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Hospital consumption of direct oral anticoagulants in regions of the Russian Federation in 2017–2022

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The aim of the study was to investigate the dynamics of inpatient consumption of direct oral anticoagulants in different regions of the Russian Federation for the period from 2017 to 2022.

Materials and methods. This study is a non-interventional, retrospective analysis of the electronic database records of Cursor Marketing LLC (Russia) about the announced by medical organizations and executed contracts for the purchase of direct oral anticoagulants (DOACs). The consumption was calculated on the basis of a DDD (defined-daily-dose) and estimated DDDTID (defined-daily-dose/1000-inhabitants/day) for each DOACs: rivaroxaban, dabigatran and apixaban. The Rosstat database available on its official website were used as a source of inhabitants data for the Russian regions.

Results. A total of 57 866 records were entered into the analyzed databases of Cursor Marketing LLC (Russia) from 2017 to 2022, 47.38% of which indicated rivaroxaban as the drug being procured, 26.51% indicated dabigatran, and 26.11% indicated apixaban. Edoxaban was not procured by healthcare organizations. During the period investigated, there was an increase in the consumption of all DOACs studied, with a higher increase for apixaban (by an average of 284.6% per year), then rivaroxaban (by 144.8% per year) and, to a lesser extent, dabigatran (by 92.5% per year). The analysis of DOACs consumption in general showed that compared to 2017, the need for these drugs in medical organizations in 2022 increased by 18 times. The Urals Federal District consistently exceeds the national average in terms of DDTID consumption. Noteworthy is the consumption dynamics of the regions of the Central Federal District and the North-Western Federal District, which made it possible to achieve DDDTID values above the national average for 5 out of 6 observation years. The lowest rates of DOACs consumption were observed in the Volga Federal District, which, despite positive growth dynamics, failed to reach the national average values. A high level of consumption (>10 DDDTID) of rivaroxaban was noted for the Arkhangelsk region (2018) and the Nenets Autonomous District (in 2021), dabigatran – only for the Arkhangelsk region (in 2018). Many more regions reached high levels of the apixaban consumption, especially in 2021.

Conclusion. Despite a number of limitations, the data on the volume of DOACs procurement can be used in the analysis of the consumption at both regional and national levels. When analyzing the DOACs consumption, the impact of COVID-19 pandemic and pharmacogenetic features of patients in different regions should be taken into account. During the studied period of time, a significant part of the Russian regions achieved a consumption level of rivaroxaban and apixaban, but not dabigatran, exceeding 1 DDDTID.

Keywords: oral anticoagulants; DOACs; consumption; rivaroxaban; apixaban; dabigatran

Abbreviations: MO – medical organization; DOACs – direct oral anticoagulants; MPs – medicinal products; RF – Russian Federation; FD – Federal District; DDD – defined-daily-dose; DDDTID – defined-daily-dose/1000-inhabitants/day.

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Потребление пероральных антикоагулянтов в стационарах регионов Российской Федерации в 2017–2022 гг.

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Цель. Изучение динамики стационарного потребления прямых пероральных антикоагулянтов в разных регионах РФ за период с 2017 по 2022 год.

Материалы и методы. Данное исследование является неинтервенционным, ретроспективным анализом записей электронной базы данных ООО «Курсор Маркетинг» (Россия) об объявленных медицинскими организациями и выполненных контрактах на закупку прямых (пероральных) антикоагулянтов (ПОАК). Расчет потребления проводили на основании данных о DDD (определенная суточная доза) и расчетного показателя DDDTID (DDD на тысячу населения в день) для каждого ПОАК: ривароксабана, дабигатрана и апиксабана. В качестве источника информации по численности населения регионов Российской Федерации использовали данные Росстата, доступные на его официальном сайте.

Результаты. Всего за период с 2017 по 2022 гг. в базы данных ООО «Курсор Маркетинг» было внесено 57 866 записей, из них 47,38% записей содержали указание, что в качестве закупаемого ЛП выступал ривароксабан, 26,51% – дабигатран и 26,11% – апиксабан, эдоксабан медицинскими организациями не закупался. За изученный период наблюдался рост потребления всех изученных ПОАК, причем в большей степени для апиксабана (в среднем на 284,6% в год), затем для ривароксабана (на 144,8% в год) и, в меньшей степени, для дабигатрана (на 92,5% в год). Анализ потребления ПОАК в целом показал, что в сравнении с 2017 годом, потребность в этих препаратах в медицинских организациях в 2022 году возросла в 18 раз. Стабильно выше среднего по стране показатель потребления DDDTID наблюдался в Уральском федеральном округе. Заслуживает внимания динамика потребления регионов Центрального и Северо-Западного федеральных округов, которая позволила добиться значений DDDTID выше средних по стране значений на протяжении 5 из 6 лет наблюдения. Наиболее низкие показатели потребления ПОАК наблюдались в Приволжском федеральном округе, в котором, несмотря на положительную динамику роста, так и не удалось достичь средних по стране значений. Высокий уровень потребления (>10 DDDTID) ривароксабана отмечен для Архангельской области (2018 г.) и Ненецкого автономного округа (в 2021 г.), дабигатрана – только для Архангельской области (в 2018 г.). Намного больше регионов достигло высокого уровня потребления апиксабана, особенно в 2021 году.

Заключение. Несмотря на ряд недостатков, данные об объеме закупок ПОАК можно использовать в анализе потребления как на региональном, так и на государственном уровнях. При анализе потребления ПОАК следует учитывать влияние пандемии COVID-19 и фармакогенетические особенности пациентов разных регионов. За исследуемый период времени в значительной части регионов РФ удалось достигнуть уровня потребления ривароксабана и апиксабана, но не дабигатрана, превышающего 1 DDDTID.

Ключевые слова: пероральные антикоагулянты; ПОАК; потребление; ривароксабан; апиксабан; дабигатран

Список сокращений: МО – медицинская организация; ПОАК – прямые (пероральные) антикоагулянты; ЛП – лекарственный препарат; РФ – Российская Федерация; ФО – федеральный округ; DDD – определенная суточная доза; DDDTID – определенная суточная доза на 1000 человек в день.

INTRODUCTION

The study of medicine demand in the healthcare system is crucial in clinical pharmacology. It is an effective method to investigate the rationality of pharmacotherapy, particularly to assess its compliance with regulatory and/or medical organizations (MOs) approved guidelines and standards, as well as to evaluate the safety and efficacy of prescribed medicines. [1, 2]. The ability to forecast a consumption and optimize a future procurement is an important consequence of drug demand studies. The methodology for such studies was published by the World Health Organization (WHO) in 2003. The formulation of principles and approaches to the analysis of the consumption data, the involvement of experts from related fields of medicine, recommendations on the introduction of the ATC/DDD classification into the widespread practice, and a consideration of social and economic factors affecting the consumption of medicines, were the outcomes of the work of an international expert group [1].

Modern oral anticoagulants known as direct oral anticoagulants (DOACs) are important in contemporary regimens for the treatment and prevention of thromboses (including ischaemic stroke) that are a frequent complication of cardiovascular disease (CVD) (the leading cause of death in the population for many years) [3]. DOACs include dabigatran (the international birth date is 2009), rivaroxaban, apixaban (first approved in 2011) and edoxaban (2013). As a result of clinical studies of these drugs, the most optimal safety and efficacy profiles were demonstrated in comparison with their previous generation (warfarin, acenocoumarol, phenylin, etc.). The convenience of their use including less frequent intake and no need for monitoring of the international normalized ratio, is also important for ensuring a better adherence to therapy, particularly in elderly patients [4–6]. According to the Russian Scientific Medical Society of Therapists (RSMST), the Gastroenterological Scientific Society of Russia (GSSR), and the National Society for Preventive Cardiology, approximately 2% of the population takes oral anticoagulants [7, 8]. The increase in DOACs prescriptions can also be explained by their economic efficacy, which has been demonstrated by numerous studies, including those conducted in Russian settings in patients with various pathologies [9–13].

The use of DOACs as an effective class of drugs for the prevention and treatment of thrombotic complications is increasing worldwide, and the COVID-19 pandemic can be considered a significant driver of their increased consumption [14, 15].

THE AIM of the study was to investigate the dynamics of inpatient consumption of direct oral anticoagulants in different regions of the Russian Federation for the period of 2017–2022.

MATERIALS AND METHODS

Study Design

This is a retrospective, non-interventional study which is an analysis of records from an electronic database on MOs announced and executed contracts for DOACs procurement. The information source on DOACs consumption in hospitals in different regions of Russia was the Kursor Marketing LLC database[1], which monitors a healthcare procurement in the Russian Federation. The authors analyzed an array of 57 866 records performed for the period from 01 January 2017 to 31 December 2022.

The inclusion criteria for the record in the final analysis were as follows: the customer should belong to the budgetary MOs of the Russian Federation; a correct indication of the region where the MO was located; the date of the contract in the period from 2017 to 2022; the inclusion some DOACs (rivaroxaban, dabigatran, apixaban or edoxaban) as a procured drug.

Consumption calculation

The consumption was calculated according to the WHO methodological recommendations based on the technical unit of consumption – DDD (defined daily dose) for each of the DOACs inclusion criteria. DDD values from the website of the WHO Collaborating Centre on the Methodology for Drug Statistics in Oslo, Norway[2] were used. The current version of the ATC / DDD classifier as of August 2023 was applied.

According to the approach described by Yan VKC et al [16], the DDD data obtained for each region of the Russian Federation were converted into a surrogate unit of consumption – DDDTID (DDD per 1 000 persons per day).

The population data for the different Russian regions were sourced from the official website of the Federal State Statistics Service (Rosstat)[3]. It was not possible to calculate DDDTID on a monthly or weekly basis, as the service provides annual data on 1 January only. The population at the beginning of the year was assumed to remain constant until the end of the year. A correction for the leap year (an additional day) was applied for 2020.

Ethical review

The database analyzed does not contain personal data of patients or healthcare providers, and the study did not involve any medical interventions. Therefore, the Ethical Committee approval was not necessary for this study.

Statistical processing

The data preparation was performed using MS Excel Software (Microsoft Corporation, USA), while the data processing and analysis were carried out using Orange Data Mining (University of Ljubljana, Slovenia)[4] to calculate descriptive (median, quartiles), comparative (one proportion test, confidence intervals of multinomial

[1] Kursor Marketing LLC database. Available from: https://www.cursor-is.ru. Russian

[2] WHO Collaborating Center for Drug Statistics Methodology. Available from: https://www.whocc.no

[3] Federal State Statistics Service of the Russian Federation. Demography. Available from: https://rosstat.gov.ru/folder/127815. Russian

[4] Data Mining Fruitful and Fun. Open-source machine learning and data visualization. Available from: https://orangedatamining.com/

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proportions using the Wald test) and statistical indicators of time series (extended Dickey–Fuller test to determine stationarity of time series, the detection of trends using the Mann–Kendall test). Median and 1st and 3rd quartile values (25th and 75th percentiles) are used to present the mean values as Me (Q1; Q3). The data are presented as absolute and percentage values. All the obtained data were considered non-parametrically distributed.

RESULTS AND DISCUSSION

During the study period, a total of 57 866 records meeting the stated inclusion criteria were entered into Kursor Marketing LLC database. Of these, 27 422 (47.38%; 95% CI=46.98; 47.79) contracts contained rivaroxaban as the procured drug, 15 338 (26.51%; 95% CI=26.15; 26.86) mentioned dabigatran, and 15 108 (26.11%; 95% CI=25.75; 26.47) contained apixaban. Notably, no edoxaban was procured by the Russian MOs in 2017–2022.

Figure 1 displays the monthly procurement volumes, expressed in millions of DDD, for each of the DOACs. The data shows that the procurement volumes of dabigatran remained relatively stable over the period, with an average annual increase of 92.5% (95% CI=71.65; 459.45). However, there was a significant increasing trend (p <0.001, Mann–Kendall test). In addition, the time series reflecting the procurement volume of dabigatran showed stationarity (p < 0.0001, extended Dickey–Fuller test), suggesting that fluctuations in dabigatran procurement volume may have been due to random. In contrast to dabigatran, the time series of contract volumes in DDD for rivaroxaban and apixaban were non-stationary (p=0.953 and p=0.187, respectively). The mean annual increase for rivaroxaban was 144.8% (95% CI=105.35; 311.9), while for apixaban it was 284.6% (95% CI=70.1; 1059). These findings are consistent with those of foreign researchers [16–19]. It is worth noting that in 2020, the contract volume of apixaban (107 977 million DDD) surpassed that of rivaroxaban (78 535 million DDD), resulting in a change in the leading position of the two drugs in hospital procurement. This aligns with the previous predictions made by Russian researchers, based on their analysis of clinical trial trends [20].

The analysis of DOACs consumption revealed that the demand for these drugs in MOs increased by 18.35 times compared to 2017, with a consumption peak in 2021 when the need was 28.5 times higher than in 2017. Although DOACs consumption in hospitals increased in all regions, the growth rate was not equal across all Federal Districts (FDs). The Urals Federal District consistently exhibited a DDDTID consumption rate above the national average. The consumption dynamics of the Central Federal District (CFD) and North-Western Federal District (NWFD) regions are noteworthy. These regions achieved DDD contract volume values above the national average for five out of six years of observation, except 2022 for NWFD and 2018 for CFD. A significant increase in DOACs procurement in NWFD hospitals in 2018 requires further investigation, in particular an increase of 37.912 million DDD, with the Arkhangelsk region accounting for 36.132 million DDD (an increase by 95.307% (95% CI=95.3;95.313)), warrants attention. It is this region that explain the initial peak in the purchase growth in the fall of 2018 (Fig. 1). With the population of the Arkhangelsk Region as of January 1, 2018, was 1 049 080, which represents only 7.525% (95% CI=7.511; 7.538) of the population, the detection of a statistically significant deviation from the expected proportional value of the volume of purchases (p <0.0001 test of one proportion) can be stated. The reason for this can be partially explained by the activity of clinical pharmacology services in the region and the peculiarities of the implementation of the anticoagulant therapy monitoring programme, which was introduced into practice in Arkhangelsk Region earlier than in other regions (since 2007) [8, 21].

The lowest rates of DOACs consumption in hospitals, based on the results of the announced tenders, were observed in the Volga FD, which, despite positive growth dynamics, failed to reach the national averages throughout the observation period. In the North Caucasus FD and Southern FD, the median consumption values were below the national average throughout the observation period, except for 2017 and 2018 for the Southern FD and 2020 for the North Caucasus FD. Figure 2 presents detailed information on DOACs consumption in the FDs.

The detailed dynamics of the individual DOACs consumption by regions of the Federal District is presented in Tables 1–8. To distinguish regions with high and low consumption levels of each of the studied drugs in the context of a single year. The consumption values of less than 1 DDDTID (group 1, a low consumption) and more than 10 DDDTID (group 3, a high consumption were analyzed. The consumption values ranging from 1 to 10 DDDTID constituted group 2.

The present analysis shows that a high consumption value of rivaroxaban was not achieved in any region in 2017, 2019, 2020, or 2022. In 2018, only the Arkhangelsk Region (31.38 DDDTID) reached this level, as the Nenets Autonomous District (10.22 DDDTID) did in 2021.

For dabigatran, the consumption above 10 DDD per 1 000 population per day was found only in the Arkhangelsk Region in 2018 (31.57 DDDTID).

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Table 1 – DDDTID values of rivaroxaban (R), apixaban (A), and dabigatran (D) for the regions of the Far Eastern Federal District for the period of 2017–2022

Period	2017			2018			2019			2020			2021			2022		
Federal Subjects	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A
Amur Region	0.02	0.01	0.00	0.05	0.02	0.00	0.23	0.08	0.00	0.91	0.53	2.07	1.89	0.89	1.84	0.83	0.37	1.19
Republic of Buryatia	0.03	0.08	0.00	0.03	0.06	0.01	0.07	0.07	0.05	0.58	0.48	2.42	1.78	0.75	10.76	0.56	0.51	0.79
Jewish Autonomous District	0.00	0.00	0.00	0.01	0.00	0.00	0.04	0.00	0.00	0.49	0.00	0.00	0.92	0.25	7.16	2.13	0.17	2.46
Zabaikalsky Territory	0.09	0.02	0.00	0.14	0.02	0.00	0.55	0.08	0.00	1.68	0.07	0.68	1.36	0.07	0.72	2.06	0.10	1.87
Kamchatka Territory	0.06	0.29	0.01	0.22	0.54	0.01	0.42	0.53	0.03	0.93	1.04	1.09	2.34	1.97	4.82	1.46	1.13	4.33
Magadan Region	0.34	0.00	0.00	0.43	0.21	0.00	0.62	0.16	0.00	0.89	0.27	2.10	1.74	1.37	7.14	1.11	0.34	5.62
Primorsky Territory	0.03	0.03	0.01	0.12	0.03	0.01	0.18	0.02	0.06	0.37	0.25	1.09	0.98	0.14	4.52	1.02	0.26	1.96
Republic of Sakha (Yakutia)	0.23	0.01	0.00	0.24	0.03	0.01	0.50	0.05	0.03	0.73	0.15	0.56	1.09	0.45	5.25	1.68	0.16	2.67
Sakhalin Region	0.38	0.14	0.00	0.53	0.08	0.06	1.06	0.15	0.00	3.66	0.62	2.24	4.87	1.72	3.31	3.11	0.65	2.76
Khabarovsk Territory	0.07	0.01	0.08	0.09	0.02	0.02	0.07	0.01	0.03	0.65	0.03	0.86	1.55	0.06	5.39	1.03	0.02	3.29
Chukotka Autonomous District	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.27	0.30	1.10	0.67	0.38	5.26	1.87	1.83	18.91

Note: fill cell – DDDTID score <1; fill cell – DDDTID >10.

Table 2 – DDDTID values of rivaroxaban (R), apixaban (A) and dabigatran (D) for the regions of the Volga Federal District for the period of 2017–2022

Period	2017			2018			2019			2020			2021			2022		
Federal Subjects	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A
Republic of Bashkortostan	0.09	0.03	0.02	0.06	0.02	0.02	0.54	0.06	0.25	0.62	1.05	0.92	0.50	0.08	2.28	0.80	0.16	1.03
Kirov Region	0.14	0.04	0.00	0.23	0.02	0.00	0.33	0.15	0.00	1.21	0.50	1.83	2.57	0.52	10.25	0.90	0.26	1.97
Mari El Republic	0.62	0.01	0.00	0.67	0.04	0.06	0.04	0.04	0.00	0.91	0.36	0.86	1.54	0.38	3.53	0.82	0.24	1.82
Republic of Mordovia	0.02	0.00	0.00	0.03	0.00	0.00	0.10	0.01	0.00	0.60	0.15	1.36	1.95	0.53	9.88	1.24	0.41	3.99
Nizhny Novgorod Region	0.39	0.22	0.01	0.48	0.28	0.02	0.41	0.15	0.01	2.32	0.73	1.60	3.63	0.53	1.33	4.13	1.15	0.54
Orenburg Region	0.10	0.05	0.00	0.17	0.01	0.00	0.75	0.50	1.09	1.68	0.89	2.44	1.20	0.22	11.59	0.73	0.00	0.81
Penza Region	0.08	0.09	0.00	0.09	0.05	0.00	0.16	0.09	0.00	0.93	0.70	0.89	1.52	0.88	1.21	1.35	0.93	0.54
Perm Territory	0.08	0.01	0.01	0.10	0.06	0.05	0.10	0.03	0.02	1.43	0.52	1.47	2.04	0.13	8.57	2.12	0.26	6.87
Samara Region	0.04	0.02	0.00	0.06	0.01	0.00	0.06	0.02	0.01	1.27	0.29	2.42	1.15	1.59	2.94	1.62	0.56	4.14
Saratov Region	0.04	0.03	0.01	0.05	0.06	0.02	0.09	0.03	0.00	1.05	0.73	0.91	1.47	0.55	0.48	1.59	0.22	1.03
Republic of Tatarstan	0.08	0.01	0.02	0.13	0.02	0.04	0.20	0.03	0.09	0.54	0.56	1.72	1.09	0.12	3.42	1.19	0.19	0.20
Udmurt Republic	0.02	0.02	0.02	0.03	0.04	0.03	0.01	0.02	0.00	0.61	1.20	1.11	0.95	0.62	4.38	0.57	0.07	1.61
Ulyanovsk Region	0.01	0.00	0.00	0.02	0.00	0.03	0.04	0.01	0.09	0.37	0.25	1.19	1.02	0.53	4.89	0.38	0.08	4.22
Chuvash Republic – Chuvashia	0.20	0.04	0.00	0.26	0.00	0.00	0.06	0.01	0.26	0.93	0.30	1.54	1.40	0.37	3.99	1.46	0.19	1.53

Note: fill cell – DDDTID score <1; fill cell – DDDTID >10.

Table 3 – DDDTID values of rivaroxaban (R), apixaban (A) and dabigatran (D) for the regions of the Northwestern Federal District and Saint-Petersburg for the period of 2017–2022

Period	2017			2018			2019			2020			2021			2022		
Federal Subjects	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A
Arkhangelsk Region	0.15	0.02	0.04	31.38	31.57	31.41	0.24	0.02	0.13	0.53	0.08	1.89	2.10	0.01	3.29	0.33	0.05	1.75
Vologda Region	0.02	0.01	0.00	0.26	0.01	0.01	0.04	0.00	0.00	0.37	0.11	0.91	1.77	0.03	7.33	0.61	0.01	1.01
Kaliningrad Region	0.05	0.03	0.00	0.10	0.02	0.01	0.26	0.03	0.07	0.61	0.32	0.63	1.72	0.02	2.15	1.64	0.26	0.53
Republic of Karelia	0.35	0.06	0.02	0.48	0.02	0.07	1.33	0.14	0.23	3.64	0.60	2.06	5.80	0.66	8.44	5.20	0.51	1.92
Komi Republic	0.43	0.13	0.11	0.61	0.22	0.00	1.31	0.22	0.27	3.98	0.59	2.38	5.95	0.33	9.22	3.34	2.24	4.75
Leningrad Region	0.00	0.01	0.00	0.02	0.01	0.00	0.03	0.03	0.00	0.01	0.02	0.01	0.27	0.15	0.28	0.11	0.00	0.08
Murmansk Region	0.06	0.12	0.05	0.07	0.03	0.15	0.15	0.05	0.21	0.51	0.39	1.94	1.25	0.01	5.77	0.71	0.19	2.77
Nenets Autonomous District	3.31	0.02	0.00	2.69	3.04	0.00	7.25	0.74	0.01	7.90	0.98	0.18	10.22	1.06	1.31	2.14	0.10	0.03
Novgorod Region	0.03	0.00	0.00	0.28	0.02	0.00	0.66	0.00	0.00	1.54	0.24	1.01	2.50	0.20	2.50	2.18	0.00	1.78
Pskov Region	0.40	0.04	0.00	0.70	0.09	0.08	1.38	0.08	0.27	2.52	0.29	3.09	4.00	0.35	10.07	2.49	0.22	5.36
Saint-Petersburg	0.32	0.03	0.02	0.33	0.03	0.04	0.64	0.22	0.10	1.16	0.60	1.79	2.49	0.40	8.23	1.71	0.44	5.73

Note: fill cell – DDDTID score <1; fill cell – DDDTID >10.

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Table 4 – DDDTID values of rivaroxaban (R), apixaban (A), and dabigatran (D) for the regions of the North Caucasus Federal District for the period of 2017–2022

Period	2017			2018			2019			2020			2021			2022		
Federal Subjects	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A
Republic of Dagestan	0.00	0.00	0.00	0.01	0.01	0.00	0.01	0.02	0.00	0.32	0.20	0.75	0.68	0.09	1.59	0.22	0.05	0.29
Republic of Ingushetia	0.02	0.19	0.00	0.10	0.01	0.00	0.12	0.02	0.00	4.30	0.04	0.06	0.81	0.10	1.05	0.74	0.01	0.49
Kabardino-Balkarian Republic	0.02	0.09	0.01	0.36	0.12	0.10	0.58	1.45	0.04	0.55	0.26	0.85	0.43	0.28	5.39	0.33	0.04	0.19
Karachay-Cherkess Republic	0.01	0.00	0.00	0.02	0.04	0.00	0.03	0.02	0.00	3.75	0.29	1.51	0.88	0.09	3.74	0.17	0.05	2.76
Republic of North Ossetia–Alania	0.03	0.02	0.00	0.09	0.01	0.01	0.12	0.03	0.00	1.47	0.39	2.31	1.87	0.46	5.23	0.50	0.11	1.58
Stavropol Territory	0.22	0.02	0.00	0.08	0.01	0.01	0.17	0.41	0.05	1.50	0.91	1.04	2.70	0.39	4.49	1.86	0.29	3.67
Chechen Republic	0.00	0.01	0.00	0.00	0.01	0.00	0.11	0.03	0.01	0.54	0.04	0.31	0.16	0.06	0.26	0.10	0.09	0.18

Note: fill cell – DDDTID score <1.

Table 5 – DDDTID values for rivaroxaban (R), apixaban (A) and dabigatran (D) for the regions of the Siberian Federal District for the period of 2017–2022

Period	2017			2018			2019			2020			2021			2022		
Federal Subjects	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A
Altai Republic	0.04	0.01	0.00	0.54	0.04	0.16	0.39	0.00	0.21	0.77	0.18	0.60	1.75	0.04	6.82	1.88	0.26	1.75
Altai Territory	0.06	0.03	0.06	0.33	0.05	0.01	0.28	0.12	0.09	1.26	0.38	1.36	2.47	0.77	4.89	1.14	0.46	1.73
Irkutsk Region	0.23	0.03	0.02	0.03	0.02	0.04	0.03	0.03	0.25	0.64	0.13	1.97	1.65	0.40	4.93	1.35	0.13	3.23
Kemerovo Region	0.01	0.03	0.01	0.04	0.06	0.01	0.14	0.04	0.02	1.68	0.60	1.82	2.20	0.45	4.09	2.31	0.74	3.08
Krasnoyarsk Territory	0.04	0.03	0.00	0.08	0.02	0.01	0.36	0.25	0.40	2.98	1.14	7.11	3.80	0.21	13.27	6.12	0.53	7.22
Novosibirsk Region	0.13	0.12	0.07	0.25	0.20	0.27	0.36	0.30	0.32	1.08	0.40	2.67	1.00	0.23	4.83	1.27	0.41	3.26
Omsk Region	0.14	0.27	0.01	0.02	0.02	0.01	0.04	0.03	0.04	0.29	0.67	2.75	1.20	0.03	7.38	0.57	0.11	0.25
Tomsk Region	0.20	0.31	0.07	0.30	0.14	0.20	0.31	0.06	0.14	0.98	0.22	2.38	1.15	0.15	4.90	1.57	0.18	3.24
Tyva Republic	0.02	0.00	0.00	0.06	0.00	0.00	0.11	0.03	0.08	0.30	0.07	0.77	1.62	0.18	1.74	0.87	0.16	0.34
Republic of Khakassia	0.04	0.04	0.00	0.04	0.05	0.03	0.09	0.16	0.33	0.50	0.52	4.87	0.66	0.09	6.52	0.98	0.30	5.34

Note: fill cell – DDDTID score <1; fill cell – DDDTID >10.

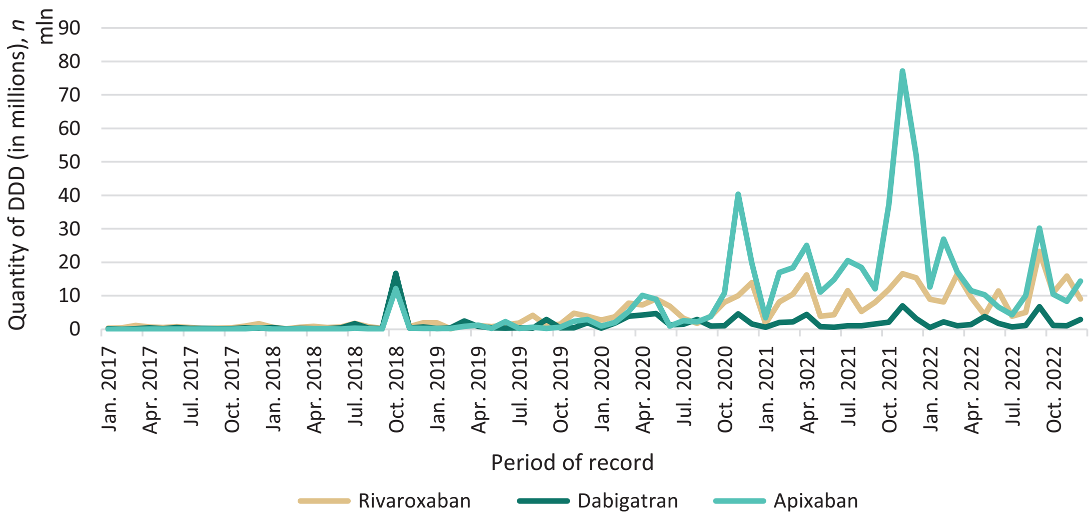

Figure 1 – Dynamics of change in monthly volumes of announced procurement of DOACs in the Russian Federation (in millions of DDD)

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Table 6 – DDDTID values for rivaroxaban (R), apixaban (A) and dabigatran (D) for the regions of the Urals Federal District for the period of 2017–2022

Period	2017			2018			2019			2020			2021			2022		
Federal Subjects	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A
Kurgan Region	0.14	0.48	0.00	0.22	0.11	0.00	0.35	0.12	0.00	1.08	0.65	1.03	1.80	0.74	9.85	1.65	0.40	0.12
Sverdlovsk Region	0.05	0.04	0.02	0.09	0.04	0.06	0.20	0.05	0.09	1.00	0.34	0.90	1.79	0.11	9.41	1.67	0.39	1.72
Tyumen Region	0.15	0.05	0.01	0.16	0.10	0.02	0.27	0.19	0.38	1.65	0.84	2.06	2.48	0.57	9.42	1.93	0.91	4.93
Khanty-Mansi Autonomous District	0.17	0.01	0.01	0.14	0.03	0.00	0.41	0.01	0.01	1.68	0.39	4.40	1.89	0.14	3.58	1.72	0.21	4.74
Chelyabinsk Region	0.02	0.03	0.01	0.10	0.10	0.02	0.13	0.05	0.12	1.01	0.28	1.95	1.63	0.52	7.66	0.81	0.29	4.56
Yamal-Nenets Autonomous District	0.16	0.46	0.00	0.59	1.58	0.01	0.31	1.62	0.01	1.68	1.63	3.06	2.44	0.81	19.72	1.34	0.95	3.62

Note: fill cell – DDDTID score <1; fill cell – DDDTID >10.

Table 7 – DDDTID values of rivaroxaban (R), apixaban (A) and dabigatran (D) for the regions of the Central Federal District and the city of Moscow for the period of 2017–2022

Period	2017			2018			2019			2020			2021			2022		
Federal Subjects	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A
Belgorod Region	0.02	0.00	0.00	0.02	0.01	0.00	0.03	0.04	0.03	1.45	0.42	3.16	1.58	0.40	12.76	1.16	0.32	6.87
Bryansk Region	0.15	0.16	0.00	0.24	0.02	0.00	0.51	0.04	0.02	1.36	0.53	1.09	3.00	0.42	5.35	2.42	0.06	5.42
Vladimir Region	0.04	0.01	0.00	0.07	0.01	0.00	0.08	0.01	0.00	0.83	0.43	0.35	1.59	0.51	6.52	1.56	0.03	2.74
Voronezh Region	0.04	0.03	0.00	0.73	1.57	0.21	0.07	0.06	0.02	1.01	0.35	0.98	1.53	0.44	5.94	0.57	0.35	0.79
Ivanovo Region	0.08	0.03	0.00	0.23	0.06	0.00	0.24	0.06	0.02	2.72	0.27	1.93	0.50	0.38	15.45	2.33	1.15	7.47
Kaluga Region	0.80	0.00	0.04	0.60	0.02	0.07	1.20	0.05	0.48	2.72	0.68	2.47	3.70	0.29	5.99	9.57	0.56	33.25
Kostroma Region	0.01	0.00	0.00	0.02	0.08	0.00	0.04	0.10	0.03	0.34	0.55	1.52	0.10	0.15	4.28	0.10	0.08	1.11
Kursk Region	1.56	0.02	0.00	0.18	0.07	0.00	0.16	0.08	0.00	0.40	0.95	0.76	1.68	0.64	2.21	0.77	0.36	2.00
Lipetsk Region	0.06	0.01	0.00	0.04	0.02	0.00	0.06	0.02	0.03	0.90	0.85	2.65	1.13	0.20	7.20	1.83	0.59	1.62
Moscow	0.28	0.16	0.13	0.82	1.06	0.10	2.13	1.22	1.57	4.04	1.29	3.11	6.00	1.69	10.51	5.95	1.27	6.35
Moscow Region	0.06	0.07	0.00	0.15	0.09	0.03	0.41	0.17	0.09	2.05	0.40	1.30	2.14	0.52	3.60	9.04	1.25	2.98
Orel Region	0.01	0.01	0.00	0.09	0.03	0.08	0.06	0.01	0.01	0.65	0.10	2.05	0.46	0.04	10.68	0.61	0.07	2.22
Ryazan Region	0.05	0.01	0.00	0.08	0.00	0.00	0.13	0.02	0.00	0.61	0.18	0.40	6.09	0.54	2.44	2.09	0.55	3.20
Smolensk Region	0.09	0.00	0.00	0.14	0.00	0.00	0.19	0.01	0.03	0.14	0.00	0.14	0.38	0.01	2.97	0.32	0.07	1.91
Tambov Region	0.08	0.01	0.00	0.22	0.03	0.00	0.20	0.05	0.01	1.19	0.48	1.34	2.49	0.88	5.78	0.84	0.21	1.37
Tver Region	0.17	0.10	0.05	0.20	0.05	0.02	0.74	0.21	0.21	1.46	0.62	1.91	2.40	0.59	6.17	0.90	0.27	0.85
Tula Region	0.85	0.04	0.00	0.07	0.08	0.00	0.45	0.01	0.00	1.19	0.34	1.62	2.09	0.19	1.64	1.42	0.17	2.22
Yaroslavl Region	0.11	0.05	0.01	0.16	0.03	0.05	0.11	0.03	0.11	0.93	0.28	2.17	0.55	0.08	4.88	0.73	0.33	2.20

Note: fill cell – DDDTID score <1; fill cell – DDDTID >10.

Table 8 – DDDTID values for rivaroxaban (R), apixaban (A) and dabigatran (D) for the regions of the Southern Federal District and the city of Sevastopol for the period of 2017–2022

Period	2017			2018			2019			2020			2021			2022		
Federal Subjects	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A	R	D	A
Republic of Adygea	1.53	0.00	0.00	0.11	1.81	0.00	0.29	2.07	0.52	0.34	0.38	1.48	0.66	0.16	2.76	0.80	0.55	4.04
Astrakhan Region	0.12	0.04	0.01	0.11	0.01	0.00	0.66	0.16	0.11	0.81	0.36	1.65	2.35	1.19	4.63	1.65	0.01	1.57
Volgograd Region	0.14	0.02	0.01	0.21	0.30	0.01	0.11	0.03	0.01	1.32	0.10	14.91	1.43	0.02	4.95	2.36	0.10	0.81
Republic of Kalmykia	0.10	0.03	0.00	0.10	0.00	0.00	0.26	0.02	0.00	1.09	0.03	1.13	2.06	0.20	1.23	1.52	0.03	0.25
Krasnodar Territory	0.07	0.03	0.00	0.07	0.04	0.02	0.07	0.04	0.03	0.62	0.32	2.08	0.65	0.44	3.00	0.83	0.23	0.93
Republic of Crimea	0.40	0.12	0.00	0.16	0.01	0.00	0.22	0.00	0.00	2.06	0.16	0.14	1.01	0.19	2.40	1.61	0.10	0.73
Rostov Region	0.06	0.07	0.00	0.22	0.06	0.01	0.12	0.04	0.03	0.95	0.66	0.75	1.24	0.44	6.46	1.37	0.38	1.75
Sevastopol	0.50	0.00	0.00	1.14	0.01	0.00	3.44	0.03	0.00	4.77	0.48	0.42	3.82	0.19	2.12	5.53	0.02	0.16

Note: fill cell – DDDTID score <1; fill cell – DDDTID >10.

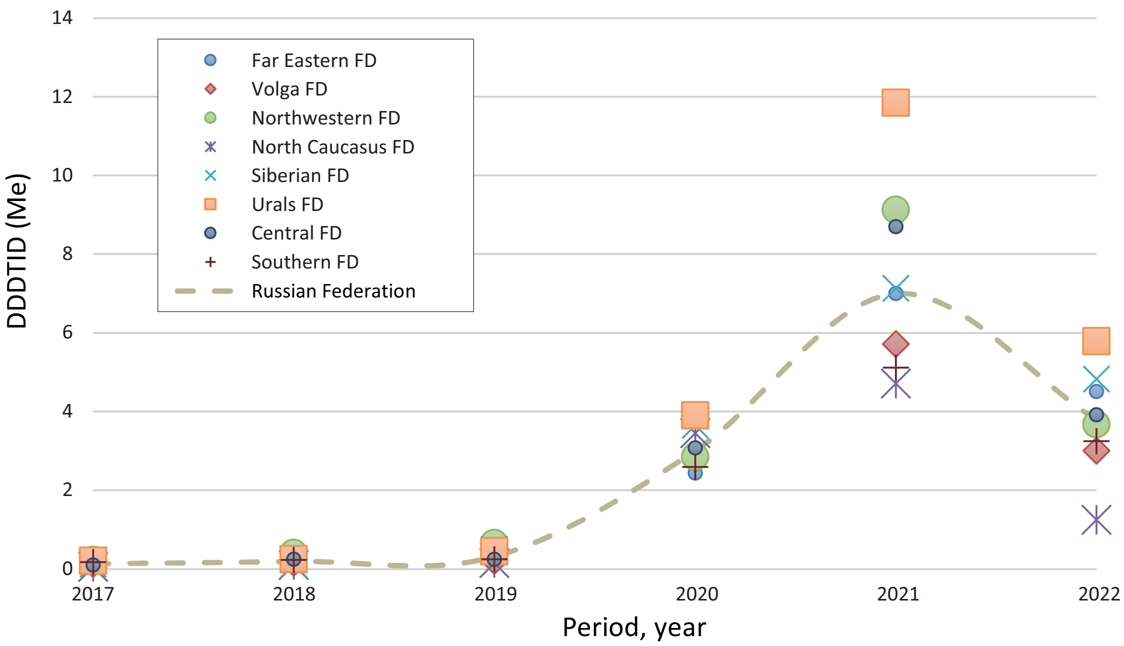

Figure 2 – DOACs consumption in federal districts of the Russian Federation in 2017-2022 (Me DDDTID)
Note: FD – federal district.

Group 3 includes the following regions for apixaban: Arkhangelsk Region in 2018 (31.41 DDDTID), Volgograd Region in 2020 (14.91 DDDTID), Republic of Buryatia (10.76 DDDTID), Kirov Region (10.25 DDDTID), Orenburg Oblast (11.59 DDDTID), Pskov Oblast (10. 07 DDDTID), Krasnoyarsk Territory (13.27 DDDTID), Yamalo-Nenets Autonomous District (19.72 DDDTID), Belgorod Region (12.76 DDDTID), Ivanovo Region (15.45 DDDTID), Orel Region (10.68 DDDTID), and the federal city of Moscow (10.51 DDDTID). In 2022, only Kaluga Region (33.25 DDTID) and Chukotka Autonomous District (18.91 DDTID) were in this group. The changes in the apixaban consumption can be explained by the announcement of the COVID-19 pandemic and the inclusion of the DOAC in the Temporary Methodological Recommendations for Prevention, Diagnosis and Treatment of New Coronavirus Infection (COVID-19)[5] of the Ministry of Health of the Russian Federation in 2020.

The national average consumption of all DOACs expressed in DDDTID was 0.132 (0.057; 0.317) in 2017; 0.195 (0.105; 0.404) in 2018; 0.315 (0.146; 0.667) in 2019;in 2020 – 3.0 (2.246; 4.401), 6.998 (5.201; 9.985), and 3.79 (2.263; 6.133) in 2021 and 2022, respectively.

Since 2018, only one region in the Russian Federation, Moscow, has exhibited a consistent average consumption of all DOACs. The reason for this can be attributed to the intensive work of the Department of Healthcare of Moscow to standardize and implement effective anticoagulant therapy in hospital practices, as well as the high density of federal-level medical organizations in the region. These organizations provide medical care not only to residents of the capital, but also to patients from other parts of the country.

Study limitations

The study's main limitations include the lack of accounting for outpatient prescribing and the ambulatory use of DOACs, which may constitute a significant portion of consumption. Unfortunately, the data on the pharmacy segment of DOACs sales are not publicly available and are subject to monitoring and commercial use by specialized organizations.

At the same time, it is known that in the Russian Federation the ratio between hospital and pharmacy (aka outpatient) segment of drug sales is 16 and 84%, respectively [22]. In addition, it is obvious that the drugs received by the MO as a result of procurement are not sold immediately, i.e. at once. It is spent over a long period of time, as patients are admitted to the hospital. At the same time, it is possible that a drug purchased during one period (a calendar year, for example) will be used in the next time period, as far as the shelf life of the purchased drug allows.

The genetic features related to the DOACs pharmacotherapy should be also considered. According to the Russian multi-ethnic studies, doses of anticoagulants, in particular dabigatran, can vary significantly depending on the patient's ethnicity [23]. Therefore, analyzing the DDDTID consumption without considering the patient's ethnic group, especially in the North Caucasus, Siberian, Ural, Southern, and Far Eastern Federal Districts, may not accurately reflect the actual consumption of DOACs [20, 23–25].

[5] Provisional methodological recommendations. Prevention, diagnosis and treatment of novel coronavirus infection (COVID-19). 8 ed. Ministry of Health of the Russian Federation, 2020. Available from: https://static-0.minzdrav.gov.ru/system/attachments/attaches/000/051/777/original/030902020_COVID-19_v8.pdf. Russisan

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CONCLUSION

The data on DOACs procurement by inpatients in the Russian Federation considered in this study, can be used to analyze the consumption of these drugs at both regional and national levels. The study revealed a consistent increase in DOACs consumption in the Russian Federation from 2017 to 2022, with the highest consumption rate in 2021. The consumption of rivaroxaban, apixaban, and dabigatran varies across different regions of the country. Although from 2017–2019, it was generally low in most regions of the Russian Federation, from 2020–2022, the consumption of rivaroxaban and apixaban (but not dabigatran) increased to 1 or more DDDTIDs in most regions of the country.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS' CONTRIBUTION

All authors confirm that they meet the ICMJE international criteria for the authorship. They have made substantial contributions to the conceptualization, conduct of the study, and preparation of the article. They have also read and approved the final version before the publication. Alexander V. Matveev – the idea and concept of the study, conducted the research, systematized and analyzed the data, statistical data analysis, wrote and edited the manuscript, and formulated the conclusions; Sergey V. Glagolev – the idea and concept of the study, conducted the research, systematized and analyzed the data, wrote and edited the manuscript, and formulated the conclusions; Ksenia N. Koryanova – conducted a critical analysis of the results and systematized the data, while also editing the manuscript; Dmitry A. Sychev – developed the study's concept, conducted a critical analysis of the results, wrote and edited the manuscript.

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