THE HIV/AIDS EPIDEMIOLOGICAL SITUATION AMONG MEN AND WOMEN IN SERBIA IN THE PERIOD 2007–2017: JOINPOINT REGRESSION ANALYSIS

Aleksandra Nikolić, Ana Božić, Danijela Simić, Sandra Šipetić Grujičić

1 Institute of Epidemiology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia
2 Faculty of Medicine, University of Belgrade, Belgrade, Serbia
3 Institute of Public Health of Serbia "Dr Milan Jovanović Batut"

ABSTRACT

Introduction: Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS) is a global major health problem. According to the data for 2018, there were 37.9 million people living with HIV/AIDS in the world, and the number of deaths related to AIDS was about 770,000.

Aim: The aim of this study was to analyze the trend of newly diagnosed HIV-infected people, AIDS patients and AIDS-related deaths among men and women in Serbia, for the period 2007–2017.

Materials and methods: Data on newly diagnosed HIV-infected people, AIDS patients and AIDS-related deaths were taken from the Report on Infectious Diseases in the Republic of Serbia. Age-specific and standardized mortality and incidence rates (standardized according to the world population) were calculated based on the data obtained. Joinpoint regression analysis was used to examine the trend.

Results: The average standardized rates of newly diagnosed HIV-infected people (per 100,000) in Serbia, for the period 2007–2017, were 3.4 for men and 0.8 for women. There was a significant annual increase in standardized rates of newly diagnosed HIV-infected people: 7.0% for men and 21.1% for women. The average standardized rates of AIDS incidence were 0.9 for men and 0.2 for women. There was a significant annual increase of 4.9% in the standardized incidence rate of AIDS in men, and a significant decrease of -12.2% in women. The average standardized mortality rates from AIDS (per 100,000) for men (0.9%) were higher than those for women (0.2%).

Conclusion: Further work is needed, primarily in advancing preventive measures, particularly by educating young people about transmission pathways and risks, but also in the early detection of HIV-infected persons and timely treatment.

Keywords: HIV, AIDS, joinpoint regression analysis, trend
UVOD

Infekcija virusom humane immunodeficijencije (engl. *Human Immunodeficiency Virus* – HIV) i dalje predstavlja jedan od vodećih javnozdravstvenih izazova u svim zemljama sveta. Takođe, veliki problem predstavlja i sindrom stečene immunodeficijencije (engl. *Acquired Immunodeficiency Syndrome* – AIDS), poslednji i najteži stadijum HIV infekcije, koji se razvija posle sedam do deset godina, ukoliko se infekcija ne leći.

Procenjuje se da je u svetu oko 37,9 miliona ljudi živelo sa HIV/AIDS-om u 2018. godini, dok je broj umrlih usled bolesti i stanja povezanih sa AIDS-om bio 770,000. Poslednjih decenija veliki decenija veliki su uticaji na okončanje epidemije HIV/AIDS-a, koja je zvanično započela pre nešto više od trideset i osam godina. Prema globalnoj strategiji Zajedničkog programa Ujedinjenih naracija za HIV i AIDS (engl. United Nations Programme on HIV/AIDS – UNAIDS), “90-90-90”, bilo je planirano da do 2020. godine 90% ljudi koji žive sa HIV-om poznaje svoj pozitivan status na HIV, da je 90% ljudi koji znaju svoj pozitivan status na HIV na antiretrovirusnoj (ARV) terapiji, i da 90% ljudi koji su na ARV terapiji ima stabilnu virusnu supresiju [1]. Na globalnom nivou dolazi do opadanja broja novoinficiranih HIV-om za 16% tokom poslednjih osam godina. Međutim, i pored toga, svet je daleko od realizacije cilja da do 2020. godine poslužit ćejo novoinficiranih HIV-om bude manji od 500,000 [2].

U 2018. godini je više od polovine (54%) novoinficiranih HIV-om, uzrasta 15 – 49 godina, bilo među ključnim populacijama i njihovim partnerima – 18% među klijentima seksualnih radnika/radnica i seksualnim partnerima drugih ključnih populacija; 17% među muškarcima koji imaju seksualni odnos sa muškarcima (engl. *men who have sex with men* – MSM); 12% među osobama koje injektiraju droge; 6% među seksualnim radnicima/radnicama, a 46% iz opšte populacije [2]. U regionima sa visokom prevalencijom HIV infekcije, kao što su istočna i južna Afrika, HIV se pretežno javlja kod osoba iz opšte populacije, a u regionima sa nižom prevalencijom među osobama iz ključnih populacija i njihovim seksualnim partnerima.

Zabrinjava procena da u svetu značajan broj osoba pozitivnih na HIV ne zna da je inficirano HIV-om, pri čemu se taj procenat kreće od 30 do 50% u regionu Evrope. U periodu od 1984. do kraja 2017. godine u Republici Srbiji registrovane su 3.664 osobe inficirane HIV-om, od kojih je 1.901 osoba oboljele od AIDS-a, a 1.100 osoba je umrlo od AIDS-a. Procene UNAIDS-а i Svetske zdravstvene organizacije (SZO) ukazuju da je krajem 2018. godine u Srbiji 3.000 (2.200 – 3.800) osoba živelo sa HIV-om, od kojih 400 do 1.200 osoba nije znalo da je inficirano HIV-om [3].

Sve navedeno ukazuje da je, uprkos brojnim novim saznanjima iz virusologije, farmakologije, intenzivnog

INTRODUCTION

Infection with the Human Immunodeficiency Virus (HIV) remains one of the leading public health challenges in all of the countries in the world. Also, acquired immunodeficiency syndrome (AIDS) constitutes a great problem as the last and most severe stage of HIV infection, which develops within 7 to 10 years, if the infection is left untreated.

The estimation is that, in 2018, around 37.9 million people were living with HIV/AIDS worldwide, while 770,000 died as the result of AIDS-related diseases and conditions. In the previous decades, great efforts have been made to end the HIV/AIDS epidemic, which officially started a little over 38 years ago. According to the global 90-90-90 strategy of the United Nations Programme on HIV/AIDS – UNAIDS, it was planned that, by the year 2020, 90% of people living with HIV would be aware of their HIV positive status, that 90% of the people aware of their HIV positive status would be on antiretroviral (ARV) therapy, and that 90% of those on ARV therapy would have stable viral suppression [1]. Globally, in the previous 8 years, there has been a 16% decrease in the number of newly infected HIV patients. Nevertheless, the world is still far from achieving the goal set for 2020, i.e. reducing the number of people newly infected with HIV below 500,000 [2].

In 2018, more than half (54%) of people newly infected with HIV, aged 15 – 49 were amongst the key populations and their partners – 18% were sex worker clients and sexual partners of other key groups; 17% were men who have sex with men (MSM); 12% were people injecting themselves with drugs; 6% were sexual workers; 46% were from the general population [2]. In regions with a high prevalence of HIV infection, such as Eastern and Southern Africa, HIV was primarily present in persons from the general population, while in regions with a lower prevalence of HIV it was primarily present amongst persons from key populations and their sexual partners.

The estimation that a significant number of people in the world who are HIV positive are not aware of that fact is a cause for concern, with this percentage ranging from 30% to 50% in the European region. In the period between 1984 and the end of 2017, 3,664 HIV positive persons were registered in the Republic of Serbia, of whom 1,901 developed AIDS, and 1,110 died of AIDS. UNAIDS and WHO estimations indicate that, at the end of 2018, in Serbia, 3,000 (2,200 – 3,800) were living with HIV, of whom between 400 and 1,200 were not aware that they had been infected [3].

All the above stated indicates that, despite numerous new developments in virology and pharmacology, despite intensive efforts in therapy, early diagnostics and prophylaxis, HIV remains one of the greatest
The HIV/AIDS epidemiological situation among men and women in Serbia in the period 2007–2017: Joinpoint regression analysis

MATERIAL AND METHODS

Data on newly diagnosed HIV positive persons (hereinafter: HIV-infected persons), persons who had developed AIDS, and persons who had died of AIDS, were taken from the Reports on Infectious Diseases in the Republic of Serbia for the period between 2007 and 2017, which are annually issued by the Institute of Public Health of Serbia Dr Milan Jovanović Batut, and are available on the Institute’s website [4].

Data on infectious sexually transmitted diseases are collected as a part of epidemiological monitoring, which is organized and implemented by 24 different public health institutes, in cooperation with health institutions, and in keeping with the law. The Rulebook on Reporting Infectious Diseases defines the dynamics and method of delivering data collected as part of epidemiological surveillance. [3]. At the Institute of Public Health of Serbia Dr Milan Jovanović Batut data are collected in the form of aggregated reports, on a weekly and monthly basis, with the exception of data on newly registered cases of anti-HIV antibody carriers and cases of patients developing or dying of AIDS, which are continuously reported by health institutions, via special individual report, to the Institute of Public Health of Serbia Dr Milan Jovanović Batut (Central Register of HIV-infected persons in the Republic of Serbia, as of 2002, and the Central Register of Persons Suffering from and Dying of AIDS in the Republic of Serbia, as of 1985). Within the annual reports from the 24 public health institutes in Serbia, which have mandates on the territories of the 25 districts, more detailed data are submitted regarding the sex and age of persons suffering from and dying of sexually transmitted diseases [4].

Based on the data obtained, age-specific and standardized rates of newly diagnosed HIV-infected persons were calculated, as well as age-specific and standardized rates of AIDS incidence and mortality rates of AIDS. Standardized rates were calculated via the direct method of standardization, while Segi’s world population was applied for the standard population [5]. The trends of standardized incidence and mortality rates were calculated by means of the joinpoint regression analysis (Joinpoint Regression Program, Version 4.7.0.0. February, 2019; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute), applying the method by Kim et al. [5]. The average annual percent change (AAPC) was calculated by means of the joinpoint regression analysis. Years was set as an
**RESULTS**

In Serbia, in the period between 2007 and 2017 there were 1,411 men and 148 women infected with HIV (Table 1). On average, 127 men and 13 women were infected with HIV, annually. The highest age-specific rates of newly diagnosed HIV-infected persons (per 100,000)

| Age   | Number of newly diagnosed HIV-infected persons for the period 2007–2017 | Average rates of newly diagnosed HIV-infected persons | AAPC (95% CI) | Number of newly diagnosed HIV-infected persons for the period 2007–2017 | Average rates of newly diagnosed HIV-infected persons | AAPC (95% CI) |
|-------|-------------------------------------------------|-----------------------------------------------------|---------------|-------------------------------------------------|-----------------------------------------------------|---------------|
| 0–14  | 7                                               | 0.1                                                 | -8.3 (-37.1, 33.6) | 4                                               | 0.1                                                 | -             |
| 15–19 | 18                                              | 0.8                                                 | 23.7 (-16.4, 83.1) | 0                                               | 0.1                                                 | -             |
| 20–24 | 169                                             | 6.7                                                 | 7.6 (-0.5, 16.4)  | 15                                              | 1.4                                                 | 22.2 (-21.2, 89.4) |
| 25–29 | 320                                             | 11.8                                                | 5.0 (-1.4, 11.8)  | 21                                              | 2.1                                                 | 2.8 (-34.4, 44.1) |
| 30–39 | 478                                             | 8.6                                                 | 8.7^ (5.5, 11.9)  | 44                                              | 2.0                                                 | 9.7 (-15.1, 41.8) |
| 40–49 | 246                                             | 4.6                                                 | 9.6^ (3.0, 16.6)  | 34                                              | 1.2                                                 | 18.3 (-18.6, 71.9) |
| 50–59 | 122                                             | 2.1                                                 | 15.4^ (1.8, 30.9) | 19                                              | 0.5                                                 | 26.8 (-14.2, 87.2) |
| 60+   | 51                                              | 0.6                                                 | 4.3 (-6.0, 15.6)  | 11                                              | 0.2                                                 | 4.3 (-6.0, 15.6)  |
| Uкупно/Total | 1,411                                             | 3.6 (3.4^)                                         | 7.0^ (3.9, 10.3^) | 148                                             | 0.8 (0.8^)                                           | 22.1^ (2.4, 45.5^) |

AAPC – average annual percent change, for the period 2007–2017; ^ AAPC is significantly different from 0 by alpha 0.05; 95% CI – 95% confidence interval; * standardization stopa prema populaciji sveta; - nemoguće izračunati trend zbog malih vrednosti stopa.
100.000) bile su u uzrastnim grupama 25 – 29 godina (muškarci 11,8 i žene 2,1) i 30 – 39 godina (muškarci 8,6 i žene 2,0). Prosečne standardizovane stope novodijagnostikovanih osoba inficiranih HIV-om bile su 4,3 puta veće za muškarce (3,4/100.000) nego za žene (0,8/100.000). Značajan porast stopa novodijagnostikovanih osoba inficiranih HIV-om, u posmatranom periodu 2007 – 2017, zabeležen je kod muškaraca za uzraste: 30 – 39 godina od 8,7% godišnje, 40 – 49 godina od 9,6% godišnje, i 50 – 59 godina od 15,4% godišnje, dok kod žena nije uočen značajan porast po uzrastnim grupama. Kada se posmatraju svi uzrasti zajedno, uočava se značajan porast standardizovanih stope novodijagnostikovanih osoba inficiranih HIV-om, kod muškaraca od 7% godišnje, a kod žena od 22,1% godišnje.

U periodu od 2007. do 2017. godine u Srbiji je 458 muškaraca i 77 žena obolelo od AIDS-a (Tabela 2). Prosečno su godišnje od AIDS-a obolevala 42 muškarca i 7 žena. Najveće uzrastno-specifične stope incidencije za AIDS (na 100.000) bile su u uzrastnim grupama 40 – 49 godina (2,7 muškarci i 0,5 žene) i 30 – 39 godina (2,6 muškarci i 0,4 žene). Prosečne standardizovane stope incidencije za AIDS bile su 4,5 puta veće za manje stope incidenca za AIDS bile su, odnosno.

| Age     | Broj osoba oboljelih od AIDS-a za period 2007 – 2017 | Prosečne stope incidencije AIDS-a | AAPC (95% IP) | Broj osoba oboljelih od AIDS-a za period 2007 – 2017 | Prosečne stope incidencije AIDS-a | AAPC (95% CI) |
|---------|-----------------------------------------------------|----------------------------------|---------------|-----------------------------------------------------|----------------------------------|---------------|
| 0 – 14  | 3                                                   | 0.0                              | -             | 2                                                   | 0.0                              | -             |
| 15 – 19 | 0                                                   | 0.0                              | -             | 0                                                   | 0.0                              | -             |
| 20 – 24 | 15                                                  | 0.6                              | 2.1 (-31.3, 51.8) | 1                                                   | 0.0                              | -             |
| 25 – 29 | 54                                                  | 2.0                              | 4.6 (-8.8, 19.9) | 5                                                   | 0.2                              | -             |
| 30 – 39 | 143                                                 | 2.6                              | 7.5^ (1,14.2) | 24                                                  | 0.4                              | -27.8^ (-45.5, -4.3) |
| 40 – 49 | 141                                                 | 2.7                              | 7.2^ (0.9, 13.9) | 27                                                  | 0.5                              | -22.6 (-44.3, 7.6) |
| 50 – 59 | 71                                                  | 1.3                              | 19.8^ (6.2, 35.1) | 15                                                  | 0.3                              | 16.9 (-18.3, 67.2) |
| 60+     | 31                                                  | 0.4                              | 10.2 (-22.2, 56.3) | 3                                                   | 0.1                              | -14.3^ (-25.9, -0.8) |
| Ukupno / Total | 458                                             | 1.2 (0.9^*)                     | 4.9^ (0.6, 9.4) | 77                                                  | 0.2 (0.2^*)                     | -12.2^ (-20.7, -2.9) |

AAPC – prosečna procentualna godišnja promena za period 2007–2017; ^ AAPC je značajno različito od 0 za alfa 0,05; 95% IP – 95% interval poverenja; ^ standardizovana stope prema populaciji sveta; - nemoguće izračunati trend zbog malih vrednosti stopa

In Serbia, in the period between 2007 and 2017, 458 men and 77 women developed AIDS (Table 2). On average, 42 men and 7 women developed AIDS each year. The highest age-specific incidence rates for AIDS (per 100,000) were in the age groups: 40 – 49 years, (2.7 for men and 0.5 for women) and 30 – 39 years (2.6 for men and 0.4 for women). The average standardized incidence rates for AIDS were 4.5 times higher for men (0.9/100,000) than for women.
muškarce (0,9/100.000) nego za žene (0,2/100,000). A significant rise in AIDS incidence rates in men, during the observation period, was registered for the age groups: 30 – 39 years, amounting to 7.5% per year; 40 – 49 years, amounting to 7.2% per year; 50 – 59 years, amounting to 19.8% per year; as well as 4.9% per year for all ages combined. However, when age-specific rates are observed in women, a significant yearly decline is apparent, amounting to: -27.8%, for the age group of 30 – 39 years; -14.3%, for the age group of persons over 60 years; as well as -12.2%, for all ages combined.

U Srbiji je u periodu od 2007. do 2017. godine od AIDS-a umro 171 muškarac i 31 žena (Tabela 3). Prosečno je godišnje od AIDS-a umiralo 16 muškarca i 3 žene. Najveće stope mortaliteta (na 100.000) bile su u uzrastnoj grupi 40 – 49 godina kod muškaraca (1,1) i kod žena za uzraste 30 – 39 i 40 – 49 (0,2). Prosečne standarizovane stope mortaliteta od AIDS-a bile su četiri puta veće za muškarce (0,4/100.000) nego za žene (0,1/100.000). Kada se posmatraju trendovi kretanja uzrasno-specifičnih i standardizovanih stope mortaliteta, kod muškaraca za poslednjih jedanaest godina nema značajnih promena, dok je kod žena prisutan značajan porast stope mortalitete kod žena.

**Tabela 3.** Broj umrlih od AIDS-a, prosečne uzrasno-specifične i standardizovane stope mortaliteta* (na 100.000) i joinpoint regresiona analiza, Srbija, 2007–2017.

| Uzrast | Muškarci / Men | Žene / Women |
|--------|----------------|---------------|
| Age | Number of AIDS-related deaths for the period 2007–2017 | Average AIDS-related mortality rates | AAPC (95% CI) | Number of AIDS-related deaths for the period 2007–2017 | Average AIDS-related mortality rates | AAPC (95% CI) |
| 0 – 14 | 2 | 0.0 | - | 0 | 0.0 | - |
| 15 – 19 | 0 | 0.0 | - | 0 | 0.0 | - |
| 20 – 24 | 5 | 0.2 | - | 1 | 0.0 | - |
| 25 – 29 | 16 | 0.6 | -2.3 (-38.6, 55.4) | 1 | 0.0 | - |
| 30 – 39 | 40 | 0.7 | -0.2 (-10.4, 11.2) | 11 | 0.2 | - |
| 40 – 49 | 55 | 1.1 | -13.1 (-36.7, 19.1) | 11 | 0.2 | -25.8^ (-43.5, -2.6) |
| 50 – 59 | 35 | 0.6 | 2.9 (-10.5, 18.2) | 6 | 0.1 | - |
| 60+ | 18 | 0.2 | -13.5 (-34.8, 15.0) | 1 | 0.01 | - |
| Ukupno / Total | 171 | 0.4 (0.4*) | -1.6 (-15.9, 15.0*) | 31 | 0.1 (0.1*) | -13.9^ (-25.3, -0.7)* |

AAPC – prosečna procentualna godišnja promena za period 2007–2017; AAPC – average annual percent change, for the period 2007–2017; ^ AAPC je značajno različito od 0 za alfa 0,05; ^ AAPC is significantly different from 0 by alpha 0.05; 95% IP – 95% interval poverenja; 95% CI – 95% confidence interval; * standardizovana stopa prema populaciji sveta; * standarded rate according to the world population; - nemoguće izračunati trend zbog malih vrednosti stopa; - impossible to calculate the trend due to small rate values.
godišnji pad od -25,8% za uzrast 40 – 49 godina, kao i za sve uzraste od -13.9%.

Prema testu uporedivosti trendova stopa novodijagnostikovanih osoba inficiranih HIV-om, između polova, kao i stopa incidencije AIDS-a, između muškaraca i žena, trendovi su bili paralelni (konačni izabrani model nije uspeo da odbaci paralelizam, $p = 0.221$ za HIV i $p = 0.093$ za AIDS) (Grafikon 1, a i b). Međutim, prema testu uporedivosti, trendovi stopa mortaliteta od AIDS-a kod muškaraca i žena nisu bili paralelni (konačni izabrani model odbacio je paralelizam, $p = 0.037$) (Grafikon 1, c).
Stope mortaliteta od AIDS-a kod žena značajno su opa-
dale za 13,9% godišnje, dok kod muškaraca nije bilo zna-
čajne promene u celokupnom posmatranom periodu.

Prema načinu transmisije, tokom perioda od 2007.
do 2017. godine, kod muškaraca kojima je novodija-
gnostikovana HIV infekcija, nezaštićeni analni seksu-
alni kontakt među muškarcima je bio najčešći način
transmisije (69,0%), (Grafikon 2), zatim heteroseksu-
alni odnos (13,9%), korišćenje droge injektiranjem
rejcting parallelism, \( p = 0.037 \) (Figure 1, c). AIDS-relat-
ed mortality rates in women decreased significantly by
13.9% per year, while in men there was no significant
change in the whole observation period.

As to the modes of transmission, during the peri-
od between 2007 and 2017, in men newly diagnosed
with HIV infection, unprotected anal sexual intercourse
amongst men was the most common way of trans-
mission (69.0%) (Figure 2); followed by heterosexual

![Grafikon 2](image_url)

**Grafikon 2.** Procentualno učešće novodijagnostikovanih osoba inficiranih
HIV-om prema prijavljenom putu transmisije infekcije u odnosu na sve osobe
inficirane HIV-om, muškarci (a) i žene (b), Srbija, 2007–2017.

**Figure 2.** Percentage of newly diagnosed persons infected with HIV according
to the reported route of transmission of infection in relation to all HIV-infected
persons, men (a) and women (b), Serbia, 2007–2017.

MSM – Men who have sex with men;
IDU – Intravenous drug users;
MTCT – Mother-to-child transmission
(3,9%), transmitisja sa majke na dete (0,6%), primacii faktora koagulacije i preparata krvi usled deficita faktora koagulacije (0,1%), dok je za 12,5% muškaraca način transmitisje bio nepoznat. U posmatranom periodu, u MSM populaciji registruje se rastući trend novodijagnostikovanih muškaraca inficiranih HIV-om, dok se kod injektirajućih korisnika droga zapaža pad. Kod žena je, u posmatranom periodu, dominantan put prenosa bio nezaštićen heteroseksualni odnos (75,7%), dok je injektirajućih korisnika droga (IKD) bilo 14,2%, transmitisja sa majke na dete je bilo 2,7%, a primacna transfuzije 0,7%. Za 6,1% žena put prenosa ostao je nepoznat.

DISKUSIJA

U Srbiji su, u periodu od 2007. do 2017. godine, prosečne standardizovane stope (na 100,000) inficiranih HIV-om iznosile 3,4 za muškarce i 0,8 za žene, odnosno bile su 4,3 puta veće kod muškaraca nego žena. Kod muškaraca je, u posmatranom periodu, došlo do prosečnog godišnjeg porasta stope inficiranih HIV-om za 7%, a kod žena za 22,1%. Najveći prosečan godišnji porast (+15,4%) bio je kod muškaraca u uzrastu 50 – 59 godina, a kod žena u svim uzrasnim grupama nije postojala značajna promena.

Istraživanje sprovedeno u Rumuniji imalo je za cilj utvrdivanje situacije u Rumuniji od 2017. do 2027. godine. Utrdreno je da postoji značajna promena u stope inficiranih HIV-om od 2004. do 2016. godine, progresivna kretanja infekcije u Rumuniji od 2017. do 2027. godine. Utvrđeno je da postoji značajna promena u stope inficiranih HIV-om od 2004. do 2016. godine, kao i da se broj obolelih od AIDS-a povećao za 60,3%. Međutim, u Rumuniji, uprkos dostupnosti lekovitog lečenja i nezakonitih korisnika droga, u posmatranom periodu, u MSM populaciji registruje se rastući trend novodijagnostikovanih muškaraca inficiranih HIV-om, dok je kod žena za 22,1%.

DISCUSSION

In Serbia, in the period between 2007 and 2017, the average standardized rates (per 100,000) of HIV-infected persons were 3.4, for men, and 0.8, for women, i.e. they were 4.3 times higher in men than in women. In men, in the observation period, there was an average annual increase in the rate of HIV-infected persons of 7%, and in women this increase was 22.1%. The greatest average yearly increase (+15.4%) was in men aged 50 – 59 years, and in women, there was no significant change in any of the age groups.

Research in Romania was carried out with the aim of predicting, on the basis of data on the dynamics of AIDS between 2004 and 2016, the infection trends in Romania from 2017 to 2027. It was established that there was a significant rise, amounting to 71%, in the number of HIV-infected persons between 2004 and 2016, as well as that the number of AIDS patients increased by 60.3%. Also, despite the availability of medication, treatment and care for AIDS patients in Romania, only a negligible decrease in the number of people dying from AIDS occurred. The largest number of HIV infected persons was in the age group of 26 – 30 years, which coincides with the epidemiological situation in Serbia [9]. It is interesting that in Spain, the highest rates of newly diagnosed HIV-persons were in persons under the age of 20 years, although their absolute number was small, while the next age group with the highest rates was the one from 35 to 39 years. Jointpoint analysis showed an increase in the rate of newly diagnosed HIV-infected persons in the period between 2000 and 2009, but stratification by modes of transmission showed that a rising trend was present only in the MSM population [10]. According to the results of another study carried out in Spain, which followed the seroprevalence of the HIV infection and infection caused by the hepatitis C virus (HCV), in the period 2008 – 2012, HIV infection was more frequent in men, HIV and HCV infection rates were the highest in persons born between 1955 and 1970, and
the peaks of these infections overlapped. The seroprevalence of the HIV infection increased with the year of birth for persons born before 1965 (53.4% per year), after which it decreased by 27.1% per year. As HIV and HCV have the same pathways of transmission, it is believed that the rise can be explained by the epidemic of injection drug abuse during the eighties of the 20th century, while in recent years, the main pathway of transmission has been sexual contact (more than 90% of newly HIV-infected persons). Consequently, the prevalence of HIV infection is on the rise in the younger population [12].

In a study by Li et al., the epidemiological situation regarding HIV infection and the development of AIDS, as well as AIDS-related mortality was analyzed in China, in the period between 2004 and 2011 [12]. A continuous rise in the rate of newly diagnosed HIV-infected persons was determined. Mortality was efficiently controlled due to certain measures which were primarily directed towards therapy. Free testing was made available, as well as free therapy for economically vulnerable groups. Counselling and free antiretroviral therapy was provided for pregnant women infected with HIV. This study monitored rates in different regions of China. While the mortality rate at the level of the whole country is under control, in certain regions, such as Gansu and Ningxia, the mortality rate is on the rise. This is attributed to multiple factors, such as unfavorable economic situation, poor access to health care in these regions, poor acceptance of testing, the large number of patients affected by the disease who are hiding their health status, and the presence of numerous opportunistic infections.

The number of newly diagnosed HIV-infected persons in the WHO European Region has risen by 22% in the last decade. The rate of newly diagnosed HIV infections has risen by 14% in the previous 10 years from 14.2 in 2009 to 16.2 in 2018. This increase is primarily the result of the rise in the number of HIV-infected persons in Eastern Europe. The comparison of the number of new diagnoses with the estimated number of new HIV infections over the past decade has shown that more people contracted HIV than was diagnosed, which indicates that the number of undiagnosed HIV-infected persons in the region is rising [13].

In Serbia, in the 11-year observation period, a significant rise in the incidence of AIDS amounting to 4.9% per year occurred in men, while in women a significant decline of 12.2% per year was registered. A study from 2017, which followed the trend of AIDS in Italy from 1999 to 2014, could provide explanations for the rise in men contracting the disease. It was noted that men are more frequently unaware of being infected, which is why they begin treatment later. The study offers several potential explanations. Firstly, women are more often offered testing, for instance during pregnancy. Secondly, it is possible...
iz Španije, gde je 56% testiranih bilo ženskog pola, što je u skladu sa preporukama za prenatalko testiranje [11]. U Srbiji, najveći porast uzrastno-specifičnih sto-pa incidencije kod muškaraca bio je u uzrastu 50 – 59 godina, i to 19,8% godišnje. U Italiji je uočeno da je veća verovatnoća da se osobe uzrasta 50 i više godišnja kasno testiraju, u poredenju sa osobama uzrasta 35 – 49 godina [14]. Mogoće je da su starije osobe manje svesne rizika od inficiranja HIV-om, sa obzirom da su preventive mere i usluge prevashodno usmere-ne ka mlađoj populaciji. Pored toga, socijalna stigma i diskriminacija izraženije su kod starijih, što stvara bariju da testiranju na HIV, tako da se neke bolesti koje se javljaju kod starijih ne prepoznaju kao bolesti indikative za AIDS, što može dovesti do kasnjeg po-stavljanja dijagnoze [14,15].

U Srbiji su u periodu 2007 – 2017. godine stope mortaliteta od AIDS-a kod muškaraca bile stabilne, dok je kod žena zabeležen značajan pad od 13,9%. Kod žena se pad beleži u uzrastu 40 – 49 godina od 25,8%. Od 1997. godine visokoaktivna antiretrovirusna terapija (engl. Highly Active Antiretroviral Therapy – HAART) dostupna je i besplatna u Republici Srbiji, tj. svi troško-vi lečenja idu na teret Republikog fonda za zdravstveno osiguranje za sve zdravstvene osiguranike kojima je lečenje indikovano. U Alžiru je, od uvođenja HAART-a 1998. godine, došlo do značajnog pada stope mortaliteta od AIDS-a. Procenat osoba inficiranih HIV-om koje su bile na terapiji je rastao, da bi u 2010. godini bio naj-viši (84%). Stope mortaliteta su se sa 200,2, pre uvođe-nja HAART-a, spustile na vrednost od 91,4 na 100.000. Od 2003. godine stopa mortaliteta se, prema joinpoint analizi, smanjila za 66,1% godišnje, da bi nakon 2006. došlo do porasta [16].

U studiji koja je ispitivala trend prijema u bolnicu, ponovnog prijema, kao i smrtnost inficiranih HIV-om u periodu 1993 – 2013, u univerzitetskoj bolnici na se-verozapad Španiji, došlo je do pada mortaliteta od bolesti koje su u vezi sa AIDS-om od 49% [17]. U Brazilu se u periodu 2000 – 2011. beleži značajan pad stopa mortaliteta od tuberkuloze kod osoba sa HIV/AIDS-om od 1,7% godišnje, sa značajnim regionalnim varijacijama. Pad je značajan za muškarce (-2,4%), dok je trend stabilan za žene. Pad je značajan za uzrastne grupe 20 – 29 i 30 – 39 godina. U starijim uzrastima (50 – 59, 60 – 69, 70 – 79 godina) beleži se značajan rastući trend mortaliteta. Mortalitet u pedijatrijskim i mladim uzra-stima, kao i za uzrast 40 – 49 godina ostao je stabilan tokom perioda ispitivanja [18].

U Srbiji je u posmatranom vremenskom periodu najčešći način transmisije novodijagnostikovane HIV infekcije zabeležen među MSM populacijom (69% inficiranih). U posmatranom periodu, među MSM that women more often access healthcare than men [14]. This is also supported by data from Spain, where 56% of those tested were female, which is in keeping with rec-ommendations for prenatal testing [11]. In Serbia, the greatest rise in age-specific incidence rates in men was in the age group of 50 to 59 years, amounting to 19.8% per year. In Italy, also, it was established that it was more probable for people over 50 years to get tested late, as compared to people aged between 35 and 49 years [14]. It is possible that older persons are less aware of the risk of being infected with HIV, since preventive measures and services are primarily directed towards the younger population. Also, social stigma and discrimination are more pronounced in older people, thus creating a barrier towards HIV testing, which is why certain diseases occurring in older patients are not recognized as indicative of AIDS, which can lead to later diagnosis [14,15].

In Serbia, in the period between 2007 and 2017, AIDS-related mortality rates in men were stable, while in women, a significant decline of 13.9% was regis-tered. In women, the decline registered in the age group of 40 – 49 years was 25.8%. Since 1997, highly active antiretroviral therapy (HAART) has been available and free in the Republic of Serbia, i.e. all costs of treatment are charged to the Health Insurance Fund of the Republic of Serbia for all health insurance beneficia ries indicated for treatment. In Algeria, after the introduction of HAART, in 1998, a significant decrease in AIDS-related mortality occurred. The percentage of HIV-infected persons on therapy rose, reaching the highest value in 2010 (84%). Mortality rates dropped from 200.2, before the introduction of HAART, to 91.4, per 100,000. As of 2003, the mortality rate, according to the joinpoint analysis, decreased by 66.1% per year, only to start rising after 2006 [16].

In a study testing the trend of hospital admission, readmission, and the mortality of HIV infected persons, in the period between 1993 and 2013, at a university clinic in North-West Spain, a decrease of 49% in mor-tality from AIDS-related diseases was registered [17]. In Brazil, in the period between 2000 and 2011, a sig-nificant drop of 1.7% per year in tuberculosis mortality rates was registered in persons with HIV/AIDS, with sig-nificant regional variations. The drop was significant for men (-2.4%), while the trend was stable for women. The decrease was significant for the age groups of 20 – 29 and 30 – 39 years. In the older age groups (50 – 59, 60 – 69, 70 – 79) a significant rising mortality trend was registered. Mortality in pediatric and younger adult age groups, as well as for the age group of 40 – 49 years re-mained stable during the observation period [18].

In Serbia, during the observation period, the most fre-quent mode of transmission of newly diagnosed HIV in-fection was noted in the MSM population (69% of infected
populacijom registruje se rastući trend novodijagnosticiranih i testiranih osoba pozitivnih na HIV, dok se kod injektirajućih korisnika droga zapaža pad. Kod žena je, u posmatranom periodu, dominantan put prenosa bio nezaštiten heteroseksualni odnos (75,7%). MSM populacija čini više od polovine novodijagnosticiranih osoba inficiranih HIV-om u zapadnoj i centralnoj Evropi, kojoj pripada i Srbija. Heteroseksualni kontakt (72%) i konzumiranje droga injektiranjem (23%) i dalje su glavni put prenošenja HIV-a u istočnoj Evropi [13].

Zabrinjava podatak iz Italije da je kod skoro dve trecine obolelih od AIDS-a, koji su se inficirali seksualnim kontaktom, kasno postavljena dijagnoza. Posebno visok rizik za kasnu dijagnozu imali su heteroseksuali, u poređenju sa injektirajućim korisnicima droge (IKD). Pretpostavlja se da programska prevencija nedovoljno pažnje posvećuju pojedincima koji imaju nisku svest o rizičnom seksualnom ponašanju i, na taj način, povećavaju verovatnoću zakasnelog testiranja na HIV [14].

Planirani ciljevi globalne strategije UNAIDS-a „90-90-90”, do ovog trenutka nisu dostignuti. U svetu je u 2018. godini bilo 79% osoba koje su živele sa HIV-om i koje su znale svoj pozitivan status, 62% osoba koje su znale svoj status bilo je na ARV terapiji, a 53% ljudi na ARV terapiji imalo je supresijusirusa. Procenjuje se da je u Srbiji krajem 2018. godine 3.000 osoba živele sa HIV-om, od kojih je 2.597 (86,6%) znalo svoj pozitivan status na HIV, dok je 72,5% dajagnostikovanih osoba inficiranih HIV-om bilo na ARV terapiji. I nakon 2020. godine ciljevi „90-90-90” ostaju najvažniji, signalizujući da su potrebna dodatna dodatna ulaganja u testiranja na HIV i programe lečenja. U svetu je 2018. godine 79% obolelih od AIDS-a, koji su se inficirali putem heteroseksualnog odnosa (75.7%). MSM populacija, uključujući njihove partnere, kao i žene, koje su se inficirale prijelaznom putem, bilo je u Srbiji 2018. godine 79% obolelih od HIV-a.

Ograničavajući faktor u našem istraživanju jeste činjenica da se u Srbiji, kao i u drugim zemljama sveta, registriraju samo novodijagnosticirane i prenovodijagnosticirane osobe inficirane HIV-om pri čemu se ne zna koliko dugo imaju infekciju, odnosno kada su inficirane. Trend novodijagnosticiranih stanovnika Hrvatske u svom većem delu je usklađen s užetima standardima Ljubljana, iako se može izraziti iznimno izuzetna situacija u vidu raste u novodijagnosticiranosti u novom epidemijskom letu 2020. godine.

In the observation period, a rising trend of newly diagnosed HIV positive men was registered in the MSM population, while a decline was registered amongst the population of injection drug users. In women, during the observation period, the dominant pathway of transmission was unprotected sexual intercourse (75,7%). The MSM population constituted more than half of newly diagnosed HIV-infected persons in Western and Central Europe, which Serbia is a part of. Heterosexual intercourse (72%) and injection drug abuse (23%) remained the main pathways of HIV transmission in Eastern Europe [13].

The data from Italy indicating that almost two thirds of AIDS patients, who had become infected through sexual intercourse, were diagnosed late, is alarming. Heterosexuals had a particularly high risk of late diagnosis, as compared to injection drug users (IDUs). The assumption is that prevention programs do not pay enough attention to individuals with low level of awareness regarding risky sexual behavior and, in that way, the probability of late HIV testing is increased [14].

Planned goals of the global UNAIDS 90-90-90 strategy have not as yet been achieved. Globally, in 2018, there were 79% of people living with HIV who were aware of their HIV positive status, 62% of people with HIV positive status were on ARV therapy, and 53% of people on ARV therapy had viral suppression. It is estimated that, in Serbia, at the end of 2018, 3,000 persons were living with HIV, 2,597 (86.6%) of whom were aware of their HIV positive status, while 72.5% of diagnosed HIV-infected persons were on ARV therapy. Even after 2020, the 90-90-90 goals remain of utmost importance, indicating that additional efforts and investments need to be made in HIV testing and treatment programs, in order to end AIDS epidemic by 2030.

A limiting factor in this study is the fact that in Serbia, just like in other countries in the world, newly diagnosed HIV-infected persons are only registered, without any definite knowledge as to how long the patients have been infected, i.e. when the infection was contracted. The trend of newly diagnosed cases of HIV infection depends on the efficiency of the infection that persons are diagnosed in, as well as on the scope of testing for persons at increased risk of HIV infection; thus it does not reflect HIV infection incidence in the population, nor does it represent the overall prevalence of the HIV infection. Consequently, it is not clear whether the rise in the number of newly diagnosed HIV-infected persons is the result of an increase in the number of newly infected persons, or the result of more comprehensive testing, especially amongst key populations, which are at increased risk. The latest WHO recommendations require of Serbia, as well, to take such steps that would enable the first, most important one, and that is to provide free and open access to voluntary confidential counselling services and HIV testing, with
paralelno smanjivanje stigme i diskriminacije za osobe inficirane HIV-om, kao i uspešno sprečavanje prenošenja HIV infekcije, posebno u ključnim populacijama u visokom riziku za HIV.

ZAKLJUČAK

Za posmatran period od 2007. do 2017. godine u Srbiji utvrđena je znatno veća stopa novodijagnostikovanih osoba inficiranih HIV-om kod muškaraca nego kod žena. Pad oboljevanja i umiranja od AIDS-a nije istovremeno praćen i smanjenjem broja novodijagnostikovanih osoba inficiranih HIV-om, pa uz produžen životni vek raste i ukupan broj osoba koje žive s HIV-om, dok udeo osoba koje ne znaju svoj pozitivan status na HIV predstavlja rizik za dalju transmisiju infekcije. Javnoodržavstvene mere prvenstveno treba da budu usmerene na prevenciju nastanka infekcije. Potrebno je dalje raditi na unapređenju preventivnih mera, posebno edukaciji mladih o putevima prenosjenja i rizicima, kao i na ron u otkrivanju osoba inficiranih HIV-om i pravovremenom lečenju. Važno je povećati broj savetovanih i testiranih osoba iz ključnih populacija pod povećanim rizikom za HIV. Rano dijagnostikovanje HIV infekcije i pravovremena terapija doprinose smanjivanju transmisije infekcije na osetljivu populaciju.

Zahvalnica: Ovaj rad je finansiran sredstvima projekta br. 175042 Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije.

Sukob interesa: Nije prijavljen.

LITERATURA / REFERENCES

1. UNAIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic [Internet]. Geneva, Switzerland: UNAIDS; 2014. [citirano jul 2020.]. Dostupno na: http://www.unaids.org/en/resources/documents/2014/90-90-90.
2. UNAIDS. UNAIDS data 2019. Joint United Nations Programme on HIV/AIDS [Internet], Geneva, Switzerland: UNAIDS; 2019. [citirano jul 2020.]. Dostupno na: https://www.unaids.org/sites/default/files/media_asset/2019-UNAIDS-data_en.pdf
3. Institut za javno zdravlje „Dr Milan Jovanović Batut“. Izveštaj o zaraznim bolestima u Republici Srbiji za 2018. godinu [Internet]. Beograd, Republika Srbija: Institut za javno zdravlje „Dr Milan Jovanović Batut“; 2019. [citirano jul 2020.]. Dostupno na: http://www.batut.org.rs/index.php?content=1997
4. Institut za javno zdravlje „Dr Milan Jovanović Batut“. Izveštaj o zaraznim bolestima u Republici Srbiji (2007–2017. godina). Beograd, Republika Srbija: Institut za javno zdravlje „Dr Milan Jovanović Batut“; 2007–2017. [citirano jul 2020.]. Dostupno na: http://www.batut.org.rs/index.php?category_id=140
5. Segi M. Cancer mortality for selected sites in 24 countries (1950–57). Sendai, Japan: Department of Public Health, Tohoku University of Medicine; 1960.
6. Kim H-J, Fay MP, Barrett MJ, Feuer EJ. Comparability of segmented line regression models. Biometrics. 2004; 60(4):1005–14.
7. Felicia A. Trends of HIV/AIDS Phenomenon Dynamics in Romania from 2017-2027. Iran J Public Health, 2019; 48(10):1903–9.
8. Diez M, Bleda MJ, Varela JR, Ordonana J, Azpiri MA, Vall M, et al. Trends in HIV testing, prevalence among first-time testers, and incidence in most-at-risk populations in Spain: the EPI-VIH Study, 2000 to 2009. Euro Surveill. 2014; 19(47):20971.
9. Mena A, Morales L, Mejide H, Cañizares A, Castro-Iglesias A, Delgado M, et al. Seroreivalence of HCV and HIV infections by year of birth in Spain: impact of US CDC and USPSTF recommendations for HCV and HIV testing. PLoS ONE. 2014; 9(12): e113062.
10. Li M, Shen Y, Jiang X, Li Q, Zhou X, Lu H. Clinical epidemiology of HIV/AIDS in China from 2004–2011. Biosci Trends. 2014; 8(1):52–8.
11. European Centre for Disease Prevention and Control/WHO Regional Office for Europe. HIV/AIDS surveillance in Europe 2019 – 2018 data. Stockholm, Sweden: ECDC; 2019. [citirano jul 2020.]. Dostupno na: https://www.ecdc.europa.eu/en/publications-data/hiv-aids-surveillance-europe-2019-2018-data
12. Taborelli M, Virdone S, Camoni L, Regine V, Zucchetto A, Frova L, et al. The persistent problem of late HIV diagnosis in people with AIDS: a population-based study in Italy, 1999-2013. Public Health. 2017; 142:39–45.

CONCLUSION

For the observation period from 2007 to 2017, in Serbia, a significantly higher rate of newly diagnosed HIV-infected persons was registered for men than for women. The decline in the number of patients developing AIDS and in AIDS-related mortality was not simultaneously followed by a decrease in the number of newly diagnosed HIV-infected persons, which is why, with a prolonged life span, the total number of persons living with HIV is increasing, while the portion of people unaware of their HIV positive status represents a risk factor for further infection transmission. Public health measures need to primarily be directed towards the prevention of infection. It is necessary to work further on improving preventive measures, especially on educating the young population on the pathways of transmission and the risks, as well as on early detection of HIV-infected persons and timely treatment. It is important to increase the number of counselled and tested persons in the key populations, who are at a higher risk of HIV infection. Early diagnosis of the HIV infection and timely treatment contribute to the decrease in infection transmission in vulnerable populations.

Acknowledgements: This paper was funded by project No. 175042 of the Ministry of Education, Science and Technological Development of the Republic of Serbia.

Conflict of interest: None declared.
15. Emlet CA. “You’re awfully old to have this disease”: experiences of stigma and ageism in adults 50 years and older living with HIV/AIDS. Gerontologist. 2006; 46(6):781–90.

16. Chaabna K, Newton R, Vanhems P, Laouar M, Forman D, Boudiaf Z, et al. Cancer incidence and all-cause mortality in HIV-positive patients in North-eastern Algeria before and during the era of highly active antiretroviral therapy. J Cancer Res Ther. 2016; 12(2):576–81.

17. Meijide H, Mena Á, Rodríguez-Osorio I, Pértega S, Castro-Iglesias Á, Rodríguez-Martínez G, et al. Trends in hospital admissions, re-admissions, and in-hospital mortality among HIV-infected patients between 1993 and 2013: Impact of hepatitis C co-infection. Enferm Infec Microbiol Clin. 2017; 35(1):20–6.

18. Lima M da S, Martins-Melo FR, Heukelbach J, Alencar CH, Boigny RN, Ramos AN. Mortality related to tuberculosis-HIV/AIDS co-infection in Brazil, 2000-2011: epidemiological patterns and time trends. Cad Saude Publica. 2016; 32(10): e00026715.