# ЭПИДЕМИОЛОГИЯ
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## HIV-INFECTION IN THE RUSSIAN FEDERATION: CURRENT DIAGNOSTIC TRENDS

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**The aim of the study:** to analyse diagnostic trends of HIV-infection in the Russian Federation in the period 2017–2022.
**Materials and methods.** The study used data obtained from reports from the Federal Register of persons infected with the human immunodeficiency virus (FRHIV). The circumstances in HIV diagnosis and clinical and epidemiological characteristics of newly diagnosed patients, including CD4+ T-lymphocyte counts, were analysed. A likely time window between presumed infection and confirmation of HIV diagnosis was also determined. Categorical data evaluated in the study were presented as proportions and caparisoned using the chi-square test ($\chi^2$). In case of multiple comparisons, the Bonferroni correction for multiplicity was used. Quantitative data were tested for normality using the Kolmogorov-Smirnov criterion. In most cases, nonparametric characteristics of distributions — median and interquartile range — were applied, as well as the Mann-Whitney criteria for comparison of two independent groups and the Kraskell-Wallis criteria for comparison more than two groups, followed by pair wise comparisons using the Mann-Whitney criterion with Bonferroni multiplicity correction. A $p$-value<0.05 was considered statistically significant. Data analysis and graphical visualization was performed using the statistical software R version 4.1.1 and its libraries.
**Results and discussion.** The results showed an increase in HIV detection through voluntary testing, preventive medical examination, and clinical indications. The proportion of injecting drug users (IDUs) decreased over time, while the involvement of women in the epidemic process and heterosexual transmission increased. Additionally, there was an increase in the proportion of patients aged 35 years and older. The analysis of CD4-cell counts revealed significant differences among gender and age subgroups. Women had higher absolute CD4-lymphocyte counts throughout the follow-up period. Patients aged 0–14 years had the highest proportion of CD4-lymphocytes over 500 cells/μL, while patients over 50 years old had the highest proportion of CD4-lymphocytes less than 200 cells/μL. Men who have sex with men and people infected through mother-to-child transmission had the highest mean baseline CD4-cell counts. IDUs and heterosexuals had a statistically significant decrease in CD4-cell counts over the follow-up period and also had the longest median time from infection to disease detection — 24 and 20 months, respectively.
**Conclusion:** Thus, this study helps identify the most significant risk groups of HIV-infected individuals in Russia at present.

**Key words:** HIV-infection; circumstances in HIV diagnosis; CD4-cell counts; the Russian Federation

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## ВИЧ-ИНФЕКЦИЯ В РОССИЙСКОЙ ФЕДЕРАЦИИ: СОВРЕМЕННЫЕ ТЕНДЕНЦИИ ДИАГНОСТИКИ

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**Цель:** проанализировать тенденции диагностики ВИЧ-инфекции в Российской Федерации в период 2017–2022 гг.
**Материалы и методы.** В исследовании использовались данные, полученные из отчетов Федерального регистра лиц, инфицированных вирусом иммунодефицита человека (ФРВИЧ). Были проанализированы обстоятельства диагностики ВИЧ, а также клинико-эпидемиологические характеристики впервые выявленных пациентов, в том числе количество CD4+ Т-лимфоцитов. Также был определен вероятный временной интервал между предполагаемым инфицированием и подтверждением диагноза «ВИЧ-инфекция». Категориальные данные, оцененные в исследовании, были представлены в виде пропорций и сравнены с использованием критерия хи-квадрат ($\chi^2$). В случае множественных сравнений использовалась поправка Бонферрони. Количественные данные проверялись на нормальность с использованием критерия Колмогорова–Смирнова. В большинстве случаев применялись непараметрические характеристики распределений — медиана и межквартильный размах, а также критерий Манна–Уитни для сравнения двух независимых групп и критерий Краскела–Уоллиса — для сравнения более двух групп с последующими попарными сравнениями с использованием критерий Манна–Уитни с поправкой Бонферрони. Значение $p<0,05$ считалось статистически значимым. Анализ данных и графическую визуализацию проводили с использованием статистического программного обеспечения R версии 4.1.1 и его библиотек.
**Результаты и их обсуждение.** Результаты показали рост выявляемости ВИЧ при добровольном тестировании, а также при профилактических медицинских осмотрах и по клиническим показаниям. Доля потребителей инъекционных наркотиков (ПИН) со временем снизилась, а вовлеченность женщин в эпидемический процесс и доля инфицирования при гетеросексуальных контактах возросли. Кроме того, наблюдалось увеличение доли пациентов в возрасте 35 лет и старше. Анализ количества CD4-клеток выявил существенные различия между подгруппами по признаку пола и возраста. У женщин было более высокое абсолютное количество CD4-лимфоцитов на протяжении всего периода наблюдения. У пациентов в возрасте 0–14 лет была самая высокая доля CD4-лимфоцитов (более 500 клеток/мкл), тогда как у пациентов старше 50 лет была самая высокая доля CD4-лимфоцитов (менее 200 клеток/мкл). Мужчины, практикующие секс с мужчинами, и люди, инфицированные в результате передачи вируса от матери ребенку, имели самый высокий средний исходный уровень CD4-клеток. У ПИН и гетеросексуалов наблюдалось статистически значимое снижение количества CD4-клеток в течение периода наблюдения, а также самое продолжительное среднее время от заражения до выявления заболевания — 24 и 20 мес соответственно.
**Заключение.** Таким образом, данное исследование позволяет выявить наиболее значимые группы риска ВИЧ-инфицированных в России в настоящее время.

**Ключевые слова:** ВИЧ-инфекция; обстоятельства диагностики ВИЧ; количество CD4-клеток; Российская Федерация

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**Introduction.** Currently, HIV-infection remains a global public health issue. According to UNAIDS, about 1.3 million people were newly diagnosed with HIV-infection in 2022[1]. Rates of HIV-infection and HIV testing vary widely around the world and depend on the region [1]. However, the World Health

[1] https://www.unaids.org/en/resources/fact-sheet [Internet]. Accessed on 28.12.2023.

Organization (WHO) estimates that as of 2022, 5.5 million people with HIV-infection still did not know their HIV status. To ensure an effective HIV testing service, the WHO recommends reaching the greatest number of people with HIV who remain undiagnosed and reaching the population groups with higher risk of HIV-infection[1]. The selection of testing groups requires in-depth knowledge and understanding of HIV-infection trends among countries, regions and key populations. A recent study in the Russian Federation showed a significant downward trend in HIV incidence and a significant upward trend in HIV testing coverage [2].

In order to monitor the epidemiological situation, the Ministry of Health of the Russian Federation maintains the Federal Register of persons infected with the human immunodeficiency virus (FRHIV) which contains clinical and epidemiological information about HIV-infected patients, including data on the circumstances under which HIV-infection was detected[2]. Thus, in the FRHIV the following groups of circumstances in HIV diagnosis can be distinguished: preventive medical examination, examination during pregnancy, medical examination for clinical indications, medical examination for epidemiological indications, after medical contact with HIV-infected persons; as well as HIV detection in narcological dispensaries, in skin and venereological dispensaries and in places of deprivation of liberty, voluntary testing for HIV-infection. In the Russian Federation, preventive medical examination for HIV-infection is required for donors of blood, biological fluids, organs and tissues, employees of certain professions (doctors, medical personnel, scientists and specialists in contact with HIV, persons performing military service)[3,4,5]. Persons in places of deprivation of liberty are also subjects to mandatory medical examination for HIV-infection[6]. In addition, according to clinical guidelines, it is recommended to test for HIV-infection twice during pregnancy[7]. Patients of narcological dispensaries and skin and venereological dispensaries are screened for HIV as vulnerable groups[8,9]. Persons diagnosed with HIV during medical examination for epidemiological indications and after medical contact with HIV-infected persons include those who have had direct contact with infected persons and participants in emergencies involving the introduction of virus-containing material into the blood and/or mucosal surfaces during the performance of professional medical activities, respectively[9]. Medical examination for clinical indications includes persons who have been referred by a doctor for HIV testing because they have signs of the acute phase of HIV-infection or AIDS-associated diseases[9]. The group of people undergoing voluntary HIV testing is large and diverse. It includes people who have been

[1] https://iris.who.int/bitstream/handle/10665/336323/9789241550581-eng.pdf?sequence=1 [Internet]. Accessed on 28.12.2023.

[2] Decree of the Government of the Russian Federation No. 426. On Approval of the Rules for Maintaining the Federal Register of Persons Infected with the Human Immunodeficiency Virus and the Federal Register of Persons with Tuberculosis. https://base.garant.ru/71654250/ [Internet]. Accessed on 28.12.2023. (In Russ.).

[3] Federal Law No. 38-FZ. On Preventing the Spread in the Russian Federation of Disease Caused by the Human Immunodeficiency Virus. https://base.garant.ru/10104189/ [Internet]. Accessed on 28.12.2023. (In Russ.).

[4] Order of the Ministry of Health of the Russian Federation No. 1129n. On Approval of the Rules for Mandatory Medical Examination for Detection of Human Immunodeficiency Virus. https://base.garant.ru/74886862/ [Internet]. Accessed on 28.12.2023. (In Russ.).

[5] Resolution of the Chief State Sanitary Doctor of the Russian Federation No. 4. On Approval of Sanitary Rules and Norms SanPiN 3.3686-21 "Sanitary and Epidemiological Requirements for the Prevention of Infectious Diseases". https://base.garant.ru/400342149/ [Internet]. Accessed on 28.12.2023. (In Russ.).

[6] Order of the Ministry of Health of the Russian Federation No. 1175n. On Approval of the Rules for Mandatory Medical Examination of Persons in Prison for Detection of Human Immunodeficiency Virus. https://base.garant.ru/74996001/ [Internet]. Accessed on 28.12.2023. (In Russ.).

[7] Clinical Guideline "HIV Infection in Pregnant Women". https://cr.minzdrav.gov.ru/schema/717_1 [Internet]. Accessed on 28.12.2023. (In Russ.).

[8] Order of the Ministry of Health of the Russian Federation No. 1034n. On Approval of the Procedure for the Provision of Medical Care in the Profile "Psychiatry-Narcology" and the Procedure for Dispensary Monitoring of Persons with Mental Disorders and (or) Behavioural Disorders Associated with the Use of Psychoactive Substances. https://base.garant.ru/71360612/ [Internet]. Accessed on 28.12.2023. (In Russ.)

[9] Methodological Guidelines "Epidemiological Surveillance of HIV-Infection". https://www.rospotrebnadzor.ru/documents/details.php?ELEMENT_ID=7883&ysclid=lqkrbd9mn839043931 [Internet]. Accessed on 28.12.2023. (In Russ.).

recommended by their doctors to undergo HIV testing: partners of pregnant women, children born to HIV-infected women, men who have sex with men (MSM), sex workers, and adults as part of medical examinations for epidemiological and clinical indications care or when seeking medical etc. This group also includes persons who decide to undergo HIV testing on their own6. Understanding the proportions of risk groups among newly diagnosed HIV-infected patients, as well as the circumstances in HIV diagnosis in the Russian Federation at the present stage is an important task.

In addition to analyzing the circumstances in HIV diagnosis among newly diagnosed HIV-infected patients, their clinical characteristics also play an important role. Thus, human infection with HIV-1 occurs when virus-containing material enters directly into the blood and/or mucosal surfaces. The main targets of HIV-1 are CD4+ T cells of the immune system and macrophages [3]. A central characteristic of acute HIV infection is a surge in viral load (VL) and the resulting damage to CD4+ T-lymphocytes. Then HIV-specific CD8+ T-cells for killing HIV-infected T-cells are produced and this led to VL declines and to partial restoration of CD4-cell level [1,4,5]. This is followed by a chronic phase characterised by a progressive decline in the CD4+ T-cells by an average of 50–100 cells/μL per year[1] [1,6]. The result of disorders in the immune system is a decrease in the organism resistance as a whole, as well as the development of a wide range of secondary diseases. Previous studies highlight the importance of monitoring CD4 counts in newly diagnosed HIV-infected individuals for epidemiological monitoring of HIV-infection [7–11].

According to the Center for Diseases Control and Prevention (CDC), the classification system for HIV-infection is based on the three ranges CD4+ T-lymphocytes counts and three clinical categories[12].

The three ranges CD4+ T-lymphocytes counts are defined as follows[2]:

Category 1: greater than or equal to 500 cells/μL;

Category 2: 200–499 cells/μL;

Category 3: less than 200 cells/μL.

Analysis of clinical and epidemiological data can help to identify the characteristics of newly diagnosed HIV-infected patients and to develop HIV prevention and treatment strategies targeting transmission groups. To date, several studies have been conducted in the Russian Federation to investigate the immune status of newly diagnosed HIV-infected [12]. However, the limitations of these studies were the small sample size or the study of the immune status of patients in a particular region of the country.

**The purpose** of this study was to analyse diagnostic trends of HIV-infection in the Russian Federation in the period 2017–2022: circumstances in HIV diagnosis and clinical and epidemiological characteristics of newly diagnosed patients, including CD4+ T-lymphocyte counts. This marks the first comprehensive examination of the diagnostic trends of HIV-infection in the Russian Federation.

**Materials and methods.** The following reports from the Federal Register of persons infected with the human immunodeficiency virus (FRHIV) were used:

— Report 168 — Log of patients entered in the FRHIV;

— Report 171 — Report on new cases of HIV-infection;

— Report 129 — Analytical report on patients with HIV+tuberculosis co-infection (additionally).

The data contained sociodemographic characteristics and blood test results at the first visit, as well as circumstances in HIV diagnosis. The sociodemographic characteristics data contained the following information: gender; the year of first visit; age at that time; route of infection (mother-to-child transmission (MTCT), heterosexual, men who have sex with men (MSM), injecting drug users (IDUs) and others); circumstances in HIV diagnosis (preventive medical examination, examination during pregnancy, medical examination for clinical indications, medical examination for epidemiological indications, after medical contact with HIV-infected persons; as well as HIV detection in narcological dispensaries, in skin and venereological dispensaries and in places of deprivation of liberty, voluntary testing for HIV-infection) and information on the estimated time of infection. The blood test results contained the CD4 cell counts. The data was uploaded on October 3, 2023 and merged using the outer join method using Python.

A likely time window between presumed infection and confirmation of HIV diagnosis was determined. Selection criteria: 1. availability of information on the estimated time of infection, 2. the difference (window:

[1] Clinical Guideline “HIV Infection in Adults”. https://cr.minzdrav.gov.ru/schema/79_1 [Internet]. Accessed on 28.12.2023. (In Russ.).

[2] https://www.cdc.gov/mmwr/preview/mmwrhtml/00018871.htm [Internet]. Accessed on 28.12.2023.

from... to...) in the estimated dates of infection was no more than 1 year. The first of the two dates of possible infection was used for the analyses.

We summarised all data descriptively and calculated the proportions of the components in each category for each year. To statistically determine whether a significant difference existed between proportions, the chi-square test ($\chi^2$) was employed. In case of multiple comparisons, the Bonferroni correction for multiplicity was used.

Quantitative data were tested for normality using the Kolmogorov-Smirnov criterion. In most cases, the distributions significantly differed from normal; therefore, nonparametric characteristics of distributions — median and interquartile range — were applied, as well as the Mann-Whitney criteria for comparison of two independent groups and the Kraskell-Wallis criteria for comparison more than two groups, followed by pair wise comparisons using the Mann-Whitney criterion with Bonferroni multiplicity correction. A $p$-value<0.05 was considered statistically significant.

The statistical software R version 4.1.1 (R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/) and its libraries were used for data analysis and graphical visualization.

**Results and discussion.** This analysis of diagnostic trends of HIV-infection in the Russian Federation provides useful insights on the changing natural history of HIV-infection in Russia and helps to assess the effectiveness of measures taken to counteract its spread. One of the main objectives of the State Strategy for counteracting the spread of HIV-infection in the Russian Federation is to reduce the number of new cases of infection[1]. A recent study conducted in Russia showed a significant downward trend in HIV incidence as well as an increase in HIV-testing coverage from 21.8% in 2016 to 32.2% in 2022 [2]. At the same time, it is very important to conduct HIV testing in the target groups. In the first part of this study we assessed the effectiveness of HIV testing in the Russian Federation by analysing the circumstances in HIV diagnosis among newly diagnosed HIV-infected patients. Thus, the results obtained showed a decrease in the detection of HIV-infection in pregnant women, in persons in places of deprivation of liberty, in patients of narcological dispensaries and skin and venereological dispensaries ($p<0.001$, $\chi^2$ test with Bonferroni correction) (Table 1).

These are vulnerable groups under constant surveillance, so the decrease in the proportion of these circumstances in HIV diagnosis can be explained by the decline in the incidence of HIV-infection in the Russian Federation[2,3,4]. An important result of our study is the finding of an increase in the proportion of HIV detection during preventive medical examination and voluntary HIV testing ($p<0.001$, $\chi^2$ test with Bonferroni correction). Such results in the case of preventive medical examination are explained by the expansion of the list of professions, industries, enterprises, institutions and organisations, whose employees undergo medical examination for HIV-infection as part of compulsory pre-employment and periodic medical examinations[5]. The increase in the detection of HIV-infection through voluntary HIV testing marks the greater involvement of medical personnel in HIV prevention issues, as well as education activities among the entire population of the country. Herewith, currently, the partners of pregnant women are actively involved in HIV testing[2]. As part of the regular medical examination of the adult population, information is

[1] Order of the Government of the Russian Federation No. 3468-r. http://government.ru/docs/all/131802/ [Internet]. Accessed on 28.12.2023. (In Russ.).

[2] Clinical Guideline "HIV Infection in Pregnant Women". https://cr.minzdrav.gov.ru/schema/717_1 [Internet]. Accessed on 28.12.2023. (In Russ.).

[3] Order of the Ministry of Health of the Russian Federation No. 1034n. On Approval of the Procedure for the Provision of Medical Care in the Profile "Psychiatry-Narcology" and the Procedure for Dispensary Monitoring of Persons with Mental Disorders and (or) Behavioural Disorders Associated with the Use of Psychoactive Substances. https://base.garant.ru/71360612/ [Internet]. Accessed on 28.12.2023. (In Russ.)

[4] Methodological Guidelines "Epidemiological Surveillance of HIV-Infection". https://www.rospotrebnadzor.ru/documents/details.php?ELEMENT_ID=7883&ysclid=lqkrbd9mn839043931 [Internet]. Accessed on 28.12.2023. (In Russ.).

[5] Order of the Ministry of Labour and Social Protection of the Russian Federation No. 885n. On Approval of the List of Certain Occupations, Industries, Enterprises, Institutions and Organisations Whose Employees Undergo Compulsory Medical Examination to Detect HIV Infection during Compulsory Preliminary Medical Examinations upon Entering Employment and Periodic Medical Examinations. https://base.garant.ru/400105354/ [Internet]. Accessed on 28.12.2023 (In Russ.).

provided on the possibility of being tested for HIV-infection, including anonymously [13]. It is worth noting that socially oriented non-profit organisations are actively involved in educational work with risk groups[1].

among injecting drug users[3] [14]. This study showed a decrease in the proportion of IDUs among newly diagnosed HIV-infected patients over time ($p<0.001$, $\chi^2$ test) (Figure 1).

**Circumstances in HIV diagnosis among**

**Обстоятельства выявления диагноза «ВИЧ-инфекция»**

| Year of diagnosis confirmation | Voluntary testing for HIV-infection | | Preventive medical examination | | Examination during pregnancy | | Medical examination for clinical indications | | Medical examination for epidemiological indications | |
|---|---|---|---|---|---|---|---|---|---|---|
| | abs. | % | abs. | % | abs. | % | abs. | % | abs. | % |
| 2017 | 11 851 | 21,98 | 2482 | 4,60 | 3376 | 6,26 | 15 717 | 29,14 | 5897 | 10,94 |
| 2018 | 14 396 | 24,44 | 2978 | 5,06 | 3326 | 5,65 | 18 497 | 31,40 | 6513 | 11,06 |
| 2019 | 17 493 | 27,32 | 3209 | 5,01 | 3218 | 5,03 | 21 333 | 33,32 | 6762 | 10,56 |
| 2020 | 12 494 | 26,76 | 2830 | 6,06 | 2688 | 5,76 | 15 482 | 33,16 | 4925 | 10,55 |
| 2021 | 12 549 | 26,00 | 3156 | 6,54 | 2625 | 5,44 | 16 289 | 33,75 | 5056 | 10,48 |
| 2022 | 13 152 | 26,50 | 3584 | 7,22 | 2133 | 4,30 | 18 238 | 36,75 | 5119 | 10,32 |

There was also an increase in the detection of HIV-infection during medical examinations for clinical indications, which may be associated with regular additional professional education of medical workers in the Russian Federation and, as a consequence, increased vigilance of primary care specialists with regard to HIV infection in patients[2]. In total, the current trend in the proportion of circumstances in HIV diagnosis, as well as, as previously reported, the increase in HIV testing coverage and the decrease in the number of new HIV-infections indicate the effectiveness of measures taken to combat the disease.

In the second part of this study we analysed the clinical and epidemiological characteristics of newly diagnosed HIV-infected patients in the period of 2017–2022 in the Russian Federation. Historically, the global HIV-infection spreading that began in the mid-1990s in Russia was caused by the introduction of the virus and its further widespread distribution (up to 90–95%)

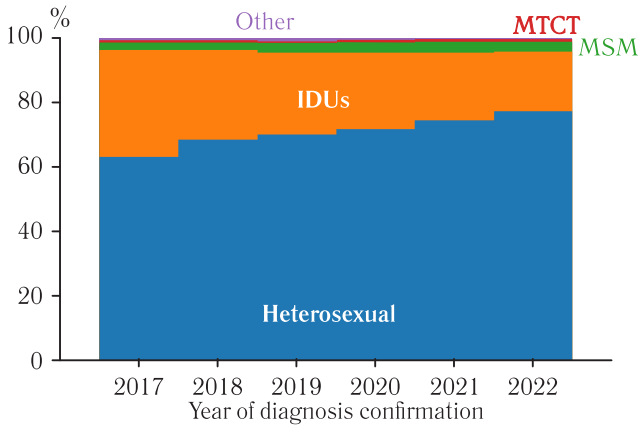


**Fig. 1.** The composition of route of infection among newly diagnosed HIV-infected patients in dynamics (2017–2022). Abbreviations: IDUs, intravenous drug users; MSM, men who have sex with men; MTCT, mother-to-child transmission

**Рис. 1.** Структура путей заражения среди впервые выявленных ВИЧ-инфицированных пациентов в динамике (2017–2022 гг.). Аббревиатуры: ПИН — потребители инъекционных наркотиков; МСМ — мужчины, практикующие секс с мужчинами; ПМР — передача ВИЧ-1 от матери ребенку

[1] Methodological Recommendations on Ensuring Access of Socially Oriented Non-Profit Organisations to the Provision of Services within the Framework of the Russian Federation State Programme "Health Care Development" for the Main Measure "Prevention of HIV-Infection, Viral Hepatitis B and C" and Implementation of Regional Health Care Development Programmes, 2018. https://de.yanao.ru/documents/active/3764/?ysclid=lqkv605vh5169796808 [Internet]. Accessed on 28.12.2023 (In Russ.).

[2] Order of the Ministry of Health of the Russian Federation No. 922n. On Approval of the Procedure and Terms for the Formation, Approval and Maintenance of Action Plans for the Organisation of Additional Professional Education of Medical Workers under Advanced Training Programmes, as Well as for the Acquisition and Repair of Medical Equipment, the Composition of the Information to Be Included in Them, the Procedure and Terms for the Formation and Submission of Applications for the Inclusion of Measures in Such Action Plans, as Well as the Forms of These Applications. https://base.garant.ru/402900347/ [Internet]. Accessed on 28.12.2023 (In Russ.).

[3] http://www.hivrussia.info/wp-content/uploads/2023/09/Spravka-VICH-v-Rossii-na-31.12.2022.pdf [Internet]. Accessed on 28.12.2023 (In Russ.).

Thus, in the period 2017–2022, there was an approximate 50%-decline in the number of new HIV-diagnoses among IDUs, while the number of newly diagnosed HIV-infected patients with a heterosexual route of infection increased from 63.19% to 77.20% (p<0.001, $\chi^2$ test). This is consistent with recent literature indicating that heterosexual transmission of HIV-infection has become dominant in the Russian Federation [2,15]. An increase in the proportion of MSM was also noted ($p$<0.001, $\chi^2$ test). It can be explained by improved epidemiological research and greater "openness" of this cohort to physicians[1].

There was also an slow, but significant increase in the involvement of women in the epidemic process from 38.6% in 2017 to 40.7% in 2022 ($p$<0.001, the Mann Whitney test) (Figure 2) and, as a consequence, an increase in the proportion of heterosexual transmission, which is consistent with earlier findings [16].

In 2017, CD4-lymphocyte counts exceeding 500 cells/μL were detected in 35.96% of newly diagnosed HIV-infected patients (Table 2).

However, over time, the proportion of individuals with this cell count decreased to 32.08% in 2022 ($p$<0.001, $\chi^2$ test). In contrast, the proportion of patients with CD4-lymphocyte counts less than 200 cells/μL increased from 18.70% in 2017 to 23.71% in 2022 ($p$<0.001, $\chi^2$ test). The difference in CD4-lymphocyte levels across all years of follow-up was significant ($p$<0.001, $\chi^2$ test).

The differences in CD4-lymphocyte levels in both newly diagnosed male and female HIV-infected patients by years of follow-up were statistically significant ($p$<0.001 $\chi^2$ test).

In 2017, CD4-lymphocyte counts greater than 500 cells/μL were found in 33.43% and 39.26% of newly diagnosed male and female HIV-infected patients, respectively. However, there was a decrease in the proportion of individuals with this cell level over time to 30.20% in 2022 among newly diagnosed HIV-infected male patients and to 34,58% among newly diagnosed HIV-infected female patients ($p$<0.001, $\chi^2$ test for male and female).

Table 1

**newly diagnosed HIV-infected patients**

Таблица 1

**среди впервые выявленных ВИЧ-инфицированных пациенто**

| Examination after medical contact with HIV-infected persons | | HIV detection in narcological dispensaries | | HIV detection in skin and venereological dispensaries | | HIV detection in places of deprivation of liberty | | Unknown | | Total |
|---|---|---|---|---|---|---|---|---|---|---|
| abs. | % | abs. | % | abs. | % | abs. | % | abs. | % | abs. |
| 71 | 0,13 | 4665 | 8,65 | 2664 | 4,94 | 3963 | 7,35 | 3241 | 6,01 | 53 927 |
| 62 | 0,11 | 4252 | 7,22 | 2569 | 4,36 | 3525 | 5,98 | 2782 | 4,72 | 58 900 |
| 82 | 0,13 | 4254 | 6,64 | 2502 | 3,91 | 3376 | 5,27 | 1800 | 2,81 | 64 029 |
| 44 | 0,09 | 2974 | 6,37 | 1895 | 4,06 | 2147 | 4,60 | 1208 | 2,59 | 46 687 |
| 43 | 0,09 | 2987 | 6,19 | 1845 | 3,82 | 2150 | 4,46 | 1560 | 3,23 | 48 260 |
| 52 | 0,10 | 2547 | 5,13 | 1598 | 3,22 | 1946 | 3,92 | 1255 | 2,53 | 49 624 |

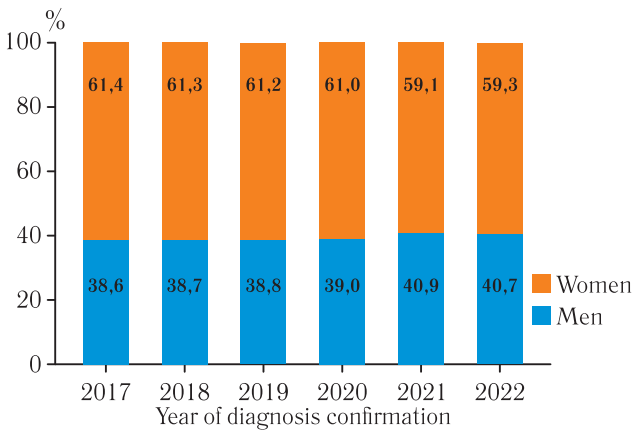


**Fig. 2.** The gender composition among newly diagnosed HIV-infected patients in dynamics (2017–2022)

**Рис. 2.** Половая структура впервые выявленных ВИЧ-инфицированных пациентов в динамике (2017–2022 гг.)

In 2017, CD4-lymphocyte counts less than 200 cells/μL were found in 20.46% and 16.42% of newly diagnosed male and female HIV-infected

[1] Zhukova E.V. Clinical and Epidemiological Features of HIV-infection in the Population of Men who Have Sex with Men in Moscow Oblast. PhD thesis, Federal State Budget Institution "National Research Centre for Epidemiology and Microbiology Named After Honorary Academician N. F. Gamaleya", the Ministry of Health of the Russian Federation, Moscow, Russia, 24 March 2023. https://gamaleya.org/upload/archive/zhukova/dis.pdf [Internet]. Accessed on 28.12.2023 (In Russ.).

patients, respectively. In contrast, there was an increase in the proportion of individuals with this cell level over time to 25.45% in 2022 among newly diagnosed HIV-infected male patients ($p<0.001$, $\chi^2$ test) and to 21,40% among newly diagnosed HIV-infected female patients ($p<0.001$, $\chi^2$ test).

The further analysis of trends in CD4-cells counts within gender subgroups revealed significant differences. The absolute number of CD4-lymphocytes was higher among women in all years of follow-up ($p<0.001$, $\chi^2$ test) (Figure 3). These obtained gender differences indicate earlier HIV diagnosis in women, which may be related to their screening during pregnancy and, as follow, their active invitation to AIDS-centres.

In recent years in the Russian Federation, HIV-infection has been detected among the population of the most active working age [17]. In our study a significant decrease in the proportion of newly detected HIV-infected patients aged 25 to 34 years and an increase in the proportion of patients aged 35 years and older (p<0.001, $\chi^2$ test) were found (Figure 4).

The median age at which patients are newly diagnosed with HIV-infection has increased significantly over time from 35 years in 2017 to 39 years in 2022 ($p<0.001$, $\chi^2$ test).

Wherein, a decrease in CD4-lymphocyte counts was observed with increasing age of patients (Figure 5).

The highest proportion of CD4-lymphocytes over 500 cells/μL was found in the group of patients aged 0–14 years (78.16%), which also is related to the dispensary monitoring of children born to HIV-infected women[1]. According to the results of our study, in contrast, the highest proportion of CD4-lymphocytes less than 200 cells/μL was found in the group of patients

**Characterization of CD4-lymphocyte levels**

**Характеристика уровней CD4-лимфоцитов среди**

| Year of diagnosis confirmation | Results of the first immune status study | | | | | |
|---|---|---|---|---|---|---|
| | less than 50 cells/μL | | 50–99 cells/μL | | 100–199 cells/μL | |
| | abs. | % | abs. | % | abs. | % |
| 2017 | 3062 | 4,77 | 2474 | 3,85 | 6473 | 10,08 |
| 2018 | 3122 | 5,13 | 2609 | 4,29 | 6184 | 10,16 |
| 2019 | 2695 | 4,78 | 2524 | 4,48 | 6027 | 10,70 |
| 2020 | 2202 | 5,27 | 1969 | 4,71 | 4472 | 10,70 |
| 2021 | 2501 | 5,64 | 2270 | 5,12 | 5019 | 11,32 |
| 2022 | 2999 | 6,45 | 2591 | 5,57 | 5434 | 11,69 |

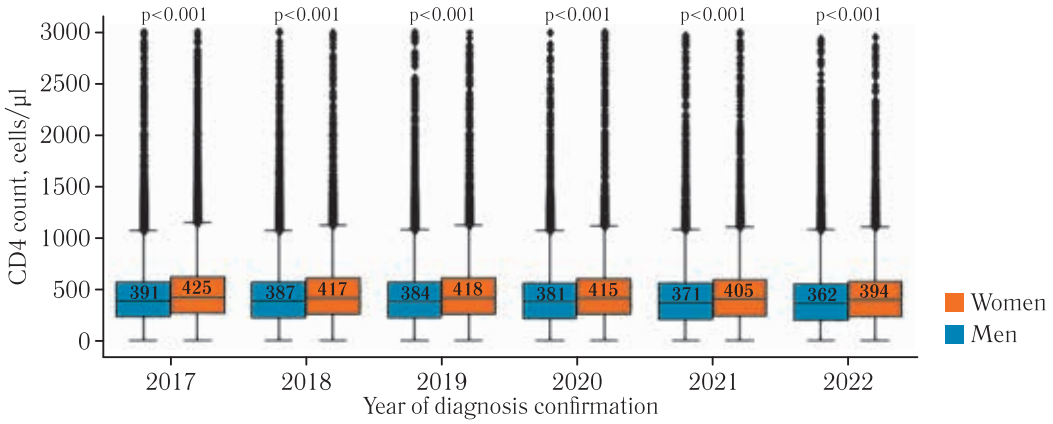


**Fig. 3.** Indicators of absolute CD4-lymphocyte counts among newly diagnosed male and female HIV-infected patients (2017–2022)
**Рис. 3.** Показатели абсолютного числа CD4-лимфоцитов среди впервые выявленных ВИЧ-инфицированных пациентов мужского и женского пола (2017–2022 гг.)

[1] Clinical Guideline "HIV-Infection in Children". https://cr.minzdrav.gov.ru/schema/459_1?ysclid=lqkw00adw4472193741 [Internet]. Accessed on 28.12.2023 (In Russ.).

aged over 50 years old (27.82%). These results are consistent with a recent study conducted in China, that surveillance and treatment and, as a result, earlier detection of HIV-infection[1]. Currently, there is a des-

Table 2

**in newly diagnosed HIV-infected patients**

Таблица 2

**впервые выявленных ВИЧ-инфицированных пациентов**

| Results of the first immune status study | | | | | | Total number of patients examined |
|---|---|---|---|---|---|---|
| 200–299 cells/μL | | 300–499 cells/μL | | over 500 cells/μL | | |
| abs. | % | abs. | % | abs. | % | abs. |
| 9025 | 14,06 | 20 085 | 31,28 | 23 091 | 35,96 | 64 210 |
| 8575 | 14,09 | 18 960 | 31,14 | 21 428 | 35,20 | 60 878 |
| 7707 | 13,68 | 17 744 | 31,49 | 19 651 | 34,87 | 56 348 |
| 5897 | 14,11 | 12 960 | 31,02 | 14 285 | 34,19 | 41 785 |
| 6215 | 14,02 | 13 605 | 30,68 | 14 728 | 33,22 | 44 338 |
| 6648 | 14,30 | 13 907 | 29,91 | 14 914 | 32,08 | 46 493 |

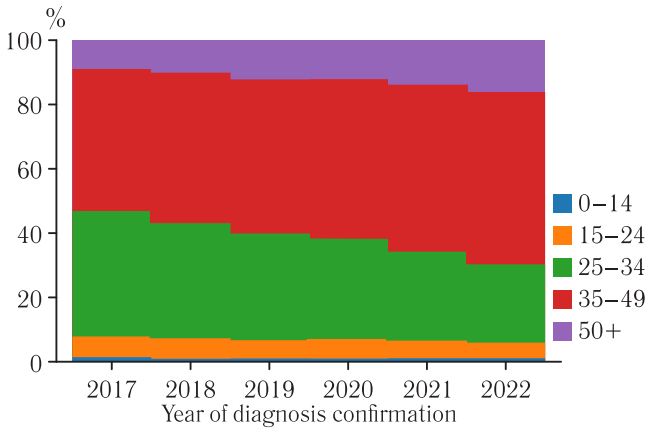


**Fig. 4.** The age composition among newly diagnosed HIV-infected patients in dynamics (2017–2022)

**Рис. 4.** Возрастной состав впервые выявленных ВИЧ-инфицированных пациентов в динамике (2017–2022 гг.)

showed an increase in the proportion of patients with CD4 counts less than 200 cells/μL and a decrease in the proportion of patients with CD4 over 500 cells/μL [18].

The two populations with the highest mean baseline CD4-cell counts were MSM ($p$<0,001, the Mann Whitney test for all years for all comparisons, with Bonferroni correction) and people infected through MTCT ($p$<0,001), suggesting improved epidemic control in these groups (Figure 6).

Studies conducted in China have also reported high median baseline CD4-lymphocyte counts among MSM compared with other risk groups [8, 19]. The MSM cohort is characterised by high adherence to tigmatising approach to MSM by medical professionals in Russia[1]. This allows not only to control the disease of each individual patient from the MSM cohort, but also acts as an anti-epidemic measure to control

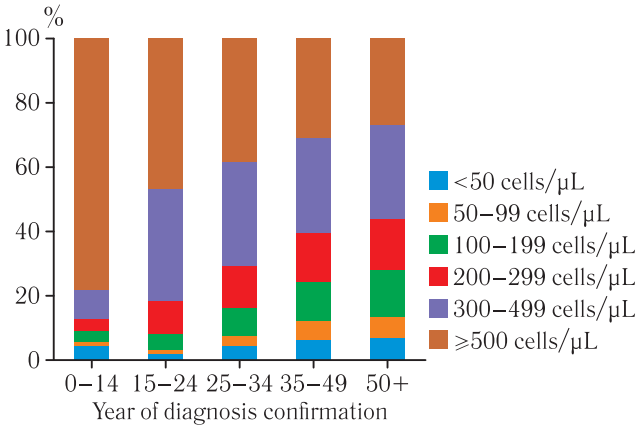


**Fig. 5.** The structure of CD4-cell counts in newly diagnosed HIV-infected patients of different ages

**Рис. 5.** Структура числа CD4-клеток у впервые выявленных ВИЧ-инфицированных пациентов разного возраста

the spread of HIV-infection in general. The high baseline CD4-cell counts in patients infected through MTCT indicates the improvement in the detection of HIV-infection during pregnancy, which has already been noted in a recent study [20].

The two populations with a statistically significant decrease in CD4-cell counts over all years of follow-up were IDUs and heterosexuals ($p$<0.001, the

[1] Zhukova E.V. Clinical and Epidemiological Features of HIV-infection in the Population of Men who Have Sex with Men in Moscow Oblast. PhD thesis, Federal State Budget Institution "National Research Centre for Epidemiology and Microbiology Named After Honorary Academician N. F. Gamaleya", the Ministry of Health of the Russian Federation, Moscow, Russia, 24 March 2023. https://gamaleya.org/upload/archive/zhukova/dis.pdf [Internet]. Accessed on 28.12.2023 (In Russ.).

Kruskall-Wallis test). These two populations were also found to have the longest median time ($p<0.001$) from infection to disease detection — 24 and 20 months, respectively (Figure 7).

Therefore, we also examined the estimated timing of HIV-infection in these risk groups during follow-up period ($p<0.001$, the Kruskall-Wallis test) (Figure 8–9).

A significant increase in the time to disease detection was found in both cases. However, in the heterosexual group, these changes were associated with a sharp increase in the period 2021–2022, which can be explained by the introduction of a self-isolation regime in the Russian Federation during the COVID-19 pandemic[1,2]. These measures have had a significant impact on reducing the number of patients visiting AIDS-centres. The risk group with the most delayed detection of HIV-infection was IDUs ($p<0.001$, the Mann Whitney test for all years) in all years of follow-up. It is important to note that IDUs have its own behavioral characteristics: the use of psycho stimulant drugs contributes to risky sexual behavior and low adherence to HIV surveillance and treatment [21]. Injecting drug use affects the pathogenesis of HIV-infection due to its immunosuppressive properties and the possibility of additional co-infection [22. Previous studies have found a high prevalence of HIV and hepatitis C co-infection in a cohort of IDUs, as well as lower CD4-cell counts with co-infection [23–25]. In our study, we also observed the highest prevalence of co-infection in the IDUs cohort, which may also have contributed to low CD4-cell counts and their significant decline over time (2.24% — for HIV/HBV vs. 0.04% (for MTCT), 0.65% (MSM), 0.72% (other) and 0.76% (heterosexual), 24.59% —

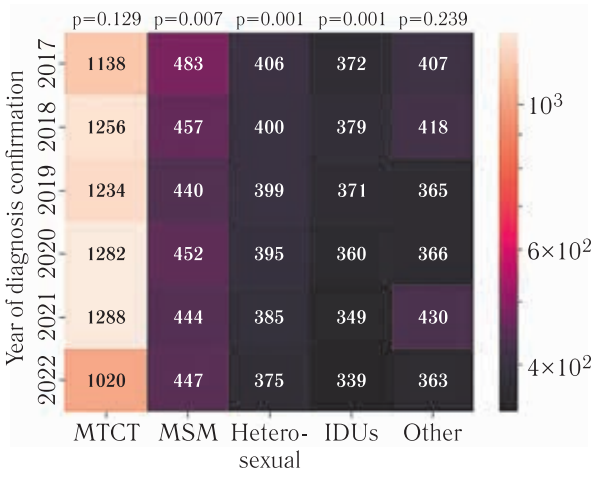


**Fig. 6.** Median CD4-lymphocyte counts in newly diagnosed HIV-infected patients with different routes of infection in the period 2017–2022

**Рис. 6.** Среднее количество CD4-лимфоцитов у впервые выявленных ВИЧ-инфицированных пациентов с различными путями заражения в период 2017–2022 гг.

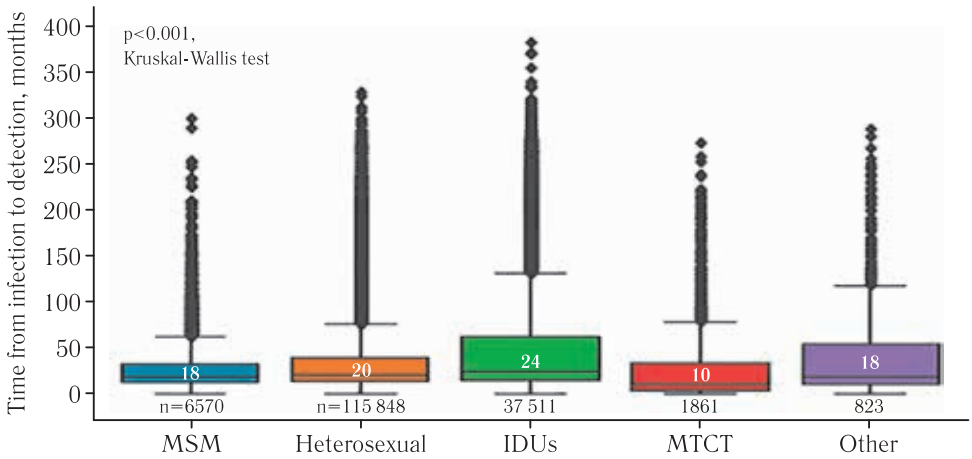


**Fig. 7.** The estimated timing of HIV-infection in patients with different routes of infection in the Russian Federation in the period 2017–2022

**Рис. 7.** Предполагаемые сроки инфицирования ВИЧ-1 среди пациентов с различными путями заражения в Российской Федерации в период 2017–2022 гг.

[1] Decree of the Chief State Sanitary Doctor of the Russian Federation No. 7. On Ensuring Isolation Regime to Prevent the Spread of COVID-2019. https://base.garant.ru/73764449/ [Internet]. Accessed on 28.12.2023 (In Russ.).

[2] Decree of the President of the Russian Federation No. 239. On Measures to Ensure Sanitary and Epidemiological Well-Being of the Population on the Territory of the Russian Federation in Connection with the Spread of a New Coronavirus Infection (COVID-19). http://publication.pravo.gov.ru/Document/View/0001202004020025?ysclid=lqpb35mqiq458148461 [Internet]. Accessed on 28.12.2023 (In Russ.).

for HIV/HCV vs. 0.51% (for MTCT), 2.91% (MSM), 6.0% (heterosexual) and 11.51% (other), 1.99% — for HIV/HBV+HCV co-infection vs. 0.0% (for MTCT), 0.08% (MSM), 0.37% (heterosexual) and 0.72% (other); 16.4% — for HIV/TB co-infection vs. 2.38% (for MSM), 4.47% (MTCT), 8.33% (heterosexual) and 10.32% (other); 0.41% — for HIV/HBV/TB vs. 0.0% (for MTCT), 0.02% (MSM), 0.08% (heterosexual) and 0.13% (other), 3.98% — for HIV/HCV/TB and vs. 0.0% (for MTCT), 0.19% (MSM), 0.72% (heterosexual) and 1.71% (other), 0.38% — HIV/HBV + HCV/TB co-infection vs. 0.0% (MSM), 0.0% (MTCT), 0.05% (heterosexual) and 0.13% (other).

Thus, it can be assumed that the observed decline in CD4-cell counts over time is associated with the detection of HIV-infection in IDUs infected in the early years of HIV-infection in the Russian Federation (in the 2010s). It correlates with ageing of newly diagnosed HIV-infected IDUs (Figure 10).

It is worth noting that in the Russian Federation, since 2016, a number of preventive measures have been taken to reduce the spread of HIV-infection: raising awareness of HIV-infection among citizens, creating a social environment that does not discriminate against people living with HIV, increasing the coverage of the population with medical testing for HIV-infection,

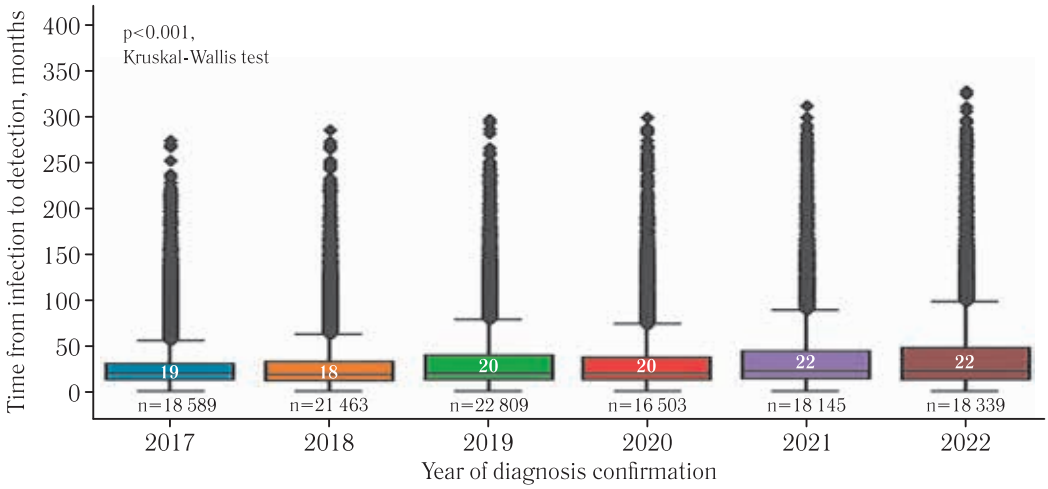


**Fig. 8.** The estimated timing of HIV-infection in patients with heterosexual route of infection in the Russian Federation in the period 2017–2022

**Рис. 8.** Предполагаемые сроки заражения ВИЧ-1 среди пациентов с гетеросексуальным путем инфицирования в Российской Федерации в период 2017–2022 гг.

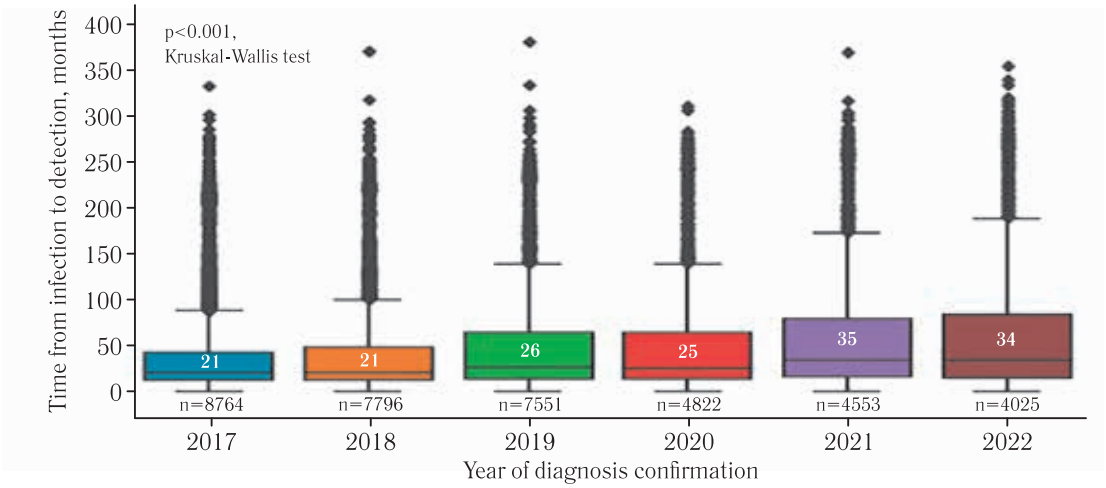


**Fig. 9.** The estimated timing of HIV-infection in patients with parenteral route of infection through injecting drug use in the Russian Federation in the period 2017–2022

**Рис. 9.** Предполагаемые сроки заражения ВИЧ-1 среди пациентов с парентеральным путем инфицирования при потреблении инъекционных наркотиков в Российской Федерации в период 2017–2022 гг.

using the achievements of science and practice to prevent HIV-infection, improving epidemiological control[1,2]. Thus, these measures contributed to attracting the interest of the population of the Russian Federation in the problem of HIV-infection and, as a consequence, to the active visitation of patients to AIDS-centres and improved detection of patients infected in the early years of HIV-infection in Russia.

It is important to note that the trends we obtained coincide with those in the report published by the European Centre for Disease Control and Prevention (CDC)[3], but there are some differences in the statistics due to the difference in the samples analysed. The material for our study was the FRHIV reports, i.e., patients on the medical register, while the data source for the CDC report was Statistical form № 61 including immunoblot-positive patients, including anonymous patients. The use of the FRHIV data not only allowed us to estimate the CD4-cells counts, but also to disaggregate by route of transmission and circumstances of HIV diagnosis.

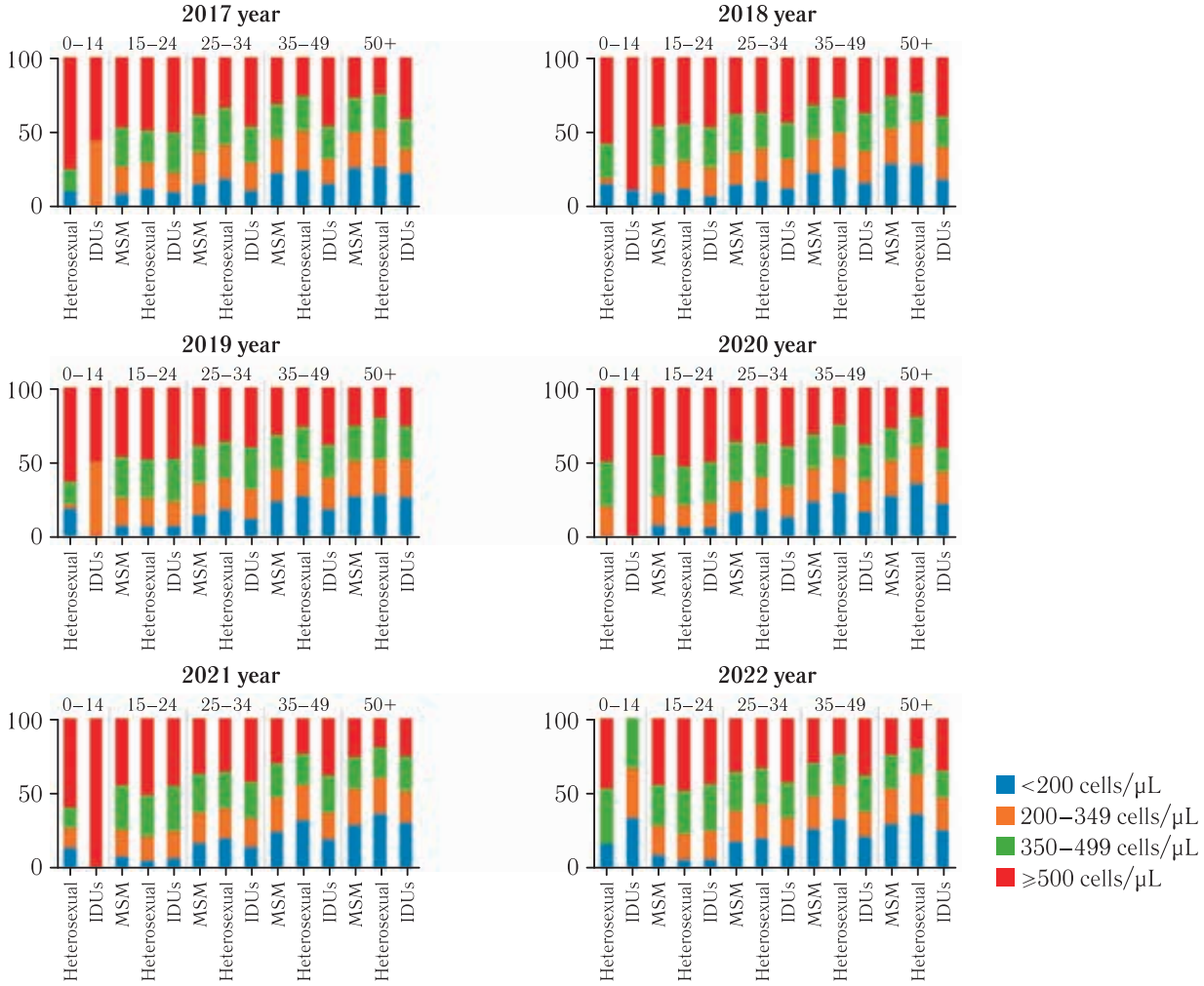


**Fig. 10.** The structure of CD4-cell counts in newly diagnosed HIV-infected patients of different ages and route of infections (2017–2022)
**Рис. 10.** Структура числа CD4-клеток среди впервые выявленных ВИЧ-инфицированных пациентов разного возраста и с разными путями заражения (2017–2022 гг.)

[1] Decree of the Government of the Russian Federation No. 426. On Approval of the Rules for Maintaining the Federal Register of Persons Infected with the Human Immunodeficiency Virus and the Federal Register of Persons with Tuberculosis. https://base.garant.ru/71654250/ [Internet]. Accessed on 28.12.2023. (In Russ.).

[2] Order of the Government of the Russian Federation No. 2203-r. On the State Strategy to Counteract the Spread of HIV-Infection in the Russian Federation for the Period until 2020 and Further Perspective. http://publication.pravo.gov.ru/Document/View/0001201610260006?ysclid=lqpbuf99uf175703933 [Internet]. Accessed on 28.12.2023 (In Russ.).

[3] HIV/AIDS surveillance in Europe 2023 (2022 data). CDC, 2023. 118 p.

**Conclusion.** This study helps to identify the most significant risk groups of people in the general population of HIV-infected people at the present stage in the Russian Federation. Thus, based on the results of the study, a portrait of a newly-diagnosed HIV-infected patient at the present stage was drawn up: a man aged 35 to 49 years, infected by heterosexual route with the median time from his infection to the diagnosis of HIV infection is 22 months.

* * *

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