;17:7650. doi:10.3390/ijerph17207650
13. Health literacy: report of the Council on Scientific Affairs. Ad Hoc Committee on Health Literacy for the Council on Scientific Affairs AMA. J Am Med Assoc. 1999;281(6):552-7.
14. Nutbeam D. Health literacy as a public goal: a challenge for contemporary health education and communication strategies into the 21st century. Health Promot Int. 2000;15(3):259-67. doi: 10.1093/heapro/15.3.259
15. Kwan B, Frankish J, Rootman I, Zumbo B, Kelly K, Begoray D, et al. The Development and Validation of Measures of "Health Literacy" in Different Populations. UBC Institute of Health Promotion Research and University of Victoria Community Health Promotion Research. 2006;4-6.
16. Bröder J, Okan O, Bauer U, Bruland D, Schlupp S, Bollweg TM, et al. Health literacy in childhood and youth: a systematic review of definitions and models. BMC Public Health. 2017;17(1):361. doi:10.1186/s12889-017-4267-y
17. Smith C, Goss HR, Issartel J, Belton S. Health Literacy in Schools? A Systematic Review of Health-Related Interventions Aimed at Disadvantaged Adolescents. Children (Basel). 2021;8(3):176. doi:10.3390/children8030176
18. Rehati P, Amaerijang N, Yang L, Xiao H, Li M, Zunong J, et al. COVID-19 Vaccine Hesitancy among Adolescents: Cross-Sectional School Survey in Four Chinese Cities Prior to Vaccine Availability. Vaccines. 2022;10(3):1-13. doi:10.3390/vaccines10030452
19. Health Literacy Tool Shed. A database of health literacy measures. [Internet]. [cited 09 August 2023] Available from: https://healthliteracy.bu.edu/
20. Guo S, Armstrong R, Waters E, Satish T, Alif SM, Browne GR, et al. Quality of health literacy instruments used in children and adolescents: a systematic review. BMJ Open. 2018;8(6):e020080. doi:10.1136/bmjopen-2017-020080
21. Chang LC, Hsieh PL, Liu CH. Psychometric evaluation of the Chinese version of short-form Test of Functional Health Literacy in Adolescents. J Clin Nurs. 2012;21(17-18):2429-37. doi:10.1111/j.1365-2702.2012.04147.x
22. Manganello JA, Colvin KF, Chisolm DJ, Arnold C, Hancock J, Davis T. Validation of the Rapid Estimate for Adolescent Literacy in Medicine Short Form (REALM-TeenS). Pediatrics. 2017;139(5):20163286. doi:10.1542/peds.2016-3286
23. Domanska OM, Bollweg TM, Loer AK, Holmberg C, Schenk L, Jordan S. Development and Psychometric Properties of a Questionnaire Assessing Self-Reported Generic Health Literacy in Adolescence. Int J Environ Res Public Health. 2020;17(8):2860. doi:10.3390/ijerph17082860
24. Bollweg TM, Okan O, Fretian AM, Broder J, Domanska OM, Jordan S, et al. Adapting the European Health Literacy Survey Questionnaire for Fourth-Grade Students in Germany: Validation and Psychometric Analysis. Health Lit Res Pract. 2020;4(3):144-59. doi:10.3928/24748307-20200428-01
25. Bechraki E, Mavrikaki E, Gialamas V, Galanaki E. Development and validation of an instrument for the health literacy assessment of secondary school students (HeLiASeSS). Health Education. 2022;122:(6):678-99. doi: 10.1108/HE-08-2021-0111
26. Manganello J, DeVellis R, Davis T, Schottler-Thal C. Development of the Health literacy Assessment Scale for Adolescents (HAS-A). J Commun Healthc. 2015;8(3):172-84.
27. Ghanbari S, Ramezankhani A, Montazeri A, Mehrabi Y. Health Literacy Measure for Adolescents (HELMA): Development and Psychometric Properties. PLoS ONE. 2016;11(2):0149202. doi:10.1179/1753807615Y.0000000016
28. Norman CD, Skinner HA. eHEALS: The eHealth Literacy Scale. J Med Internet Res. 2006;8(4):27. doi:10.2196/jmir.8.4.e27
29. Abel T, Hofmann K, Ackermann S, Buckher S, Sakarya S. Health literacy among young adults: a short survey tool for public health and health promotion research. Health Promot Int 2015;30:725–35. doi:10.1093/heapro/dat096
30. Velardo S, Drummond M. Emphasizing the child in child health literacy research. J Child Health Care 2017;21:5–13. doi:10.1177/1367493516643423

8. Visscher KL, Hutnik CM. Reprint of: health literacy in Canada and the ophthalmology patient. Can J Ophthalmol. 2015;50(1):40–6. doi:10.1016/j.jcjo.2015.04.008
9. Sørensen K, Pelikan JM, Röthlin F, Ganahl K, Slonska Z, Doyle G, et al. Health literacy in Europe: comparative results of the European health literacy survey (HLS-EU). Eur J Public Health. 2015;25(6):1053-8. doi:10.1093/eurpub/ckv043
10. Guo S. Understanding and Measuring Health Literacy among Secondary Students in Beijing and Melbourne [dissertation]. Melbourne: The University of Melbourne; 2018.
11. Australian Bureau of Statistics. 4233.0-Health Literacy, Australia, 2006. Canberra: Australian Bureau of Statistics; 2008 Jun 25 [cited 2014 Mar 23]; Available from: http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/4233.02006?OpenDocument.
12. Guo S, Yu X, Okan O. Moving health literacy research and practice towards a vision of equity, precision and transparency. Int J Environ Res Public Health. 2020;17:7650. doi:10.3390/ijerph17207650
13. Health literacy: report of the Council on Scientific Affairs. Ad Hoc Committee on Health Literacy for the Council on Scientific Affairs AMA. J Am Med Assoc. 1999;281(6):552-7.
14. Nutbeam D. Health literacy as a public goal: a challenge for contemporary health education and communication strategies into the 21st century. Health Promot Int. 2000;15(3):259-67. doi: 10.1093/heapro/15.3.259
15. Kwan B, Frankish J, Rootman I, Zumbo B, Kelly K, Begoray D, et al. The Development and Validation of Measures of "Health Literacy" in Different Populations. UBC Institute of Health Promotion Research and University of Victoria Community Health Promotion Research. 2006;4-6.
16. Bröder J, Okan O, Bauer U, Bruland D, Schlupp S, Bollweg TM, et al. Health literacy in childhood and youth: a systematic review of definitions and models. BMC Public Health. 2017;17(1):361. doi:10.1186/s12889-017-4267-y
17. Smith C, Goss HR, Issartel J, Belton S. Health Literacy in Schools? A Systematic Review of Health-Related Interventions Aimed at Disadvantaged Adolescents. Children (Basel). 2021;8(3):176. doi:10.3390/children8030176
18. Rehati P, Amaerijang N, Yang L, Xiao H, Li M, Zunong J, et al. COVID-19 Vaccine Hesitancy among Adolescents: Cross-Sectional School Survey in Four Chinese Cities Prior to Vaccine Availability. Vaccines. 2022;10(3):1-13. doi:10.3390/vaccines10030452
19. Health Literacy Tool Shed. A database of health literacy measures. [Internet]. [cited 09 August 2023] Available from: https://healthliteracy.bu.edu/
20. Guo S, Armstrong R, Waters E, Satish T, Alif SM, Browne GR, et al. Quality of health literacy instruments used in children and adolescents: a systematic review. BMJ Open. 2018;8(6):e020080. doi:10.1136/bmjopen-2017-020080
21. Chang LC, Hsieh PL, Liu CH. Psychometric evaluation of the Chinese version of short-form Test of Functional Health Literacy in Adolescents. J Clin Nurs. 2012;21(17-18):2429-37. doi:10.1111/j.1365-2702.2012.04147.x
22. Manganello JA, Colvin KF, Chisolm DJ, Arnold C, Hancock J, Davis T. Validation of the Rapid Estimate for Adolescent Literacy in Medicine Short Form (REALM-TeenS). Pediatrics. 2017;139(5):20163286. doi:10.1542/peds.2016-3286
23. Domanska OM, Bollweg TM, Loer AK, Holmberg C, Schenk L, Jordan S. Development and Psychometric Properties of a Questionnaire Assessing Self-Reported Generic Health Literacy in Adolescence. Int J Environ Res Public Health. 2020;17(8):2860. doi:10.3390/ijerph17082860
24. Bollweg TM, Okan O, Fretian AM, Broder J, Domanska OM, Jordan S, et al. Adapting the European Health Literacy Survey Questionnaire for Fourth-Grade Students in Germany: Validation and Psychometric Analysis. Health Lit Res Pract. 2020;4(3):144-59. doi:10.3928/24748307-20200428-01
25. Bechraki E, Mavrikaki E, Gialamas V, Galanaki E. Development and validation of an instrument for the health literacy assessment of secondary school students (HeLiASeSS). Health Education. 2022;122:(6):678-99. doi:10.1108/HE-08-2021-0111
26. Manganello J, DeVellis R, Davis T, Schottler-Thal C. Development of the Health literacy Assessment Scale for Adolescents (HAS-A). J Commun Healthc. 2015;8(3):172-84.
27. Ghanbari S, Ramezankhani A, Montazeri A, Mehrabi Y. Health Literacy Measure for Adolescents (HELMA): Development and Psychometric Properties. PLoS ONE. 2016;11(2):0149202. doi:10.1179/1753807615Y.0000000016
28. Norman CD, Skinner HA. eHEALS: The eHealth Literacy Scale. J Med Internet Res. 2006;8(4):27. doi:10.2196/jmir.8.4.e27
29. Abel T, Hofmann K, Ackermann S, Buckher S, Sakarya S. Health literacy among young adults: a short survey tool for public health and health promotion research. Health Promot Int 2015;30:725–35. doi:10.1093/heapro/dat096
30. Velardo S, Drummond M. Emphasizing the child in child health literacy research. J Child Health Care 2017;21:5–13. doi:10.1177/1367493516643423

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# ETIČKI ASPEKTI TRANSPLANTACIJE ORGANA I TRANSPLANTACIJSKI TURIZAM

**Damir Peličić** [1,2]

[1] Centar za nauku, Klinički centar Crne Gore, Podgorica, Crna Gora
[2] Medicinski fakultet Univerziteta Crne Gore, Podgorica, Crna Gora

[*] Korespondencija: dr sc. med. Damir Peličić, Centar nauke, Klinički centar Crne Gore, Podgorica, Crna Gora; Medicinski fakultet, Univerzitet Crne Gore, Ljubljanska bb, 18000 Podgorica, Crna Gora; e-mail: damir.pelicic@t-com.me

**SAŽETAK**

Savremena medicina i tehnologija su od sredine dvadesetog veka znatno napredovale, ali transplantacijska medicina je još uvek tema o kojoj se raspravlja, kako na medicinskom, tako i na religijskom, pravnom i etičkom polju. Da bi se izvršila transplantacija organa, bilo da je reč o srodnoj, nesrodnoj ili kadaveričnoj transplantaciji potrebno je da se ispuni niz uslova kako bi se uradila adekvatna priprema bolesnika i potencijalnog donora. Za ovaj pregledni rad služili smo se relevantnim literaturalnim podacima koristeći baze, kao što su: PubMed, SCOPUS, Srpski citatni indeks i dr. Sve publikacije odnosile su se na etičke principe i pravne aspekte transplantacije i donacije organa, kako u svetu tako i u Crnoj Gori. Osvrnuli smo se na Istanbulsku deklaraciju koju je potpisala i Crna Gora.

**Ključne reči:** Donacija organa, Istanbulska deklaracija, transplantacija, religija, etika

## Uvod

Transplantacija i donacija organa je započela da se primenjuje u drugoj polovini dvadesetog veka i ovaj modalitet zamene funkcije solitarnih organa je znatno produžio život bolesnika i poboljšao njihov kvalitet života, ali transplantacijska medicina i pored biomedicinskih i tehnoloških dostignuća, još uvek predstavlja složenu etičku dilemu (1). Savremena medicina i tehnologija su znatno napredovale, ali transplantacijska medicina je još uvek tema o kojoj se raspravlja, kako na medicniskom, tako i na religijskom, pravnom i etičkom nivou (1). Transplantacija je prihvaćena kao tretman izbora za bolesnike sa terminalnim stadijumom bolesti solidnih organa (2), ali bez obzira na etičke i pravne dileme, transplantacija organa je jasno definisana i medicinski opravdana intervencija (3). Određivanje prioriteta u odluci o transplantaciji organa može biti i etička dilema uzrokovana nedostatkom organa, kao i religijskim i filozofskim poimanjem smisla života i smrti (4,5).

## Etički aspekti transplantacije organa i transplantacijski turizam

Kroz istoriju medicine razvijale su se nove terapijske metode lečenja koje su omogućavale transplantaciju tkiva i organa uspešnom, ali takođe ovo polje medicine je stalno pod pritiskom brojnih etičkih i moralnih dilema (6). Trgovina organima strogo je zabranjena od strane nekoliko nefroloških društava u mnogim zemljama sveta, kao i u Crnoj Gori. Istraživanja nam sugeriše da je ova praksa široko rasprostranjena i toleriše se u mnogim zemljama, pa su u nedostatku univerzalnog zakona moguće i određene zlouptrebe (7). Uprkos Istanbulskoj deklaraciji koja je strogo definisala stav protiv trgovine organima, kontroverza oko plaćenog doniranja organa u nekim državama ostaje otvorena (8). Što se tiče religijskih aspekata, Islam je religija koja podrazumeva da svaki pojedinac poseduje dušu i telo. Etička pitanja vezana za transplantaciju i doniranje organa u Islamu proizilaze iz islamskih principa, a Časni Kur'an kaže „A

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PROFESSIONAL ARTICLE

# ETHICAL ASPECTS OF ORGAN TRANSPLANTATION AND TRANSPLANTATION TOURISM

**Damir Peličić** [1,2]

[1] Center for Science, Clinical Center of Montenegro, Podgorica, Montenegro
[2] Faculty of Medicine, University of Montenegro, Podgorica, Montenegro

[*] Correspondence: Damir Peličić, RN, PhD, Center of sience, Clinical centre of Montenegro, Podgorica, Montenegro; Faculty of Medicine, University of Montenegro, Ljubljanska bb, 18000 Podgorica, Montenegro; e-mail: damir.pelicic@t-com.me

**SUMMARY**

Modern medicine and technology have advanced significantly since the mid-twentieth century, but transplant medicine is still a hotly debated topic, both medically and religiously, legally and ethically. In order to carry out an organ transplant, whether it is related, unrelated or cadaveric transplantation, a number of conditions must be met in order to adequately prepare the patient and the potential donor. For this review, we used relevant literary data using databases such as: PubMed, SCOPUS, Serbian Citation Index, etc. All publications related to ethical principles and legal aspects of transplantation and organ donation, both in the world and in Montenegro. We referred to the Istanbul Declaration, which was also signed by Montenegro.

**Key words:** Organ donation, Istanbul Declaration, transplantation, religion, ethics

## Introduction

Transplantation and organ donation began in the second half of the twentieth century and this modality of replacing the function of solitary organs extends significantly the lives of patients and improves their quality of life, however, transplantation medicine, despite its biomedical and technological achievements, still presents a complex ethical dilemma (1). Modern medicine and technology have improved considerably, but transplantation medicine is still a topic of debate at the medical, religious, legal and ethical level (1). Transplantation has been accepted as the treatment of choice for patients with terminal disease of solid organs (2), but regardless of ethical and legal dilemmas, organ transplantation is a clearly defined and medically justified intervention (3). Determining priorities while making decision about organ transplantation can be an ethical dilemma caused by the lack of organs, as well as by religious and philosophical understanding of the meaning of life and death (4,5).

## Ethical aspects of organ transplantation and transplant tourism

Throughout the history of medicine, new therapeutic methods of treatment were developed, which enabled successful tissue and organ transplantation, however, this field of medicine is also constantly under the pressure of numerous ethical and moral dilemmas (6). Trade in organs has been strictly prohibited by several societies of nephrology in many countries of the world, as well as in Montenegro. Research suggests that this practice is widespread and that it is tolerated in many countries, and therefore, in the absence of universal law, certain abuses are possible (7). Despite the Istanbul Declaration, which strictly defined the position against organ trafficking, the controversy related to the paid organ donation in some countries remains open (8). As far as religious aspects are concerned, Islam is a religion that assumes that each individual has a body and a soul. Ethical issues related to transplantation and organ donation in Islam arise from Islamic principles, and

ko bude takav, ako ikada oživi dušu, biće kao da je dao život celom čovečanstvu" (9). Katolička crkva se ne protivi transplantaciji i doniranju organa, već se naprotiv poziva na poruku pape Ivana Pavla II, koja glasi „Ko je rekao da jeste greh zakopati sve što čoveku može poslužiti" (10). U literaturi nismo pronašli da se pravoslavna crkva protivi donaciji organa ili da o tome navodi svoj stav (11).

Svedoci smo da trgovina organima i transplantacioni turizam, postoji u svetu, a posebno u nerazvijenim zemljama (12). Istanbulska deklaracija sugeriše da su siromašni ljudi prinuđeni da prodaju svoje organe i da su time eksploatisani od strane ljudi koji dolaze iz bogatih zemalja da bi im se uradila transplantacija. Učesnici samita u Istanbulu su zaključili da transplantacijski komercijalizam, koji cilja na ranjive grupe ljudi iz siromašnih zemalja, treba sistem da zaštiti od eksploatacije i potrebno je razvijati Nacionalne programe za transplantaciju i doniranje organa, kako bi se ovaj trend smanjio ili eliminisao (13). Studije rađene u Sjedinjenim Američkim Državama (SAD) ukazuju da zbog stalnog nedostatka donora organa, transplantacijski turizam se sve više razvija i do danas nije bilo dovoljno objavljenih radova koji bi pomogli u adekvatnom vođenju programa američkih transplantacijskih centara u vezi s transplantacijskim turizmom (14,15). Prema procenama svetske zdravstvene organizacije (SZO), u nekim azijskim zemljama, poput Indije, Indonezije, Izraela, Kine, Pakistana i latinoameričkim zemljama, poput Ekvadora i Bolivije, svake godine se uradi oko 10.000 protivzakonitih transplantacija i godišnja zarada od ovih kriminalnih radnji dostiže oko milijardu američkih dolara (16).

Najveća smrtnost od posledica infekcije i rano odbacivanje transplantiranog organa, pojava dijabetesa kao posledice neadekvatnog doziranja kortiko i imunosupresivne terapije dešava se kod pacijenata kojima je nelegalno urađena transplantacija organa (17).

Vlada Narodne Republike Kine je osudila organizacije za transplantaciju i proglasila je nezakonitim davanje organa za transplantaciju stranim turistima od zatvorenika nad kojima je izvršena egzekucija (18). U Indiji trenutno postoji preko 120 centara za transplantaciju organa gde se obavi od 3.500 do 4.000 transplantacija bubrega godišnje. Uprkos zakonu o transplantaciji koji je donet u Indiji 1994. godine, indijski mediji redovno izveštavaju o trgovini organima, a posebno trgovini bubrega (19). Kako bi se zaustavio transplantacijski turizam i obezbedio optimalan tretman za građane sa terminalnom bubrežnom insuficijencijom, Crna Gora je u septembru 2012. godine izvršila prvu kadaveričnu transplantaciju bubrega.

Uprkos činjenici da je transplantacija organa produžila i poboljšala živote mnogih bolesnika širom sveta, rasprostranjeni nedostatak donora i dalje je glavni faktor koji je doveo do trgovine organima. Procenjuje se da 10% transplantacija organa u svetu uključuje ovu praksu, što čini čak dve trećine transplantacija u Pakistanu za primaoce organa iz inostranstva (20-23). Skupština Svetske zdravstvene organizacije je 2004. godine pozvala države članice da zaštite siromašno i ugroženo stanovništvo od eksploatacije kroz praksu ilegalne trgovine organima, koja je postala raširena širom sveta. U 2008. godini, Međunarodna zajednica za transplantaciju organa sazvala je samit stručnjaka za transplantaciju iz oblasti, pravnih stručnjaka i etičara za borbu protiv trgovine organima, transplantacijskog turizma i komercijalizma iste, što je rezultiralo Istanbulskom deklaracijom (22).

Milijić i sardanici navode da je uzrok malog broja donora organa u Srbiji povezan sa neobaveštenošću, zatim sa strahom od doniranja organa i dilemama oko etičkih i pravnih pitanja vezanih za transplantaciju organa (24). Studija preseka sprovedena u Crnoj Gori, autora Peličića i saradnika, na populaciji od 400 ispitanika, zdravstvenih radnika i opšte populacije koja se odnosi na socio-demografske i verske aspekte transplantacije organa, ukazuje da zdravstveni radnici i opšta populacija u Crnoj Gori smatraju da religija nema uticaja na negativne stavove prema transplantaciji i doniranju organa, ali da su zabrinuti da se organi neće koristiti u prave svrhe (25). Studija o etičkim aspektima transplantacije u Crnoj Gori ukazuje da je u predlogu mera potrebno osmisliti strategiju kako bi se povećalo poverenje da će se doniranje organa vršiti samo u prave svrhe, kako bi se izbegle zloupotrebe i gubitak poverenja od strane građana (26). Od septembra 2012. godine, kada je uz podršku Kliničko bolničkog centra u Zagrebu i medicinskog tima Kliničkog centra Crne Gore u Podgorici, obavljena prva transplantacija organa, smanjen je broj pacijenata koji su plaćali organe, a posebno bubrege, u odnosu na period pre uvođenja ovog programa transplantacije. Međutim, ako kontinuirano ne razvijamo program transplantacije organa od preminulog donora, u budućnosti se

the holy Quran says: “and whoever is like that, if he ever revives soul, it will be as if he gave life to all mankind” (9). The Catholic Church is not opposed to transplantation and organ donation, but on the contrary, it refers to the message of Pope John Paul II, which reads: “who said that it is a sin to bury everything that can be useful to a man” (10). We have not found in the literature that the Orthodox Church is opposed to organ donation or that it stated its attitude towards that (11).

We are witnesses that organ trade and transplant tourism exist in the world, especially in underdeveloped countries (12). The Istanbul Declaration suggests that poor people are forced to sell their organs and that they are exploited by people who come from rich countries to get a transplant. The participants of the summit in Istanbul concluded that transplant commercialism targets vulnerable groups of people from poor counties, who need to be protected from exploitation by the system, and that it is necessary to develop National Programs for transplantation and organ donation in order to reduce or eliminate this trend (13). Studies, which have been conducted in the United States of America (USA), indicate that, due to the constant lack of organ donors, transplant tourism is increasingly developing and there have not been enough published studies that would help to adequately manage the programs of American transplantation centers related to transplant tourism (14,15). According to the estimates of the World Health Organization (WHO) in some Asian countries, such as India, Indonesia, Israel, China, Pakistan and Latin American countries, such as Ecuador and Bolivia, about 10,000 illegal transplants are carried out every year, while the annual income from these criminal activities reaches about billion US dollars (16).

The highest mortality as a result of infection and early rejection of the transplanted organ, the occurrence of diabetes as a result of inadequate dosing of corticosteroids and immunosuppressive therapy appears in patients who illegally underwent organ transplantation (17).

The government of the People’s Republic of China condemned transplant organizations and declared that it is illegal to give organs from executed prisoners to foreign tourists (18). There are currently more than 120 centers for organ transplantation in India, where 3,500 to 4,500 renal transplantations are done annually. Despite the transplant law, which was passed in India in 1994, the media in India regularly report on organ trafficking, especially kidney trafficking (19). In order to stop transplant tourism and ensure the optimal treatment for citizens with terminal kidney failure, the first cadaveric kidney transplant was done in Montenegro in 2012.

Despite the fact that organ transplantation has prolonged and improved the lives of many patients around the world, the widespread lack of donors is still a major factor that has led to organ trafficking. It has been estimated that 10% of organ transplants worldwide include this practice, which makes as many as two-thirds of transplants in Pakistan for foreign organ recipients (20-23). In 2004, the Assembly of the World Health Organization called member states to protect the poor and endangered population from the exploitation through the practice of illegal organ trade, which has become widespread around the world. In 2008, the International Organ Transplantation Community convened a summit of transplantation experts from that field, legal experts and ethicists to combat organ trafficking, transplant tourism and commercialism, which resulted in the Istanbul Declaration (22).

Milijić and associates claim that the cause of the small number of donors in Serbia is related to lack of information, followed by fear of organ donation and dilemmas regarding ethical and legal issues related to organ transplantation (24). A cross-sectional study by Peličić and associates, which was conducted in Montenegro on the population of 400 respondents, including healthcare workers and general population, and which referred to the socio-demographic and religious aspects of organ transplantation, showed that health workers and general population in Montenegro believe that religion has no influence on negative attitudes towards transplantation and organ donation, but that they are worried that the organs will not be used for the right purposes (25). A study on the ethical aspects of transplantation in Montenegro indicates that a strategy needs to be developed within the proposed measures in order to increase trust that organ donation will be done only for the right purposes, so that the abuses would be avoided, as well as loss of trust of citizens (26). Since 2012, when the first organ transplant was performed with the support of the Clinical Hospital Center in Zagreb and the medical

može očekivati transplantacijski turizam, a naša država treba da uloži više napora ukoliko želimo da unapredimo program transplantacije u Crnoj Gori (26). Iz svega navedenog, nameće se pitanje, šta to nauka može da uradi za dobrobit bolesnika i šta zdravstveni radnik sme da uradi za njega, kako bi mu olakšao i produžio životni vek i poboljšao njegov kvalitet života, a da time ne ugrozi život potencijonalnih donora i primaoca organa (27).

## Zaključak

Ovo je složena tema koja zahteva informacije, ne samo iz oblasti medicinskih istraživanja, već i na pravnom, religijskom i etičkom polju. Prilikom pripreme donora i recipijenta za transplantaciju organa, pored medicinskih indikacija, potrebno je poštovati Istanbulsku deklaraciju, posebno etičke i pravne norme kako bi se izbegle zloupotrebe u vezi sa transplantacijom organa. Ova tema je predmet kontinuiranog razmatranja mnogih naučnika i istraživača, jer ni jedno polje u biomedicini nije toliko osetljivo po pitanju etičkih, pravnih i religijskih dilema, kao što je to transplantacijska medicina. Naučnici u svetu navode da je transplantacijski turizam u stalnom porastu i pacijenti mogu biti izloženi riziku od većeg broja posttransplantacijskih komplikacija (najčešće infekcija koje su rezistentne na antibiotike, neadekvatne primene imunosupresivne tarapije, neadekvatne nege i rizika od krvlju prenosivih infekcija).

## Konflikt interesa

Autor je izjavio da nema konflikta interesa.

## Reference


1. Nierste D. Issues in organ procurement, allocation, and transplantation. J Christ Nurs. 2013;30(2):80-7; quiz 88-9. doi: 10.1097/cnj.0b013e3182839b47.
2. Beauchamp TL. Methods and principles in biomedical ethics. J Med Ethics. 2003;29(5):269–74. doi: 10.1136/jme.29.5.269.
3. Ambagtsheer F, Weimar W (ur.). Trafficking in Human Beings for the Purpose of Organ Removal. Lengerich: Pabst Science Publish-ers; 2016.
4. Padmapriya ST, Parthasarathy S. Ethical Data Collection for Medical Image Analysis: a Structured Approach. Asian Bioeth Rev. 2023;16(1):1-14. doi: 10.1007/s41649-023-00250-9.
5. Tong A, Sautenet B, Chapman JR, Harper C, MacDonald P, Shackel N, et al. Research priority set-ting in organ transplantation: a systematic review. Transpl Int.2017;30:327-43.
6. Eurotransplant (ET). Annual Report 2016. Eurotransplant International Foundation. Leiden, the Netherlands: Eurotransplant Foundation; 2016.
7. Ivanovski N, Masin J, Rambabova-Busljetic I, Pusevski V, Dohcev S, Ivanovski O, Popov Z. The outcome of commercial kidney transplant tourism in Pakistan. Clin Transplant. 2011 Jan-Feb;25(1):171-3. doi: 10.1111/j.1399-0012.2010.01299.x
8. World Medical Association (WMA). Rescinded: WMA statement on human organ donation and transplantation, 2017. Available at: https://www.wma.net/policies-post/wma-statement-on-human-organ-donation-and-transplant ation/. (Accessed December 12, 2019.)
9. Jedličková A. Ethical aspects of tissue and organ transplantation. Cas Lek Cesk. 2023;162(4):152-9.
10. JPII Pope. Address of John Paul II to the 18th International Congress of the Transplantation Society. Med Etika Bioet 2001;8(1–2):12–4.
11. Bruzzone P. Religious aspects of organ transplantation. Transplant Proc. 2008;40(4):1064-7. doi: 10.1016/j.transproceed.2008.03.049.
12. International Summit on Transplant T, Organ T. The Declaration of Istanbul on organ trafficking and transplant tourism. Kidney Int 2008;74(7):854–9.
13. Piccoli GB, Sacchetti L, Verzè L, Cavallo F; Working group of the students of the Torino Medical School. Doctor can I buy a new kidney? I've heard it isn't forbidden: what is the role of the nephrologist when dealing with a patient who wants to buy a kidney? Philos Ethics Humanit Med. 2015;10:13. doi: 10.1186/s13010-015-0033-x.
14. Schiano TD, Rhodes R. Transplant tourism. Curr Opin Organ Transplant. 2010;15(2):245-8. doi: 10.1097/mot.0b013e328337353e.
15. Schiano TD, Rhodes R. The dilemma and reality of transplant tourism: an ethical perspective for liver transplant programs. Liver Transpl. 2010;16(2):113-7. doi: 10.1002/lt.21967.
16. Zibar L, Šunić K. Transplantacijski turizam. Medicina Fluminensis [Internet]. 2020 [pristup 23.03.2024.]; 56(4):522-528. Available: https://doi.org/10.21860/medflum2020_245228
17. Pavli A, Maltezou HC. Infectious complications related to medical tourism. J Travel Med. 2021;28(1):taaa210. doi: 10.1093/jtm/taaa210.
18. Rhodes R, Schiano T. Transplant tourism in China: a tale of two transplants. Am J Bioeth. 2010;10(2):3-11. doi: 10.1080/15265160903558781.
19. Shroff S. Legal and ethical aspects of organ donation and transplantation. Indian J Urol. 2009;25(3):348-55. doi: 10.4103/0970-1591.56203.
20. Larijani B, Zahedi F, Taheri E. Ethical and legal aspects of organ transplantation in Iran. Transplant Proc. 2004;36(5):1241-4. doi: 10.1016/j.transproceed.2004.05.065.
21. International Summit on Transplant Tourism and Organ Trafficking. The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. Clin J Am Soc Nephrol. 2008;3(5):1227-31. doi: 10.2215/CJN.03320708. Epub 2008 Aug 13.

team from the Clinical Center of Montenegro in Podgorica, the number of patients who paid for organs, especially kidneys, has decreased in the period before the introduction of this transplant program. However, if we do not continuously develop the program of organ transplantation from a deceased donor, transplant tourism can be expected in the future, and our country should make more efforts if we want to improve the transplantation program in Montenegro (26). Based on the above mentioned, the question arises, what can science do for the benefit of patients, and what the healthcare worker is allowed to do to make his life easier, to extend his life and improve his quality of life, not endangering the lives of potential donors and organ recipients (27).

## Conclusion

This is a complex topic that requires information, not only from the fields of medical research, but also from legal, religious and ethical fields. During the preparation of donors and recipients for organ transplantation, in addition to medical indications, it is necessary to respect the Istanbul Declaration, especially ethical and legal norms in order to avoid abuses related to organ transplantation. This issue is the topic of continuous considerations of numerous scientists and researchers, because no field in biomedicine is as sensitive to ethical, legal and religious dilemmas as transplantation medicine. Scientists in the world state that transplant tourism is constantly increasing and patients may be exposed to the risk of a greater number of post-transplantation complications (most frequently infections that are resistant to antibiotics, inadequate implementation of immunosuppressive therapy, inadequate care and the risk of blood-borne infections).

## Competing interests

The author declared no competing interests.

## References


1. Nierste D. Issues in organ procurement, allocation, and transplantation. J Christ Nurs. 2013;30(2):80-7; quiz 88-9. doi: 10.1097/cnj.0b013e3182839b47.
2. Beauchamp TL. Methods and principles in biomedical ethics. J Med Ethics. 2003;29(5):269–74. doi: 10.1136/jme.29.5.269.
3. Ambagtsheer F, Weimar W (ur.). Trafficking in Human Beings for the Purpose of Organ Removal. Lengerich: Pabst Science Publish-ers; 2016.
4. Padmapriya ST, Parthasarathy S. Ethical Data Collection for Medical Image Analysis: a Structured Approach. Asian Bioeth Rev. 2023;16(1):1-14. doi: 10.1007/s41649-023-00250-9.
5. Tong A, Sautenet B, Chapman JR, Harper C, MacDonald P, Shackel N, et al. Research priority set-ting in organ transplantation: a systematic review. Transpl Int.2017;30:327-43.
6. Eurotransplant (ET). Annual Report 2016. Eurotransplant International Foundation. Leiden, the Netherlands: Eurotransplant Foundation; 2016.
7. Ivanovski N, Masin J, Rambabova-Busljetic I, Pusevski V, Dohcev S, Ivanovski O, Popov Z. The outcome of commercial kidney transplant tourism in Pakistan. Clin Transplant. 2011 Jan-Feb;25(1):171-3. doi: 10.1111/j.1399-0012.2010.01299.x
8. World Medical Association (WMA). Rescinded: WMA statement on human organ donation and transplantation, 2017. Available at: https://www.wma.net/policies-post/wma-statement-on-human-organ-donation-and-transplant ation/. (Accessed December 12, 2019.)
9. Jedličková A. Ethical aspects of tissue and organ transplantation. Cas Lek Cesk. 2023;162(4):152-9.
10. JPII Pope. Address of John Paul II to the 18th International Congress of the Transplantation Society. Med Etika Bioet 2001;8(1–2):12–4.
11. Bruzzone P. Religious aspects of organ transplantation. Transplant Proc. 2008;40(4):1064-7. doi: 10.1016/j.transproceed.2008.03.049.
12. International Summit on Transplant T, Organ T. The Declaration of Istanbul on organ trafficking and transplant tourism. Kidney Int 2008;74(7):854–9.
13. Piccoli GB, Sacchetti L, Verzè L, Cavallo F; Working group of the students of the Torino Medical School. Doctor can I buy a new kidney? I've heard it isn't forbidden: what is the role of the nephrologist when dealing with a patient who wants to buy a kidney? Philos Ethics Humanit Med. 2015;10:13. doi: 10.1186/s13010-015-0033-x.
14. Schiano TD, Rhodes R. Transplant tourism. Curr Opin Organ Transplant. 2010;15(2):245-8. doi: 10.1097/mot.0b013e328337353e.
15. Schiano TD, Rhodes R. The dilemma and reality of transplant tourism: an ethical perspective for liver transplant programs. Liver Transpl. 2010;16(2):113-7. doi: 10.1002/lt.21967.
16. Zibar L, Šunić K. Transplantacijski turizam. Medicina Fluminensis [Internet]. 2020 [pristup 23.03.2024.]; 56(4):522-528. Available: https://doi.org/10.21860/medflum2020_245228
17. Pavli A, Maltezou HC. Infectious complications related to medical tourism. J Travel Med. 2021;28(1):taaa210. doi: 10.1093/jtm/taaa210.
18. Rhodes R, Schiano T. Transplant tourism in China: a tale of two transplants. Am J Bioeth. 2010;10(2):3-11. doi: 10.1080/15265160903558781.
19. Shroff S. Legal and ethical aspects of organ donation and transplantation. Indian J Urol. 2009;25(3):348-55. doi:

22. Spasovski G, Busic M, Delmonico F. Improvement in kidney transplantation in the Balkans after the Istanbul Declaration: where do we stand today? Clin Kidney J. 2016;9(1):172-5. doi: 10.1093/ckj/sfv116.
23. Naqvi SA, Ali B, Mazhar F, Zafar MN, Rizvi SA. A socioeconomic survey of kidney vendors in Pakistan. Transpl Int 2007;20:934–9.
24. Milijić S, Nikolić A. Etika u transplantaciji organa. Acta Facultatis Medicae Naissensis. 2018;35(2):87-93. doi: 10.2478/afmnai-2018-0010
25. Pelicic D, Vojinovic T, Vukovic M, Bokan D, Radevic S. Sociodemographic Characteristics and the Influence of Religion on the Knowledge of Doctors, Nurses, and the General Population in Montenegro About Transplant and Organ Donation. Exp Clin Transplant. 2023;21(12):973-979. doi: 10.6002/ect.2023.0243.
26. Peličić DN, Prelević VM, Nejkov SS, Bogojević MD, Saveljić MM, Stojanović VD, et al. Attitudes about the legal and ethical aspects of organ donation among healthcare workers and the general population in Montenegro. Hospital Pharmacology Int Multidisciplinary J. 2022;9(2):1176-82. doi: 10.5937/hpimj2202176P.
27. Peličić D, Ratković M, Radunović D, Prelević V. Etički aspekti transplantacije tkiva i organa. Inspirium. 2015;(14):35-8.



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10.4103/0970-1591.56203.

20. Larijani B, Zahedi F, Taheri E. Ethical and legal aspects of organ transplantation in Iran. Transplant Proc. 2004;36(5):1241-4. doi: 10.1016/j.transproceed.2004.05.065.
21. International Summit on Transplant Tourism and Organ Trafficking. The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. Clin J Am Soc Nephrol. 2008;3(5):1227-31. doi: 10.2215/CJN.03320708. Epub 2008 Aug 13.
22. Spasovski G, Busic M, Delmonico F. Improvement in kidney transplantation in the Balkans after the Istanbul Declaration: where do we stand today? Clin Kidney J. 2016;9(1):172-5. doi: 10.1093/ckj/sfv116.
23. Naqvi SA, Ali B, Mazhar F, Zafar MN, Rizvi SA. A socioeconomic survey of kidney vendors in Pakistan. Transpl Int 2007;20:934–9.
24. Milijić S, Nikolić A. Etika u transplantaciji organa. Acta Facultatis Medicae Naissensis. 2018;35(2):87-93. doi: 10.2478/afmnai-2018-0010
25. Pelicic D, Vojinovic T, Vukovic M, Bokan D, Radevic S. Sociodemographic Characteristics and the Influence of Religion on the Knowledge of Doctors, Nurses, and the General Population in Montenegro About Transplant and Organ Donation. Exp Clin Transplant. 2023;21(12):973-979. doi: 10.6002/ect.2023.0243.
26. Peličić DN, Prelević VM, Nejkov SS, Bogojević MD, Saveljić MM, Stojanović VD, et al. Attitudes about the legal and ethical aspects of organ donation among healthcare workers and the general population in Montenegro. Hospital Pharmacology Int Multidisciplinary J. 2022;9(2):1176-82. doi: 10.5937/hpimj2202176P.
27. Peličić D, Ratković M, Radunović D, Prelević V. Etički aspekti transplantacije tkiva i organa. Inspirium. 2015;(14):35-8.



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# AKTUELNA I POTENCIJALNA PRIMENA MODERNIH TEHNOLOGIJA U MEDICINI I STOMATOLOGIJI KAO POSLEDICA INDUSTRIJE 4.0

**Radoje Jevtić**[1]

[1] Elektrotehnička škola „Nikola Tesla “, Niš, Republika Srbija

[*] Korespondencija: Radoje Jevtić, Elektrotehnička škola „Nikola Tesla”, Aleksandra Medvedeva 18, Niš, Republika Srbija; e-mail: milan.jvtc@gmail.com

**SAŽETAK**

Industrija 4.0, odnosno četvrta industrijska revolucija, je doprinela ogromnom napretku znanja i nauke u mnogim različitim oblastima života. Cilj ovog rada je da prikaže trenutne i potencijalne primene modernih tehnologija kao dirktna posledica Industrije 4.0 u medicini i stomatologiji i stvaranje koncepta Medicina 4.0 i Stomatologija 4.0. Industrija 4.0 ima veliki uticaj na sve oblasti savremene nauke, ali i na medicinu i stomatologiju. Očigledno je da se celokupno zdravstvo transformisalo u potpuno novi, moderan i drugačiji oblik - Zdravstvo 4.0 sa velikim benefitima od Industrije 4.0. To znači bolju i sigurniju budućnost u smislu optimiziranih medicinskih usluga i lečenja, mnogo veći procenat izlečenih pacijenata, virtuelnih medicinskih i stomatoloških klinika za konsultacije uz pomoć telemedicine i još mnogo toga. Takođe, industrija 4.0 je omogućila brzu i kvalitetnu poizvodnju različitih vrsta medicinskih i dentalnih implantata, što doprinosi značajnom smanjenju troškova. Upotreba novih digitalnih tehnologija, novih koncepata u radu omogućava potpuno novi pristup i mnogo bolje rezultate u medicini i stomatologiji.

**Ključne reči:** tehnologija, Industrija 4.0, Medicina, Stomatologija, Zdravstvo

## Uvod

Razvoj Industrije 4.0, odnosno četvrte industrijske revolucije, predstavlja veliki korak u ljudskoj istoriji u smislu razvoja nauke i tehnologije. Upotreba novih tehnologija dovela je čovečanstvo do nezamislivih dostignuća. Tehnologija i njene primene su toliko napredovale da su unapredile skoro sve sfere života i rada ljudi. Ove promene i inovacije su izazvale mnoge promene i inovacije u medicini i stomatologiji, tako da je postignut novi nivo i novi koncept ovih oblasti – Medicina 4.0 i Stomatologija 4.0. Medicina i stomatologija sada imaju svoj „oblak“ (eng. cloud) i virtuelne modele, kao i virtuelne pacijente (1,2). Pod „oblak“ se podrazumeva veliki broj računara sa svim mogućim resursima koji se tretiraju kao jedan virtuelan računar. Klinike, laboratorije, menadžment, osoblje, proizvodnja, lečenje, informacije i usluge su povezani i umreženi preko Interneta. Pacijenti imaju poboljšan pristup medicinskim i stomatološkim službama i klinikama. Troškovi su značajno smanjeni. Dijagnoze se postavljaju ranije, što implicira bolje lečenje, kao i bolje efekte i ishode lečenja. Za intervencije je potrebno kraće vreme. Komunikacija i zaštita podataka su na veoma visokom nivou.

Ranije, doktori nisu bili upoznati sa korišćenjem kompjutera, ali danas upotreba više kompjutera, uređaja, robota predstavlja realnost i trend. Jedna od važnih stvari je precizna i efikasna edukacija, pomoć i sugestije medicinskom i stomatološkom osoblju “na daljinu” u realnom vremenu. Takođe, značajno treba povećati produktivnost u medicinskim i stomatološkim uslugama, jer su osnova za efikasno pružanje kvalitetnih usluga (1,2). Naravno, to će zahtevati značajna finansijska sredstva, ali kada se uporede efekti i investicije, efekti jesu i biće gotovo neverovatni.

Cilj ovog rada je da prikaže trenutne i potencijalne primene modernih tehnologija kao direktna posledica Industrije 4.0 u medicini i stomatologiji i stvaranje koncepta Medicina 4.0 i Stomatologija 4.0.

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# CURRENT AND POTENTIAL APPLICATIONS OF MODERN TECHNOLOGIES IN MEDICINE AND DENTISTRY AS A CONSEQUENCE OF INDUSTRY 4.0

**Radoje Jevtić**[1]

[1] School for Electrical Engineering „Nikola Tesla “, Niš, Republic of Serbia

[*] Correspondence: Radoje Jevtić, School for Electrical Engineering Nikola Tesla, Alexander Medvedev St 18, Niš, Republic of Serbia; e-mail: milan.jvtc@gmail.com

**SUMMARY**

Industry 4.0, i.e. the fourth industrial revolution, has contributed to enormous progress of knowledge and science in many different areas of life and brought lots of benefits. The aim of this paper is to present the current and potential applications of modern technologies as direct consequence of Industry 4.0 in medicine and dentistry and designing the Medicine 4.0 and Dentistry 4.0 concept. Industry 4.0 has a great influence on every field of modern science, and also on medicine and dentistry. It is obvious that complete healthcare transforms in the totally new, modern and different form - Healthcare 4.0 with a huge benefit from Industry 4.0. This means a better and safer future in the form of optimized medical services and treatment, much bigger percentage of cured patients, virtual medical and dental clinics with telemedicine consultations and lot of other things. Also, industry 4.0 enabled the fast and high-quality production of various types of medical and dental implants, which contributes to a significant reduction in costs. The use of new digital technologies and new concepts enable a completely new approach and better results in medicine and dentistry.

**Key words:** technology, digitalisation, Industry 4.0, Medicine, Dentistry, Healthcare

## Introduction

The development of Industry 4.0, i.e. the fourth industrial revolution, presents a great step in human history in the sense of the development of science and technology. The use of new technologies has brought humanity to unimaginable achievements. Technology and its applications have advanced so much that they have improved almost all sphere of human work and life. These changes and innovations caused many changes and innovations in medicine and dentistry and therefore, a new level and new concept of these spheres - Medicine 4.0 and Dentistry 4.0 were achieved (1,2). Medicine and dentistry now have their own “cloud“ and virtual models, as well as virtual patients. The cloud means a large number of computers with all possible resources that are treated as one virtual computer. Clinics, laboratories, management, personnel, production, treatment, information and services are connected via the Internet. Patients have an improved access to medical and dental services and clinics. Expenses are significantly reduced. Diagnoses are established much earlier, which implies better treatment, as well as better treatment effects and outcomes. Interventions demand shorter time. Communication and data protection are at a very high level.

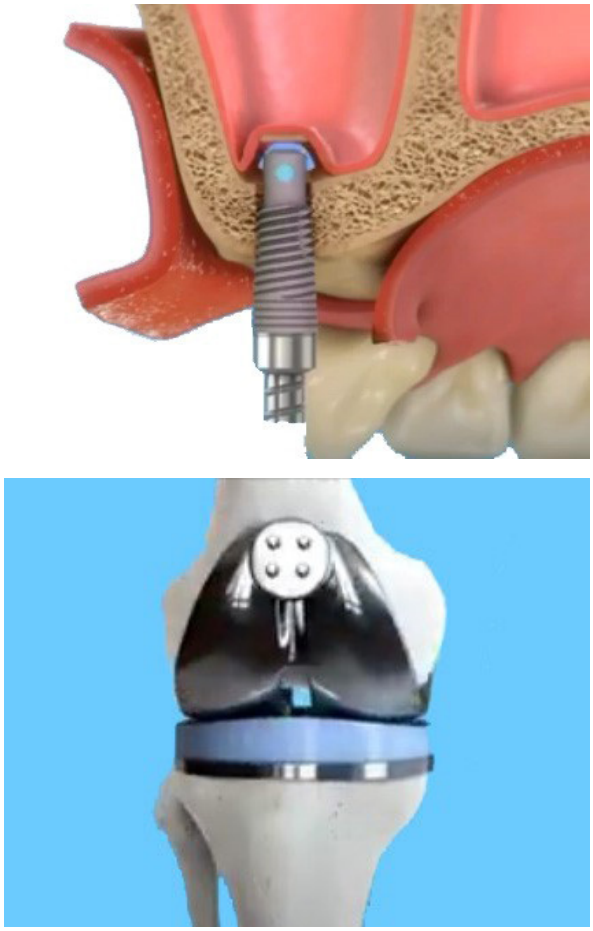
Before, doctors were not familiar with computers, but today, manipulation with more computers, devices, robots present reality and trend. One of the important things is the precise and effective education, help and suggestions given to medical and dental personnel at a distant place in real time. Also, productivity in medical and dental services should be significantly increased, because they are the basis for efficient provision of quality services (1,2). Of course, it will demand significant financial resources but, when effects and investment are compared, effects are and will be almost unbelievable.

## Primena tehnologija Industrije 4.0 u medicini i stomatologiji

Jedna od veoma interesantnih primena Industrije 4.0 su personalizovani medicinski i dentalni implantati. Zahvaljujući velikoj količini podataka, uspostavljaju se lake i brze veze između različitih pretraživača podataka. Industrija 4.0 je omogućila brzu i kvalitetnu poizvodnju različitih vrsta medicinskih i dentalnih implantata, zbog obilja različitih informacija. Takođe, kompletni troškovi su značajno smanjeni (1,2). Pravu revoluciju kada su u pitanju implantati donela je upotreba 3D štampe. Primer dentalnog i medicinskog implantata dat je na slici 1.

Pametni implantati su veliko dostignuće modernih tehnologija. Savremeni implantati koji se koriste u medicini i stomatologiji mogu se proizvoditi veoma precizno i mogu se pratiti na daljinu u realnom vremenu. Uz upotrebu pametnih materijala, implantati mogu biti složenog i različitog oblika i

**Slika 1.** Primer dentalnog i medicinskog implantata
Izvor: https://www.1888implant.com/dental-implants-procedures.html/; https://www.youtube.com/watch?v=hOMKaaCnxEc&ab_channel=UCDavisHealth



**Slika 2.** Primer pametnog implantata u medicini i stomatologiji
Izvor: https://benhvienranghammatsg.vn/cay-ghep-rang-implant-co-tot-khong/; https://www.biomag-medical.com/joint-arthroses/

mogu reagovati na određene parametre (npr. na pritisak ili temperaturu). Ovakvi implantati, koji se koriste u medicini i stomatologiji su se pokazali kao mnogo prikladniji za pacijente (1,2). Oni moraju biti napravljeni tako da budu neko vreme ili ceo život u telu čoveka. Primer pametnog implantata u stomatologiji i medicini je prikazan na slici 2.

Digitalna klinika i digitalna stomatološka ordinacija predstavljaju nove i moderne termine. Tehnologije Industrije 4.0 omogućile su najbolji način upravljanja i distribucije informacija u medicini i stomatologiji putem Interneta. Upravljanje laboratorijom, vođenje evidencije i mnoge druge prednosti su veoma važne u funkcionisanju digitalne klinike i digitalne stomatološke ordinacije. Industrija 4.0 takođe omogućava laku dijagnostiku u medicini i stomatologiji. Sistem koji predstavlja digitalnu bolnicu ili kliniku 4.0 na osnovu „cloud“ kompjuterskog modela dat je na slici 3 (1,2).

The aim of this paper is to present the current and potential applications of modern technologies as direct consequence of Industry 4.0 in medicine and dentistry and designing the Medicine 4.0 and Dentistry 4.0 concept.

## Applications of technologies of Industry 4.0 in medicine and dentistry

One of the very interesting applications of Industry 4.0 is personalized medical and dental implants. Thanks to the large amount of data, easy and fast connections between different data browsers. Industry 4.0 has enabled the fast and high-quality production of various types of medical and dental implants, due to the abundance of different information. Also, complete costs are significantly reduced (1,2). The real revolution related for dental and medical implants has been started with the use of 3D printers). An example of dental and medical implant is presented in Figure 1.

**Figure 1.** An example of dental and medical implant
Source: https://www.1888implant.com/dental-implants-procedures.html/; https://www.youtube.com/watch?v=hOMKaaCnxEc&ab_channel=UCDavisHealth

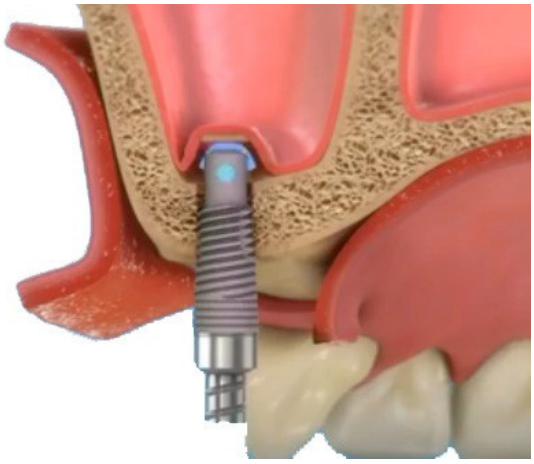
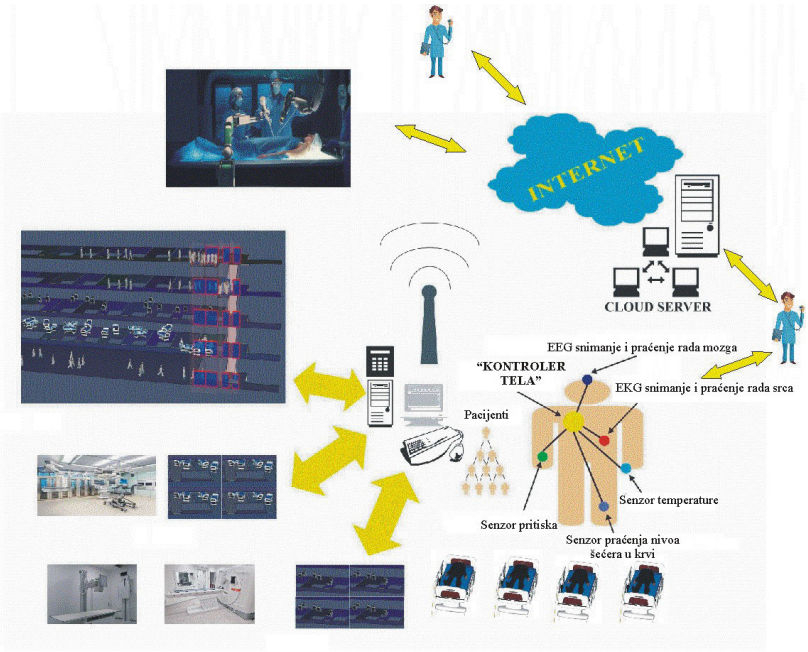


**Figure 2.** An example for smart implant in dentistry and medicine
Source: https://benhvienranghammatsg.vn/cay-ghep-rang-implant-co-tot-khong ; https://www.biomag-medical.com/joint-arthroses/

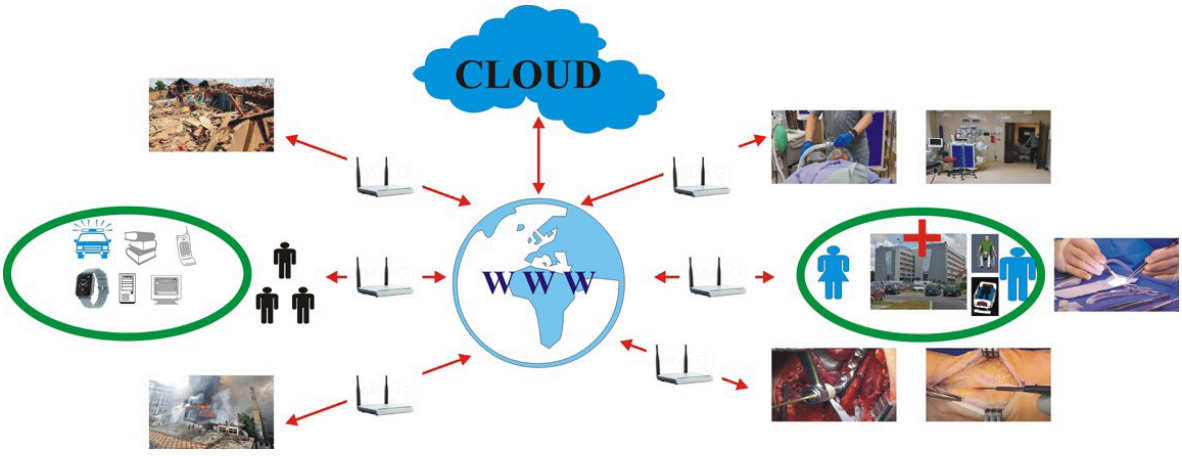
Smart implants are the great achievement of modern technologies. Modern implants used in medicine and dentistry can be produced very precisely and they can be monitored at the distant place in real time. With the use of smart materials, implants can be made to have a different and complex shape and they can react on some particular parameters (pressure or temperature, for example). Those implants, used in medicine were shown as more appropriate for patients (1,2). They must be made to be on the specific place in the human body for some time or for whole life of the patient. An example of smart implant in dentistry and medicine is presented in Figure 2.

Digital clinic and digital dental office present new and modern terms. Technologies of Industry 4.0 provided the best way of information managing and distribution in medicine and dentistry




**Slika 3.** Digitalna klinika 4.0 na osnovu „cloud" kompjuterskog modela

**Slika 4.** Primer precizne hirurgije




**Slika 5.** Značaj komunikacije u medicini i stomatologiji

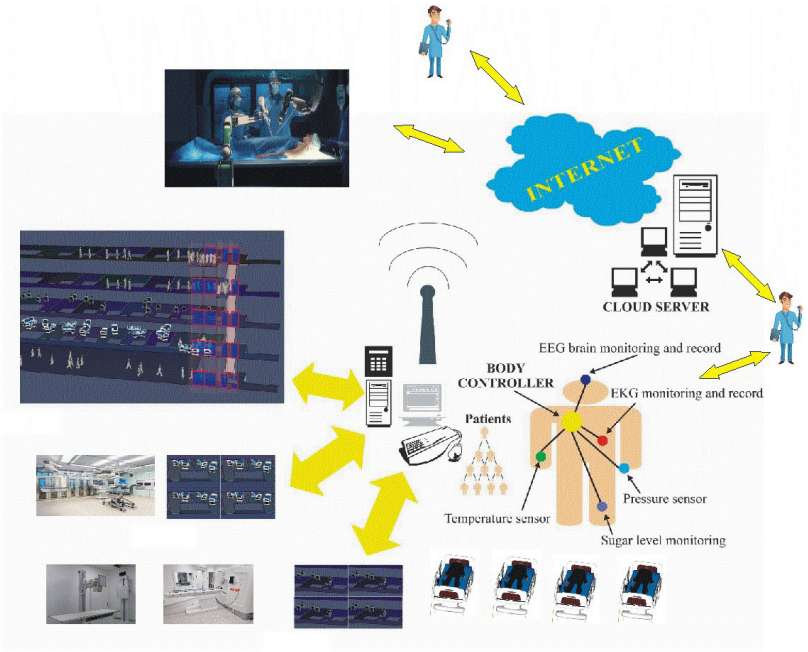



**Figure 3.** Digital clinic 4.0 related to the cloud computing model

**Figure 4.** An example for precise surgery

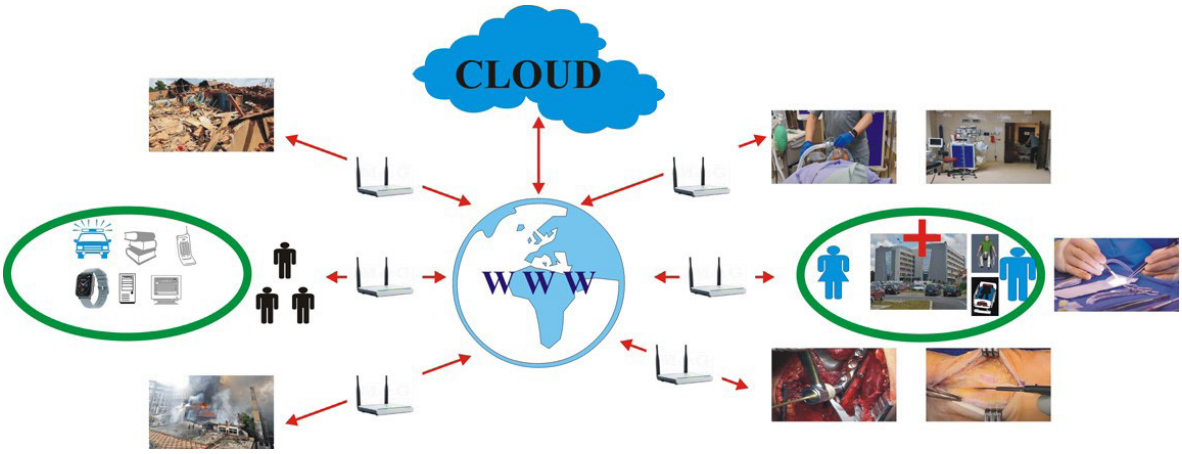



**Figure 5.** The significance of the communication in medicine and dentistry

Industrija 4.0 je obezbedila dizajn i proizvodnju hirurških alata i aparata neslućenih mogućnosti, dimenzija i efikasnosti. Ovi alati i aparati su proizvedeni upotrebom aditivne proizvodnje (stvaranje trodimenzionalnih objekata iz digitalnog modela). Njihov kvalitet, izdržljivost i završna obrada su na mnogo višem nivou nego ranije (1,2).

Jedna od interesantnih posledica Industrije 4.0 vezanih za medicinu i stomatologiju je menadžment prve pomoći. Na primer, u kritičnim situacijama, kada je potrebna brza i precizna akcija, ova tehnologija veoma lako otkriva i prepoznaje prethodnu istoriju bolesti sa svim neophodnim informacijama, poput osnovnih podataka (ime, prezime, adresa, ustanova) i važnih medicinskih informacija (krvna grupa, prosečna težina, prosečna vrednost krvnog pritiska, komorbiditeti itd.). Na ovaj način, štedi se važno i, u mnogim slučajevima, kritično vreme; određuje se i dijagnostikuje trenutna situacija. Korišćenje različitih modernih instrumenata i uređaja povećava preciznu detekciju i dijagnostiku, poput tehnika 3D snimanja (1,2).

Ekonomija i menadžment u medicini i stomatologiji imaju potpuno novi pristup. Moguća je optimizacija troškova u proizvodnji aparata, medicinskih i stomatoloških sredstava, implantata itd. Upravljanje na svakoj klinici je digitalno, što značajno povećava i ubrzava usluge koje se pružaju pacijentima. Proizvodnja se pažljivo i precizno planira i prilagođena je pacijentu. Sve se prilagođava pacijentu, i time se smanjuje rizik i povećava efikasnost (1,2).

Precizna hirurgija je postigla veliki uspeh u složenim operacijama u medicini i stomatologiji i značajno unapredila dosadašnju hirurgiju. Industrija 4.0 i pametna proizvodnja proizvele su robote i precizne mehanizme i instrumente sposobne da realizuju složene, precizne i teške operacije u medicini i stomatologiji. Na primer, jedan hirurg, koliko god da je dobar, ne može da operiše dvadeset i više sati bez pauze i bez povećane mogućnosti da napravi grešku. Roboti ne mogu da se umore; njihova preciznost i efikasnost su kontinuirani, bez uticaja bilo kakvog fizičkog ili psihičkog faktora; roboti mogu da obavljaju nekoliko zadataka u isto vreme, što je hirurgu gotovo nemoguće. Veoma složene operacije u medicini i stomatologiji su sada lake i brze (različite laparoskopske operacije, vađenje zuba itd.). Primer precizne hirurgije prikazan je na slici 4.

Komunikacija lekara ili stomatologa sa pacijentom je na znatno višem nivou. Količina informacija je znatno veća, ali je rukovanje ovim informacijama znatno lakše i brže. Kada su u pitanju dostignuća u komunikacijama, medicina i stomatologija će praćenjem moći da predvide ishode lečenja, i ako je potrebno, realizuju odgovarajuće promene vezane za ishod lečenja. Očigledno je da će ogromna količina informacija biti dostupna veoma brzo i lako zahvaljujući novim komunikacionim tehnologijama. Na primer, lekari su u mogućnosti da u realnom vremenu vrše operaciju, koju istovremeno mogu da posmatraju studenti i specijalizanti, kao i da pri tome vrše komplikovana praćenja, kao i konsultacije sa kolegama. Takođe, prilikom nesreće, moguće je da se vrši komunikacija tokom transporta pacijenta, da se prati stanje pacijenta i da se organizuje najbolji mogući njegov prihvat (1,2). Značaj komunikacije u medicini i stomatologiji na različitim nivoima prikazan je na slici 5.

Jedna od najvećih prednosti Industrije 4.0 je smanjenje rizika po zdravlje i život pacijenta. Razvoj različitih senzora omogućava bolju efikasnost tokom operacija ili tretmana, jer se problemi mogu lako i brzo detektovati i rešiti. Primena novih tehnologija, naročito simulacija i virtuelne stvarnosti omogućava prethodnu probu i proveru tako da su zahvati koji se izvode na pacijentu potpuno bezbedni i unapred isplanirani. Matematički gledano, sve potencijalne „varijable“ (pretnje) se mogu predvideti i mogu se u potpunosti kontrolisati i pratiti.

Nove tehnologije se sve intenzivnije koriste. Jedan veoma dobar i upečatljiv primer je holografija. Ova tehnologija može se koristiti za predstavljanje stanja pacijenta uz pomoć 3D tomografskog prikaza. Generalno, holografija podrazumeva kreiranje 3D slika pomoću svetlosti. Holografija je jedna od prednosti Industrije 4.0 i predstavlja veoma važan medicinski i stomatološki alat sa mnogo primena u patologiji, urologiji, kardiologiji, ortopediji, stomatologiji i protetici (1-5). Primer hologrma zuba i srca prikazani su na slici 6.

Simulacija i virtuelna stvarnost predstavljaju standard u različitim naučnim oblastima, tako da je bilo samo pitanje vremena kada će se ova tehnologija koristiti u medicini i stomatologiji. Prednosti simulacija i virtuelne realnosti su ogromne. Na primer, u protivpožarnoj zaštiti, simulacija se može koristiti za predviđanje širenja vatre, dima, plamena, što može spasiti mnoge živote. Takođe,

via the Internet. Laboratory management, record management and many other benefits are very important in the functioning of digital clinic and digital dental office. Industry 4.0 also enables easy diagnostic in medicine and dentistry. System that presents digital hospital or clinic 4.0 related to the cloud computing model is shown in Figure 3 (1,2).

Industry 4.0 enabled design and production of surgery tools and apparatus with unimaginable possibilities, dimensions and efficiency. Noted tools and apparatus were manufactured using additive manufacturing (creation of three-dimensional objects from a digital model).). Their quality, endurance and sand are at a much higher level than before (1,2).

One of the interesting consequences of Industry 4.0 related to medicine and dentistry is first-aid management. For example, in critical situations, when fast and precise action is needed, this technology very easily detects and recognizes previous illness history with all necessary information, such as basic information (name, surname, address, affiliation etc.) and important medical information (blood group, average weight, average blood pressure, comorbidities etc.). In this way, important and in many cases critical amount of time is saved; determination and diagnosis of the current situation is made. The use of different modern tools and devices significantly increases the precise detection and diagnostics, such as 3D imaging techniques (1,2).

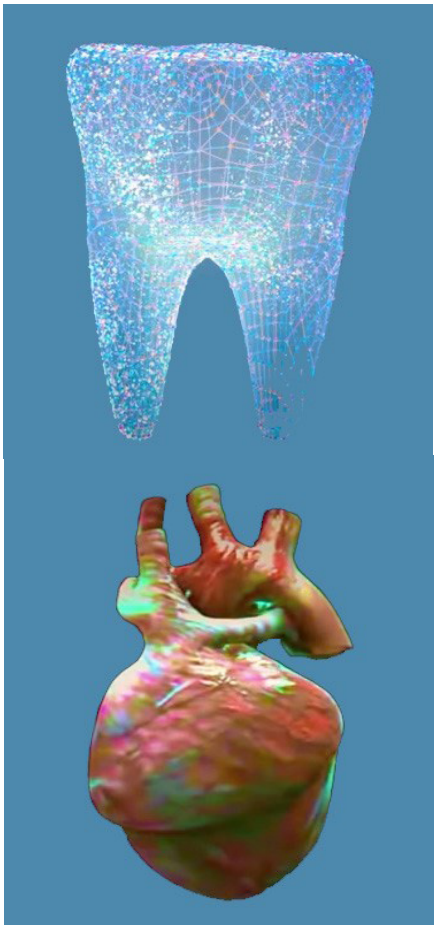
Economy and management in medicine and dentistry have a totally new approach. It is possible to realize the cost optimization in the production of devices, medicine and dentistry resources, implants etc. Management at every clinic is digital, which significantly increases and accelerates services provided to patients. Manufacturing was carefully and precisely planned and adapted to patients' needs. Everything is adapted to the patient, which reduces risks and increases efficiency (1,2).

Precise surgery has achieved great success in complex operations in medicine and dentistry and significantly improved the previous surgery. Industry 4.0 and smart manufacturing produced robots and precise mechanisms capable to realize complex, precise and hard operations in medicine and dentistry. For example, one surgeon, no matter how good he is, simply cannot operate twenty or more hours without pause and without increased potential for mistake. Robots cannot be tired; their precision and efficiency are continual, without influence of any physical or psychic factor; robots are capable of doing several tasks at the same time what is for a human surgeon almost impossible. Very complex operations in medicine and dentistry are now easy and fast (different laparoscope operations, tooth extraction etc.). An example for precise surgery is presented in Figure 4.

Communication between a doctor or a dentist with a patient are at a significantly higher level. The quantity of information is significantly greater but handling with this information is significantly easier and faster. Considering communication achievements, medicine and dentistry will be able to predict epilogues of treatment with monitoring and, if it is necessary, realize appropriate changes related to healing epilogue. When it comes to achievements in communications, medicine and dentistry will be able to predict treatment outcomes through monitoring, and if necessary, implement appropriate changes related to treatment outcomes.It is obvious that huge amount of information will be available very fast and easily thanks to new communication technologies. For example, doctors are able to realize operation in real time, where in the same time students and specialists can observing the operation, so as to realize complex monitoring and consultations with colleges. Also, in the event of an accident, it is possible to communicate during the transport of the patient, monitor his condition and organize the best possible reception (1,2). The significance of communication in medicine and dentistry at different levels is presented in figure 5.

One of the biggest benefits from Industry 4.0 is the risk reduction, related to the patients' health and life. Development of different sensors provides better efficiency during operations and treatments, because potential problems can be detected and solved fast and easily. The application of new technologies, especially simulation and virtual reality, enables preliminary testing and checking so that procedures performed on the patient are completely safe and planned in advance. From the mathematical point of view, all potentials „variables "can be predicted and can be fully controlled and monitoring.

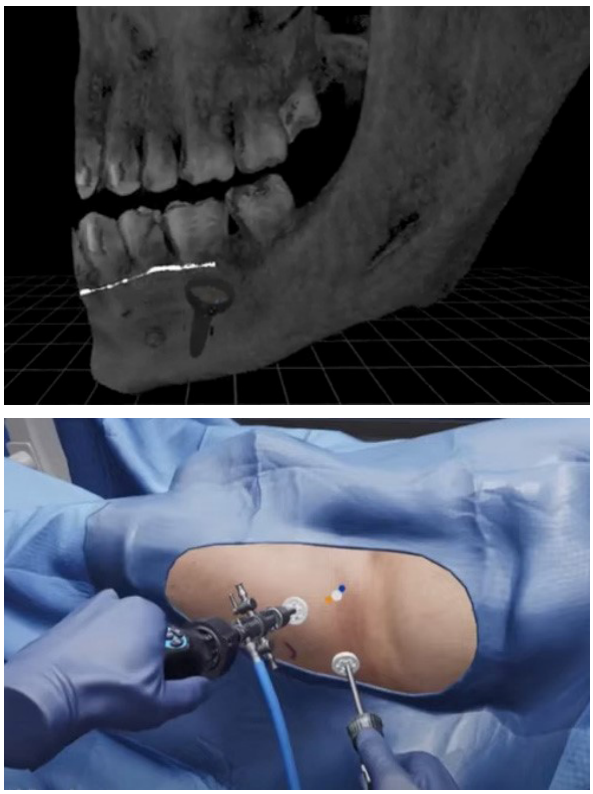
New technologies are more and more intensively used. One very good and striking example is holography. This technology can be used for the presentation of medical states of patients with 3D tomography view. Generally, holography pur-



**Slika 6.** Primer holograma zuba i srca
Izvor: https://depositphotos.com/video/hologram-screen-of-molar-tooth-299092082.html; https://free3d.com/3d-model/heart-pro-animated-textured-4653.html

kada je u pitanju protivpožarna zaštita, strategije evakuacije i scenariji evakuacije sa preciznim proračunima vremena potrebnog za evakuaciju se mogu realizovati korišćenjem simulacija i softvera za simulaciju (6,7). Naravno, postoje i mnogi drugi primeri u drugim naučnim oblastima.

Simulacije i virtuelna stvarnost imaju sjajnu ulogu u medicini i stomatologiji. Virtuelna starnost može pružiti važne informacije o pacijentima doktorima i stomatolozima. Planiranje kompleksnih aktivnosti i operacija u medicini i stomatologiji uz pomoć 3D snimaka obezbeđuje kvalitet i značajno umanjuje vreme potrebno za planiranje i realizaciju neke aktivnosti ili operacije. Ove tehnologije značajno unapređuju hirurške i manuelne veštine hirurga i stomatologa zbog mnogo boljeg prikaza i šanse da se vežba pre operacije (1,2,6,7). Upotreba simulacije i virtuelne stvarnosti prikazana je na slici 7.



**Slika 7.** Simulacija i virtuelna stvarnost u stomatologiji i hirurgiji
Izvor: https://www.youtube.com/watch?v=3t-pnRFshvsA&ab_channel=MedtronicDigitalSurgery

Posmatranje i praćenje u medicini i stomatologiji ima veliki značaj. Korišćenjem tehnologija Industrije 4.0, posmatanje i praćenje celokupnog procesa lečenja je veoma lak i efikasan. Sve važne informacije su pripremljene i dostupne. Na primer, mnogi kardiološki pacijenti mogu biti praćeni uz kompletne informacije o njihovim tegobama, bolesti, terapiji uz mogućnost da se odmah reaguje u slučaju hitnih stanja. Korišćenjem ovih tehnologija, moguće je sprovesti posmatranje i praćenje kompletne javno-zdravstvene situacije, što je od ključne važnosti za optimizaciju zdravlja, predviđanje potencijalnih kriznih situacija (pandemija, na primer), optimizaciju kvaliteta lečenja u medicini i stomatologiji, optimizaciju troškova, recikliranje medicinskog i stomatološkog otpada itd. (1,2,5,10).

Optimizirana proizvodnja različitih implantata bilo kog oblika u medicini i stomatologiji predstavlja standard. Više nije potrebno povećavati rezerve jer se implanti proizvode prema ličnim zahtevima. Primetno je i veoma veliko smanjenje papirologije. Korišćenjem digitalnih tehnologija, informacije o

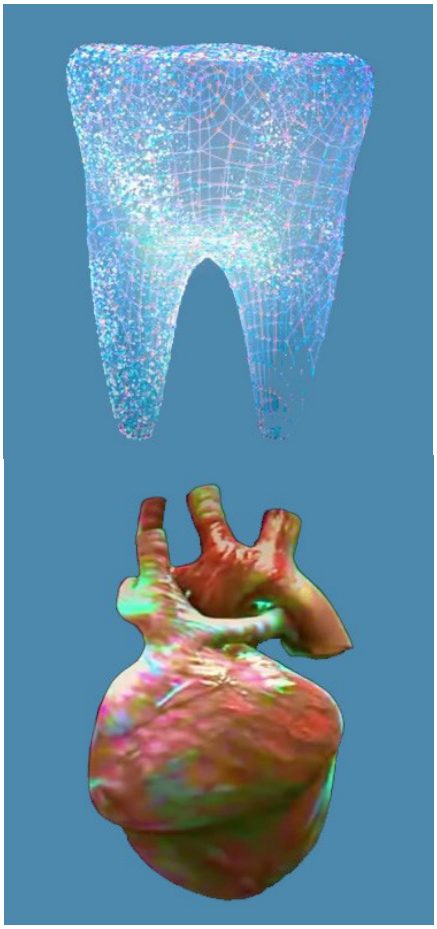


**Figure 6.** An example for hologram of tooth and heart.
Source: https://depositphotos.com/video/hologram-screen-of-molar-tooth-299092082.html; https://free3d.com/3d-model/heart-pro-animated-textured-4653.html

ports design of the 3D pictures by light. Holography presents the consequence of Industry 4.0 and presents a very important medical and dentistry tool with plenty of applications in pathology, urology, cardiology, orthopaedic, dentistry, prosthetics etc. (1-5). An example of a tooth and hart hologram is shown in Figure 6.

Simulation and virtual reality represent a standard in different fields of science, so it was just a question of time when this technology would be used in medicine and dentistry. The benefits of simulations and virtual reality are enormous. For example, in fire safety, simulation can be used to predict the spreading of fire, smoke, flame which can save many lives. Also, in relation to fire protection, evacuation strategies and evacuation scenarios with precise calculation of needed evacuation times can be realized using simulations and simulation software (6,7). Of course, there are many other examples in other fields of science.

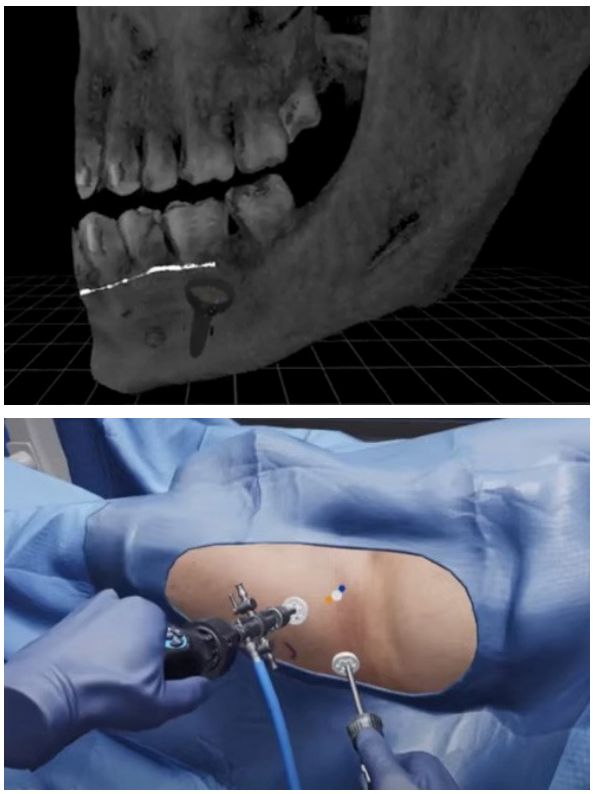


**Figure 7.** Simulation and virtual reality in dentistry and surgery
Source: https://www.youtube.com/watch?v=3t-pnRFshvsA&ab_channel=MedtronicDigitalSurgery

Simulations and virtual reality have a great role in medicine and dentistry. Virtual reality can provide important information to doctors and dentists about patients. Planning of complex actions and operations in medicine and dentistry with providing of 3D presentation of the patient enables quality and significantly reduced time needed for preparation and realization of action or operation. These technologies significantly increase operation and manual skills of surgeons and dentists because they have much better view and chance to practice before operations (1,2,6,7). The use of simulation and virtual reality in dentistry and surgery is presented in Figure 7.

Monitoring and tracking in medicine and dentistry have very important roles. With the use of Industry 4.0 technologies, monitoring and tracking of complete treatment process is very easy and effective. All important information is prepared and available. For example, many of cardiac patients can be monitored and tracked with complete in-

pacijentima se čuvaju u digitalnom obliku i mogu se lako odštampati (10).

Postoje brojni drugi primeri primene tehnologija Industrije 4.0 u medicini i stomatologiji. Očigledno je da se promene izazvane digitalnim tehnologijama pojavljuju i nepovratno menjaju mnoge sfere života i rada ljudi, pa je tako i u medicini i stomatologiji (8,10).

## Budući trendovi razvoja

Očigledno je da Industrija 4.0 ima sve više mogućnosti u smislu primene, istraživanja i inovacija. Primenjuje se korišćenjem pametne proizvodnje, integrisanog dizajna, pametnih usluga i menadžmenta i pametnog istraživanja. Pametni medicinski i stomatološki uređaji i aparati se već proizvode, a u bliskoj budućnosti će se proizvoditi mnogo bolji. To će zahtevati edukaciju medicinskog i stomatološkog kadra, ali će korist od njih biti neverovatna (1,2).

Uticaji Industrije 4.0 i njene tehnologije će takođe značiti i ogromnu pomoć i prednosti za studente medicine i stomatologije u smislu postavljanja precizne dijagnoze, lečenja, usavršavanja njihovih veština itd.

Tehnologije Industrije 4.0 će se suočiti sa enormnim količinama informacija, njihovim upravljanjem i čuvanjem. Sve potrebne informacije o pacijentu će biti pružene i dostupne u svakom trenutku.

Jedna od veoma bitnih stavki kada su u pitanju Zdravstvo 4.0, odnosno Medicina 4.0 i Stomatologija 4.0, su neograničene mogućnosti za istrživanje. Primena novih procedura, instrumenata, implanata, robota, lekova daju neslućene mogućnosti za uspostavljanje znatno efikasnijeg zdravstva u celini. Procena je da će mnoge bolesti u budućnosti biti potpuno iskorenjene ili da će preći u hronične, sa mnogo povoljnijim ishodima po pacijente.

Bolesti će se potpuno pratiti, u svim potencijalnim pravcima i sa uvek najboljim solucijama. Pretpostavlja se i da će veliki broj retkih bolesti biti potpuno eliminisan zahvaljujući neslućenim mogućnostima predikcije koje donose nove tehnologije. Mnoge operacije za koje su bili potrebni posebni uslovi (anestezija, razni neophodni instrumenti i pomagala itd.) će biti potpuno automatizovane sa unapred predviđenim pozitivnim ishodom.

Angažovanje velikog broja doktora, sestara, specijalista će drastično biti smanjeno. Naravno, to će podrazumevati efikasna rešavanja mnogih problema i izazova koji se odnose na standarde, bezbednost, privatnost, raznovrsnost podataka, mogućnosti prilagođavanja i prihvatanja, snabdevanje različitim resursima itd. Bez obzira na postojeće i potencijalne probleme, poređenje, generalno, zdravstva 4.0 sa prethodnim (zdravstvo 1.0, zdravstvo 2.0 i zdravstvo 3.0) dokazuje da je upotreba novih tehnologija nužnost, potreba i budućnost i to ne samo za istraživanje i razvoj, nego i za druge oblasti zdravstva (medicina, stomatologija) (1,2,11,12).

Zbog svega navedenog, očigledno je da će industrija 4.0 u medicini i stomatologiji povećati svoje mogućnosti, ali i potrebe. Prilagođavanje na digitalne tehnologije biće na najvišem nivou sa jasnim ciljem kreiranja pametnog, jedinstvenog zdravstvenog sistema (1, 2,7, 8, 10).

Inovativne tehnologije Industrije 4.0 će stvoriti bolju i sigurniju budućnost u smislu optimiziranih medicinskih usluga i lečenja, mnogo većeg procenta izlečenih pacijenata, virtuelnih medicinskih i stomatoloških klinika sa konsultacijama uz pomoć telemedicine i terapija i još mnogo toga (8-12).

## Zaključak

Medicina i stomatologija predstavljaju oblasti u kojima se primenjuju različiti pametni proizvodi i rešenja koja su kreirana na osnovu tehnologija Industrije 4.0. Napravljeni su mnogi složeni i efikasni medicinski i stomatološki uređaji i aparati sa mogućnostima koje se do pre nekoliko godina nisu mogle ni zamisliti. Performanse i kvalitet zdravstvenih tretmana i usluga su na veoma visokom nivou i taj nivo će biti još veći u budućnosti.

Iako je Industrija 4.0 donela mnoge prednosti, to nije kraj istraživanja i razvoja. Osnovane su veoma važne baze, pripremaju se novi trendovi istraživanja i razvoja. Istraživanja se bave novim uređajima, aparatima i implantatima koji će doprineti daljem napretku u medicini i stomatologiji i omogućiti potpunu realizaciju koncepta Medicina 4.0 i Stomatologija 4.0.

## Konflikt interesa

Autor je izjavio da nema konflikta interesa.

formation about their problems, illness, therapy and possibility to react instantly in case of emergency. Using these technologies, it is possible to realize the monitoring and tracking of complete public health situation, which has crucial importance in optimization of health, prediction of potential crisis situations (pandemics for example), optimization of quality of medical and dental treatments, optimization of costs, recycling of medical and dental waste etc (1,2,5,10).

The optimized production of different implants of any shape present a standard in medicine and dentistry. It is not necessary to increase reserves anymore because implants are produced by individual requirement. A very large reduction of paper documentation is also notable. Using digital technologies, information about patients is stored in digital form and can be easily printed (10).

There are numerous other examples of applications of Industry 4.0 technologies in medicine and dentistry. It is obvious that changes caused by digital technologies appear and irrevocably change many spheres of human work and living, including medicine and dentistry (8,10).

## Future trends of development

It is obvious that Industry 4.0 has more and more possibilities of applications, research and innovations. It is applied using smart manufacturing, integrated design, intelligent services and management and smart researching. Smart medical and dental devices and apparatus have already been produced, and in the near future, much better will be produced. It will demand the education of medical and dental staff, but the benefits of them will be unbelievable (1,2).

The influences of Industry 4.0 and its technology will also provide great help and benefits to students of medicine and dentistry in the sense of precise diagnostics, treatment solutions, improving of their skills etc.

Technologies of Industry 4.0 will face enormous quantities of information, their management and storing. Necessary information about patients will be provided and available at the moment.

One of the very important items when it comes to Health 4.0, i.e. Medicine 4.0 and Dentistry 4.0, are unlimited opportunities for research. The application of new procedures, instruments, implants, robots, and drugs provide unprecedented opportunities for the establishment of significantly more efficient health care as a whole. It is estimated that many diseases will be completely eradicated in the future or that they will become chronic, with much more favorable epilogues for patients.

Diseases will be fully monitored, in all potential directions and always with the best solutions. It is estimated that many diseases will be completely eradicated in the future or that they will become chronic, with much more favorable epilogues for patients. It is also assumed that a large number of rare diseases will be completely eliminated thanks to the unprecedented possibilities of prediction brought by new technologies. Many operations that required special conditions (anesthesia, various necessary instruments and aids, etc.) will be fully automated with a predetermined positive outcome.

The hiring of a large number of doctors, nurses, and specialists will be drastically reduced. Of course, this will involve effective solutions to many problems and challenges related to standards, security, privacy, diversity of data, possibilities of adaptation and acceptance, supply of different resources, etc. Regardless of the existing and potential problems, the comparison, in general, of healthcare 4.0 with the previous ones (health 1.0, healthcare 2.0 and healthcare 3.0) proves that the use of new technologies is a necessity, a need and the future, not only for research and development, but also for other fields of medicine (medicine, dentistry) (1,2,11,12).

Based on the above mentioned, it is obvious that industry in medicine and dentistry will increase their possibilities and needs. The adaption to digital technologies will be at the highest level with the clear aim of designing a smart unique healthcare system (1, 2, 7, 8, 10).

Innovative Industry 4.0 technologies will design a better and safer future in the form of optimized medical services and treatment, much bigger percentage of cured patients, virtual medical and dental clinics with telemedicine consultations, optimal use of medicaments and therapies and lot of other things (8-12).

## Conclusion

Medicine and dentistry present spheres where many different intelligent products and solutions

## Reference


1. Majstorović V, Đuričin D, Mitrović R. Industry 4.0-Renaissance of Engineering. Faculty of Mechanical Engineering, University in Belgrade, Belgrade, 2021: p235-260.
2. Majstorović N, Majstorović V, Mitrović R. and Mišković Ž. Industrija 4.0 i njena primena u medicini i stomatologiji, kao i borbi protiv pandemije COVID-19. Tehnika 2021;76(4):509-520. doi: 10.5937/tehnika2104509M
3. Abas ZA, Abiding ZZ, Rahman H, Pramudy G, Hamid HA. Internet of things and healthcare analytics for better healthcare solution: Applications and Challenges. IJACSA 2018;9(9):446-450. doi: 10.14569/IJACSA.2018.090956
4. Bhatt Y, Bhatt C. Internet of things in healthcare. In: Internet of things and big data technologies for next generation healthcare care. Springer, Germany; 2017:p13-33. doi: 10.1007/978-3-319-49736-5_2
5. Abdeldjali K, Estrela VV, Monteiro ACB, Franca RP, Iano Y, Razmjooy N. Applications, Management, Technologies and Review. Medical Technologies Journal 2018;2(4):262-276. doi:/10.26415/2572-004X-vol2iss1p262-276.
6. Jevtić BR. The significance and use of simulation software in fire protection, Path to a Knowledge Society-Managing Risks and Innovation PaKSoM, 3rd International Virtual conference, 2021.
7. Jevtić R. The significance and use of simulation software in evacuation, Path to a Knowledge Society-Managing Risks and Innovation PaKSoM, 3rd International Virtual conference, 2021.
8. Ivančić L, Glavan LM, Vukšić VB. A Literature Review of Digital Transformation in Healthcare. 43rd International Convention on Information, Communication and Electronic Technology (MIPRO), Opatija, Croatia, 2020: pp. 1351-5. doi: 10.23919/MIPRO48935.2020.9245259.
9. Albesher A. IoT in Health-care: Recent Advances in the Development of Smart Cyber-Physical Ubiquitous Environments. IJCSNS 2019;19(2): 181-6.
10. Javid M, Haleem A. Industry 4.0 applications in medical field: a brief review. Curr Med Res Pract 2019:9(3):102-109. doi: 10.1016/j.cmrp.2019.04.001
11. Gupta A, Singh A. Healthcare 4.0: recent advancements and futuristic research directions. Wirel Pers Commun. 2023;129(2):933-952. doi: 10.1007/s11277-022-10164-8.
12. Subiksha KP, Ramakrishnan M. Smart Healthcare Analytics Solutions Using Deep Learning AI. In: Gunjan VK, Zurada JM (eds). Proceedings of International Conference on Recent Trends in Machine Learning, IoT, Smart Cities and Applications. Advances in Intelligent Systems and Computing, Springer, Singapore, 2021 (vol 1245). Available at: https://doi.org/10.1007/978-981-15-7234-0_67

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designed by technologies of Industry 4.0. Many complex and efficient medical and dental devices and appliances have been created with possibilities that could not even be imagined until a few years ago. Performances and qualities of complete healthcare treatments and services are at a very high level and this level will be even higher in the future.

Although Industry 4.0 has brought many benefits, this is not the end of research and development. Research deals with new devices, appliances and implants that will contribute to further progress in medicine and dentistry and enable the full realization of the concept of Medicine 4.0 and Dentistry 4.0.

## Competing interests

The author declared no competing interests.

## References


1. Majstorović V, Đuričin D, Mitrović R. Industry 4.0-Renaissance of Engineering. Faculty of Mechanical Engineering, University in Belgrade, Belgrade, 2021: p235-260.
2. Majstorović N, Majstorović V, Mitrović R. and Mišković Ž. Industrija 4.0 i njena primena u medicini i stomatologiji, kao i borbi protiv pandemije COVID-19. Tehnika 2021;76(4):509-520. doi: 10.5937/tehnika2104509M
3. Abas ZA, Abiding ZZ, Rahman H, Pramudy G, Hamid HA. Internet of things and healthcare analytics for better healthcare solution: Applications and Challenges. IJACSA 2018;9(9):446-450. doi: 10.14569/IJACSA.2018.090956
4. Bhatt Y, Bhatt C. Internet of things in healthcare. In: Internet of things and big data technologies for next generation healthcare care. Springer, Germany; 2017:p13-33. doi: 10.1007/978-3-319-49736-5_2
5. Abdeldjali K, Estrela VV, Monteiro ACB, Franca RP, Iano Y, Razmjooy N. Applications, Management, Technologies and Review. Medical Technologies Journal 2018;2(4):262-276. doi:/10.26415/2572-004X-vol2iss1p262-276.
6. Jevtić BR. The significance and use of simulation software in fire protection, Path to a Knowledge Society-Managing Risks and Innovation PaKSoM, 3rd International Virtual conference, 2021.
7. Jevtić R. The significance and use of simulation software in evacuation, Path to a Knowledge Society-Managing Risks and Innovation PaKSoM, 3rd International Virtual conference, 2021.
8. Ivančić L, Glavan LM, Vukšić VB. A Literature Review of Digital Transformation in Healthcare. 43rd International Convention on Information, Communication and Electronic Technology (MIPRO), Opatija, Croatia, 2020: pp. 1351-5. doi: 10.23919/MIPRO48935.2020.9245259.
9. Albesher A. IoT in Health-care: Recent Advances in the Development of Smart Cyber-Physical Ubiquitous Environments. IJCSNS 2019;19(2): 181-6.
10. Javid M, Haleem A. Industry 4.0 applications in medical field: a brief review. Curr Med Res Pract 2019:9(3):102-109. doi: 10.1016/j.cmrp.2019.04.001
11. Gupta A, Singh A. Healthcare 4.0: recent advancements and futuristic research directions. Wirel Pers Commun. 2023;129(2):933-952. doi: 10.1007/s11277-022-10164-8.
12. Subiksha KP, Ramakrishnan M. Smart Healthcare Analytics Solutions Using Deep Learning AI. In: Gunjan VK, Zurada JM (eds). Proceedings of International Conference on Recent Trends in Machine Learning, IoT, Smart Cities and Applications. Advances in Intelligent Systems and Computing, Springer, Singapore, 2021 (vol 1245). Available at: https://doi.org/10.1007/978-981-15-7234-0_67




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**Acknowledgment**
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