

## ORIGINAL ARTICLE

# TRENDS IN ORAL ANTICOAGULANT PRESCRIPTION PATTERNS IN THE CZECH REPUBLIC: A RETROSPECTIVE ANALYSIS OF 2019–2024

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### Summary

**Background:** The patterns of oral anticoagulant (OAC) prescription have significantly changed in recent years, with direct oral anticoagulants (DOACs) gradually replacing warfarin. While this transition occurred earlier in some countries, limited data are available about its timeline in the Czech Republic.

**Objectives:** This study aimed to analyse trends in OAC prescriptions in the Czech Republic from 2019 to 2024, focusing on the shift from warfarin to DOACs and the patterns of utilisation of individual DOACs.

**Methods:** A retrospective analysis was conducted using national electronic prescription data from the State Institute for Drug Control (SÚKL). Annual drug consumption is presented as defined daily doses per thousand inhabitants per day (DDD/TID).

**Results:** Total OAC utilisation increased from 18.83 to 26.70 DDD/TID between 2019 and 2024 ( $p < 0.01$ ), with an average of  $22.99 \pm 3.05$  DDD/TID. DOACs surpassed warfarin in total prescriptions in 2021. Rivaroxaban ( $6.84 \pm 3.00$  DDD/TID) and apixaban ( $5.24 \pm 2.43$  DDD/TID) exhibited the highest growth, while dabigatran utilisation ( $3.00 \pm 0.66$  DDD/TID) showed a halt in increase after 2022.

**Conclusion:** DOACs have progressively replaced warfarin in the Czech Republic, but this transition occurred later than in other developed countries. This shift was likely influenced by local changes in prescribing restrictions. Further research is warranted to evaluate prescription patterns based on specific indications.

*Key words: DOACs; warfarin; anticoagulants; prescription trends; drug utilisation; Czech Republic*

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## **Introduction**

For a considerable period of time, warfarin and other vitamin K antagonists (VKAs) have been the primary oral anticoagulants (OACs) that are used to prevent thromboembolic complications in patients with conditions such as atrial fibrillation (AF) and venous thromboembolism (VTE) and in patients with prosthetic valves. Despite their efficacy, VKAs have significant disadvantages, including the need for regular coagulation monitoring, dietary restrictions, and a high potential for interindividual variability in drug–drug and drug–food interactions (1–3).

The introduction of direct oral anticoagulants (DOACs) in 2008 signified a pivotal paradigm shift in the domain of anticoagulation therapy for AF and VTE patients. DOACs, including dabigatran, rivaroxaban, apixaban, and edoxaban, have several advantages over VKAs, including fixed dosing, the lack of need for routine monitoring, and a decreased risk of drug interactions (4). Furthermore, DOACs have transformed the management of thromboembolic disorders owing to their efficacy and safety, which are comparable to or better than those of warfarin in treating both AF and VTE. In atrial fibrillation, major trials have demonstrated that DOACs are either noninferior or superior to warfarin for stroke prevention, with the most significant reductions observed in the risk of intracranial bleeding (5–8). Similarly, for VTE, clinical trials have confirmed the noninferiority of DOACs to warfarin in treating acute deep vein thrombosis (DVT) and pulmonary embolism (PE), while significantly reducing major bleeding events (9–12).

The results of these clinical trials have led to a gradual expansion of the indications for DOACs, which are now included in numerous international clinical guidelines. These include their use in stroke prevention in patients with nonvalvular atrial fibrillation (NVAF) (13), as well as in the treatment and secondary prevention of venous thromboembolism (14,15) and thromboprophylaxis following major orthopaedic surgery (16) as well as the prevention of cardiovascular events in high-risk populations (17,18).

Research on the utilisation of oral anticoagulants, including DOACs, frequently focuses on national trends and specific indications. For example, studies conducted in Sweden and the United Kingdom have demonstrated how policy modifications and updated guidelines influence prescribing behaviours, resulting in increased adoption of DOACs in comparison with traditional VKAs (19,20). A similar trend has been observed in the United States, where DOACs have replaced warfarin as the preferred anticoagulants in many clinical settings, driven by their improved safety profiles and ease of use (21,22). In the Czech Republic, a comprehensive analysis of the utilisation of anticoagulants during 2007–2017 revealed an increasing adoption of DOACs, which accounted for a substantial proportion of oral anticoagulant prescriptions by the end of the study period. This shift can be attributed to the influence of clinical guidelines and the expanding indications for DOACs (23). Nevertheless, further data are needed to assess the impact of more recent guidelines and to evaluate the factors that have affected prescribing patterns over the past five years.

This study aimed to build on the findings outlined in previous studies. The objective of this study was to analyse trends in the prescription of oral anticoagulants in the Czech Republic from 2019 to 2024. To our knowledge, no study has yet analysed this period. The investigation of these patterns will provide insights into the evolving role of DOACs in clinical practice in the Czech Republic.

## **Materials and methods**

This study is a retrospective analysis of oral anticoagulant utilisation in the Czech Republic from 2019 to 2024 based on open data from the State Institute for Drug Control (SÚKL). The data were sourced from the national electronic prescription system (eRecept), which has been mandatory in the Czech Republic since 2018 (24). However, data from 2018 were excluded because of a noticeable gap in data, which was likely caused by technical issues and low adherence to electronic prescribing during its initial year of implementation. Thus, the study period commenced in 2019. The availability of consistent data from this year onwards enables the identification of trends that were subsequently observed and aligns with the findings of a previous study conducted between 2007 and 2017 (23). The analysis included all oral anticoagulants prescribed in outpatient settings during the study period, specifically warfarin (the Anatomical Therapeutic Chemical (ATC) code B01AA03), dabigatran (B01AE07), rivaroxaban (B01AF01), apixaban (B01AF02), and edoxaban (B01AF03), irrespective of their indications. Inpatient

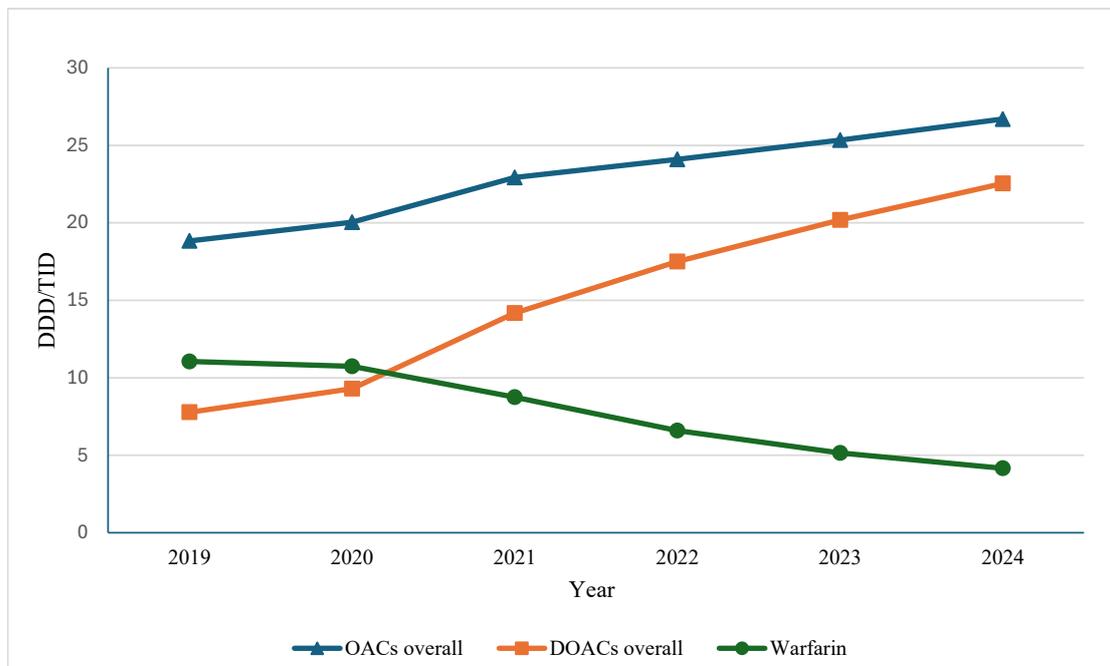
utilisation was not captured, as it does not generate electronic prescriptions in the eRecept system. Data were available for all marketed strengths of each anticoagulant. Drug utilisation is presented as defined daily doses per thousand inhabitants per day (DDD/TID) in accordance with the ATC classification and Defined Daily Dose (DDD) methodology provided by the World Health Organization Collaborating Centre for Drug Statistics Methodology (25). The DDD methodology is predicated on average maintenance doses for the primary indication in adults, inherently accounting for substances with divergent dosing schedules. Consequently, variations in the number of daily doses (e.g. once vs. twice daily regimens) are proportionally reflected in the calculated DDD/TID values. DDDs were calculated on an annual basis for each drug and for the entire class of OACs.

The data were processed using Easy CSV Editor (version 2.56, VDT Labs S.R.L.) for initial data cleaning, organisation, and preparation. Statistical analyses and visualisation of trends were conducted in Microsoft Excel (version 16.93.1, Microsoft Corporation).

Descriptive statistics were used to summarise oral anticoagulant utilisation, with the results presented as the means  $\pm$  standard deviations (SDs). Trends in utilisation were evaluated using linear regression analysis, with time (year) as the independent variable and drug utilisation (DDD/TID) as the dependent variable. The significance of trends was assessed using *p* values, with *p* < 0.05 considered to indicate statistically significant differences.

## Results

The utilisation of oral anticoagulants markedly increased during the observed study period, rising from 18.83 DDD/TID in 2019 to 26.70 DDD/TID in 2024 (*p* < 0.01). The average utilisation of OACs over the entire study period was  $22.99 \pm 3.05$  DDD/TID. This growth was primarily driven by DOAC utilisation, which increased significantly from 7.78 DDD/TID in 2019 to 22.54 DDD/TID in 2024 (*p* < 0.01). In 2019, DOAC prescriptions accounted for 41.29% of total OAC prescriptions, increasing to 84.41% by 2024. Conversely, warfarin utilisation declined significantly, from 11.06 DDD/TID in 2019 to 4.16 DDD/TID in 2024 (*p* < 0.01) (Figure 1). The mean utilisation rates over the study period were  $15.24 \pm 5.92$  DDD/TID for DOACs and  $7.74 \pm 2.89$  DDD/TID for warfarin.



**Figure 1.** Oral anticoagulants prescription trend (2019–2024).

DDD/TID, Defined daily doses per thousand inhabitants per day; DOACs, Direct oral anticoagulants; OACs, Oral anticoagulants.

Among the individual DOACs, rivaroxaban utilisation demonstrated the most significant growth, increasing from 2.95 DDD/TID in 2019 to 9.92 DDD/TID in 2024 ( $p < 0.01$ ), with an average utilisation of  $6.84 \pm 3.00$  DDD/TID. A substantial increase was also observed in the utilisation of apixaban, which increased from 2.62 DDD/TID in 2019 to 8.99 DDD/TID in 2024 ( $p < 0.01$ ), with an average utilisation of  $5.24 \pm 2.43$  DDD/TID. Dabigatran exhibited two distinct trends: a significant increase in utilisation from 2.05 DDD/TID in 2019 to 3.51 DDD/TID in 2022 ( $p < 0.05$ ), followed by stagnation between 2022 and 2024, with utilisation remaining at approximately 3.51 DDD/TID ( $p > 0.05$ ). The mean utilisation of dabigatran over the entire period was  $3.00 \pm 0.66$  DDD/TID. Edoxaban was the least utilised DOAC throughout the study period, with minimal fluctuations and no statistically significant trend observed ( $p > 0.05$ ), with an average utilisation of  $0.16 \pm 0.03$  DDD/TID (Table 1).

**Table 1.** Oral Anticoagulants Utilisation (2019–2024).

Drug (DDD/TID)	2019	2020	2021	2022	2023	2024	Mean $\pm$ SD
Warfarin	11.06	10.75	8.75	6.60	5.15	4.16	$7.74 \pm 2.89$
Rivaroxaban	2.95	3.48	6.82	8.49	9.39	9.92	$6.84 \pm 3.00$
Apixaban	2.62	3.29	4.11	5.35	7.09	8.99	$5.24 \pm 2.43$
Dabigatran	2.05	2.32	3.05	3.51	3.55	3.51	$3.00 \pm 0.66$
Edoxaban	0.15	0.21	0.19	0.16	0.15	0.11	$0.16 \pm 0.03$

DDD/TID, defined daily doses per thousand inhabitants per day; SD, standard deviation.

## Discussion

Our study confirms a persistent increase in the utilisation of oral anticoagulants in the Czech Republic, a trend that is consistent with previous findings. A similar upwards trajectory in OAC prescription has been observed in the United States (26), and a previous study in the Czech Republic conducted by Maly et al. reported a continuous increase in OAC use from 2007 to 2017 (23). According to their findings, OAC utilisation in the Czech Republic reached 17.64 DDD/TID in 2017, whereas our data show a further increase to 18.83 DDD/TID in 2019, indicating the continuation of this trend. However, direct comparison is limited by methodological differences. The previous study was based on distributor-reported data, which did not distinguish between outpatient and inpatient prescriptions, whereas our study focused exclusively on electronically prescribed outpatient prescriptions. Nevertheless, the overall trend is evident, reflecting the growing clinical need for anticoagulation prescriptions. The increasing administration of OACs is likely driven by the increasing incidence of AF and VTE, the two primary indications for anticoagulation therapy (27,28).

The utilisation of DOACs has surpassed that of warfarin as the predominant anticoagulants used in the United States since 2017 and in the United Kingdom since 2019 (20,26). This transition aligned with the 2016 European Society of Cardiology guidelines for the management of atrial fibrillation, which recommended DOACs as the preferred initial treatment option over warfarin for stroke prevention in patients with NVAf (29). However, our data suggest that this shift did not occur in the Czech Republic until 2021.

A plausible explanation for this delay is the gradual relaxation of restrictions for prescribing DOACs in the Czech Republic. The modifications implemented in 2020 and 2021 resulted in increased accessibility, thereby establishing DOACs as the preferred initial treatment for all patients with NVAf, leading to a substantial increase in their utilisation. Prior to these regulatory changes, DOACs could only be prescribed to patients with a documented contraindication to warfarin, such as the inability to maintain the international normalised ratio (INR) within the therapeutic range, a history of severe adverse effects related to warfarin therapy, or the inability to undergo regular INR monitoring. These restrictions significantly limited their widespread adoption, although international guidelines had already recommended DOACs as the preferred treatment option.

The impact of the COVID-19 pandemic and the resulting necessity for treatments that do not require regular in-person monitoring may have also been contributing factors. DOACs do not require INR checks, and as a result, their use may have been favoured over warfarin during periods of restricted health care access. A previous study suggested that the COVID-19 pandemic could have played a role in accelerating this transition to DOACs in England (30), although direct data from the Czech Republic are not available to confirm this effect.

Rivaroxaban and apixaban were the most frequently prescribed DOACs in our study, while the trend of increasing dabigatran utilisation stagnated, which is consistent with international data (20,21). A notable difference, however, is that while apixaban is the most commonly prescribed DOAC in the studies mentioned above, rivaroxaban prescriptions remain dominant in the Czech Republic. However, in these studies, rivaroxaban held the leading position as the most prescribed DOAC for a significant portion of the study period, with apixaban only surpassing it in recent years. Given the delayed adoption of DOACs in the Czech Republic, as evidenced in our study, it is conceivable that a comparable transition towards apixaban, the most frequently prescribed DOAC, may also occur in the coming years.

The stagnation of dabigatran utilisation can be attributed to several factors. As the first DOAC on the market, it initially benefited from its early availability and the introduction of a specific antidote (idarucizumab). However, newer agents such as rivaroxaban and apixaban have several advantages, including a lower risk of gastrointestinal bleeding with apixaban (31,32), better suitability for patients with renal impairment (13,33), fewer drug interactions and improved gastrointestinal tolerability (34), and, in the case of rivaroxaban and edoxaban, more convenient dosing regimens. Additionally, a reversal agent (andexanet alfa) is now available for apixaban and rivaroxaban. In the treatment of VTE, another limitation of the use of dabigatran is the requirement for at least five days of prior parenteral anticoagulation. These factors have likely contributed to the significant increase in rivaroxaban and apixaban prescriptions over dabigatran prescriptions in recent years.

### **Limitations**

Our study has several limitations that should be considered when interpreting the results. First, the data used in our analysis include only outpatient prescriptions recorded in the electronic prescribing system and do not include OAC use during hospitalisation. This may slightly influence the overall trends in OAC use.

Second, the dataset does not include information on the indication for anticoagulation therapy, so it was not possible to distinguish between prescriptions for AF, VTE, and other approved indications. Additionally, we did not analyse prescription trends on the basis of different drug strengths. However, it is important to note that the DDD/TID calculation methodology does not distinguish between specific indications or dosing regimens, as it assigns a standard DDD value to each drug.

Moreover, the dataset utilised in our study does not comprise patient-level demographic data, such as age, sex, or comorbidities. The available data are aggregated at the regional level, which limits the ability to assess changes in the structure of the target population receiving anticoagulant therapy.

Finally, owing to insufficient data coverage in 2018, our analysis starts in 2019. This means that there is no direct continuity with the previous Czech study, which analysed trends up to 2017. Although our results indicate a continuation of previously observed trends, the lack of data from 2018 limits the ability to track short-term changes in prescription patterns during the early years of the study period.

### **Conclusion**

The present study confirms a continuous increase in the utilisation of oral anticoagulants in the Czech Republic between 2019 and 2024, primarily driven by the increasing prescription of DOACs. While warfarin remained the dominant anticoagulant in the early years of the study period, the use of DOACs surpassed the use of warfarin in total use volume in 2021. The findings of this study suggest that this transition occurred at a later point in time in the Czech Republic than in other countries, a phenomenon that is presumably attributable to the gradual relaxation of prescribing restrictions that occurred during 2020–2021. The most frequently prescribed agents within the DOAC category were rivaroxaban and apixaban, whereas dabigatran prescriptions showed stagnant growth.

The findings provide valuable insights into anticoagulant prescription patterns and their evolution in response to regulatory and clinical practice changes. Further research is needed to explore prescription trends by specific indications and patient subgroups to better understand the factors influencing anticoagulant selection in the Czech Republic.

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## **Conflicts of Interest**

The authors declare that they have no conflicts of interest related to this study.

## **Adherence to Ethical Standards**

Not applicable.

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