



ORAL ANTICOAGULANTS IN THE JORDANIAN ROYAL MEDICAL SERVICES: A COMPARATIVE ANALYSIS OF DIRECT ORAL ANTICOAGULANTS AND WARFARIN

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ABSTRACT

Introduction: Thromboembolic disorders are among the most common cardiovascular disorders worldwide and are an important indication for anti-coagulation drugs, and the Direct Oral Anticoagulants (DOACs) are becoming the alternative choice to the traditional and more demanding-to-use Vitamin K Antagonists (VKAs) due to their better profile and need for less monitoring. Jordanian Royal Medical Services (JRMS) is a key player in the healthcare sector in Jordan and identifying the use and distribution of such important medicines across its premises is vital for increasing patient care and management of resources.

Methodology: In this study, a descriptive quantitative approach using secondary data on anticoagulant distribution will be used. The data that will be provided directly from the JRMS will encompass the average monthly distribution of each medication at King Hussein Hospital and Queen Alia Center for Heart Diseases, for the duration of 2020-2023. The data will be developed and analyzed using IBM SPSS 28.0 Software. The analysis will support the calculation of the total yearly distribution volume, proportion of DOACs to Warfarin distribution and individual share of each DOAC in each hospital. Year-over-year growth rates of each anticoagulant will also be calculated, which will help recognize dynamic changes in distribution. These trends will be graphically represented using the data visualization techniques thus a clear and details understanding of the trends in the distribution of anticoagulants and their utilization in the given timeframe can be achieved. The results will be analyzed to offer an insight into the consumption patterns, distribution efficiency, and possible clinical preferences in the JRMS healthcare system.

Results: Between 2020 and 2023, warfarin remained the most distributed oral anticoagulant but experienced a continuous decline in average monthly volume (-14.9% at King Hussein Hospital and -36.4% at Queen Alia Center). Conversely, listed DOAC distribution nearly doubled at both facilities (+94.9% and +93.5%, respectively). The proportion of DOACs relative to total anticoagulants rose from approximately 12% in 2020 across both sites to 23.8% at King Hussein Hospital and 30.1% at Queen Alia Center by 2023. Furthermore, distinct facility-level profiles emerged by 2023; apixaban and dabigatran were the most distributed DOACs at King Hussein, whereas dabigatran and rivaroxaban were most prominent at Queen Alia

Conclusion: The JRMS distribution network reflects a clear shift toward DOAC utilization, aligning with global clinical trends, though warfarin remains the highest-volume agent. The divergent product profiles and varying DOAC uptake rates between the two hospitals emphasize the necessity for facility-specific forecasting and procurement strategies rather than a standardized, network-wide supply formula. Integrating localized, offline web-based inventory tracking and active supply chain risk management will be essential for monitoring these shifting dispensing patterns.

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1. INTRODUCTION:

Oral anticoagulation is a key part of the prevention and treatment of thromboembolic disease particularly in patients with AF and VTE. Historically, warfarin was the primary oral anti coagulant, but administering this medication is extremely problematic due to its narrow therapeutic range, the effect of certain foods, drugs and itself on the INR, and the time course between its dose and activation. The Direct Oral Anticoagulants (DOACs) (dabigatran, rivaroxaban and apixaban) were created to offer more predictable anticoagulation with less routine monitoring. Routine clinical practice, randomized evidence, and current recommendations support the use of DOACs over warfarin in eligible patients with nonvalvular atrial fibrillation (NVAF), with some exceptions and the need to assess renal function and titrate the dose [3,4].

Changeover from warfarin to DOACs does not just depend on the clinical decision. It is also a phenomenon in the health system and supply chain. A medicine that is being more frequently chosen by clinicians should be forecast, purchased, stored, dispensed, and kept available. But at the same time some warehousing problems may occur for many reasons such as fluctuations in demand, institutional policy, procurement cycles, substitution and temporary shortage. Records of dispensing and issues are therefore valuable for providing context for patterns in dispensing, but should not be assumed to give information about levels of patient use or of prescribing.

Under the Jordanian Royal Medical Services (JRMS) hospitals and centers are connected to a huge network. In this study, two clinical points namely King Hussein Hospital and Queen Alia Center for Heart diseases were examined and the quantities discharged to them from the medical warehouses of the JRMS were studied in the period 2020-2023, with the annual average monthly issued quantities as the primary data. The first question was: (1) Will warfarin continue to be the main distributed anticoagulant? (2) How will the proportion of distribution of the DOACs change over time? (3) Do the two hospitals have different product profiles – in essence, institutional preferences? Because the data are not supplemented by information on physicians, patients' diagnoses, doses, stock-outs or prescriptions, the analysis is intentionally limited in its use of bold language to discuss these patterns.

2. Literature review:

The monitoring and pharmacological managements are different between warfarin and DOACs. It's important to note that while warfarin is closely monitored and dose adjustment are made

using INRs, the pharmacokinetics of DOACs are more predictable and there is less need for regular coagulation monitoring. While these differences can make DOACs attractive, they do not eliminate the need for clinical evaluation. When choosing the dose or drug, several patient-related factors should be taken into account, such as renal function, age, concomitant medication, indication, and others [1,2].

There have been general trends in favor of DOACs in eligible patients with AF. A patient-level network meta-analysis of pivotal randomized trials (RCTs) did not detect any significant difference between reference-dose DOACs and the warfarin arm regarding the hazards of stroke or systemic embolism, death, or intracranial bleeding [3]. Therefore, the Joint 2023 ACC/AHA/ACCP/HRS Guideline for the Management of Adults with Atrial Fibrillation recommends that DOACs be used as the preferred alternative to warfarin in most patients with AF, except in certain situations, including moderate-to-severe mitral stenosis or mechanical heart valves [4]. These results provide context for reviewing health-system distribution data to determine whether movement towards DOACs is reflected in those data. Such changes are not, however, evidence of clinically appropriate substitution, but rather of DOAC distribution.

Guidelines are more general in language than may be apparent in practice. Between 2011 and 2020, DOAC use increased while warfarin use decreased across 436,864 patients with atrial fibrillation in 88 health systems, with significant variation across health systems [5]. This result supports looking at the performance of the two JRMS sites separately rather than assuming that performance is similar across both hospitals within the JRMS network. The differences among institutions could be due to patient mix, the type of specialist practice, the formulary, medicine procurement, local protocols, or access conditions; no specific reasons can be identified with the present data.

The literature also warns against using the amount issued as actual therapy. One population-based study of patients with AF showed non-optimal adherence and differences in adherence and persistence among individual OACs [6]. A study on the use and prescribing of DOACs found a high likelihood of potentially inappropriate use, particularly regarding dose, duration, and administration, highlighting the importance of prescriber education and medication review for DOACs [1]. Therefore, distribution data can be useful for surveillance and forecasting, but must be linked to prescriptions, administration data, patient-level diagnosis data, and clinical monitoring data before conclusions about quality or physician behavior can be formed.

3. Methodology:

3.1 Analytical rationale:

Clinical trials and warehouse surveillance address different questions. Trials are established to compare treatments with definite inclusion and exclusion criteria, protocolized dosing, follow-up, and outcome ascertainment. Distribution logs indicate the flow of medicines through a health system. These are not mutually exclusive views—the evidence seen in the clinic could be driving why a system decides to expand a DOAC, while warehouse data show whether that is happening. Identifying the full pathway from clinical eligibility to treatment uptake, treatment engagement, and outcome remains difficult to achieve with either source alone.

As a rule, the three DOACs analyzed here should not be treated as interchangeable. They may have different indications, dosage regimens, renal handling, formulations, and other considerations for clinical use. The strength or dose for the DOACs is not mentioned in the study data. The dose frequency, indication, treatment duration, and number of patients are also not indicated. Therefore, it is not possible to safely convert 3,000 tablets into a number of patients or treatment-days. The unit of interpretation in this study is the average monthly issue amount as recorded in the study data.

3.2 Study design and data source:

This was a retrospective, descriptive quantitative study of secondary distribution data from the central medical stores of the JRMS. The data presents the average monthly quantities dispensed to King Hussein Hospital and Queen Alia Center for Heart Diseases for four oral anticoagulants (OACs): apixaban tablets, dabigatran tablets, rivaroxaban tablets, and warfarin 5-mg tablets during the 2020–2023 period. No JRMS or patient data, doses, prices, population denominators, or stock data were merged externally.

There is no rivaroxaban entry in the data provided for 2021. This was not considered to be zero, but was instead regarded as missing. For this reason, 2021 DOAC totals and shares are limited to the listed values for apixaban and dabigatran, and the values are explicitly reported where applicable.

Measures and calculations:

The following quantities were determined for every hospital year:

$$T_{hy} = A_{hy} + D_{hy} + R_{hy} + W_{hy}$$

T = total listed anticoagulant distribution, A = apixaban, D = dabigatran, R = rivaroxaban, and W = warfarin. DOAC distribution was calculated as (A+D+R), using only the values shown in the source table. DOAC share was calculated as DOAC distribution divided by total listed distribution $\times 100$. The DOAC-to-warfarin ratio was defined as DOAC distribution divided by warfarin distribution. Product share was calculated as each product's quantity divided by the quantities of all products listed during the hospital-year.

Year-over-year percentage change was calculated as:

$$YoY\ change = \frac{Q_t - Q_{t-1}}{Q_{t-1}} \times 100$$

In the principal comparisons, the observations were not multiplied by 12 because they are averages of monthly observations. Multiplying by 12 would give an annualized estimate, but it would not improve the comparison and might suggest greater precision than is present in the source table. No statistical tests were used to make inferences from the data, because there was one aggregate observation per drug, hospital, and year, and the data do not include patient-level or month-level variance.

Interpretive framework:

Only in a qualified sense is "consumption" used to mean the distribution pattern given in the table. "Preference" does not mean the preference of particular doctors; rather, it refers to the apparent product profile of a hospital. There are two aspects to the analysis: a level effect (more of a product is issued in absolute terms) and a composition effect (the proportion of DOACs in each hospital's total product distribution). This distinction is crucial because the absolute amount of DOACs is generally higher at Queen Alia Center, but the more important measure of therapeutic mix is the within-hospital DOAC share.

4. Results and Discussion:

The most common product listed in all hospital years was warfarin. The amount of each of the listed anticoagulants was found to be significantly more in 2020, 2021 and 2023 in Queen Alia Center than in King Hussein Hospital and was comparable in 2022. This is an absolute distribution difference, not evidence of increased per-patient usage, as patient denominators were not provided (Table 1).

Table 1: The frequency of warfarin distribution per year in study hospitals

YEAR	KING HUSSEIN TOTAL	KING HUSSEIN DOAC SHARE	QUEEN ALIA TOTAL	QUEEN ALIA DOAC SHARE
2020	33,359	12.0%	44,723	12.4%
2021	29,758	11.8%	36,394	10.6%
2022	32,968	24.9%	35,692	24.9%
2023	32,778	23.8%	35,639	30.1%

The largest overall trend was the increase in DOAC share after 2021. The share at King Hussein Hospital more than doubled, from 11.8% in 2021 to 24.9% in 2022. In parallel, at Queen Alia Center, the figure rose from 10.6% to 24.9% over the same period. The profiles then diverged in 2023: King Hussein

Hospital remained at approximately the 2022 level, while Queen Alia Center advanced further to 30.1%. This is similar to health-system variability observed in real-world studies ^[5], but the reasons for this variability cannot be confirmed from the current data (Figure 1).

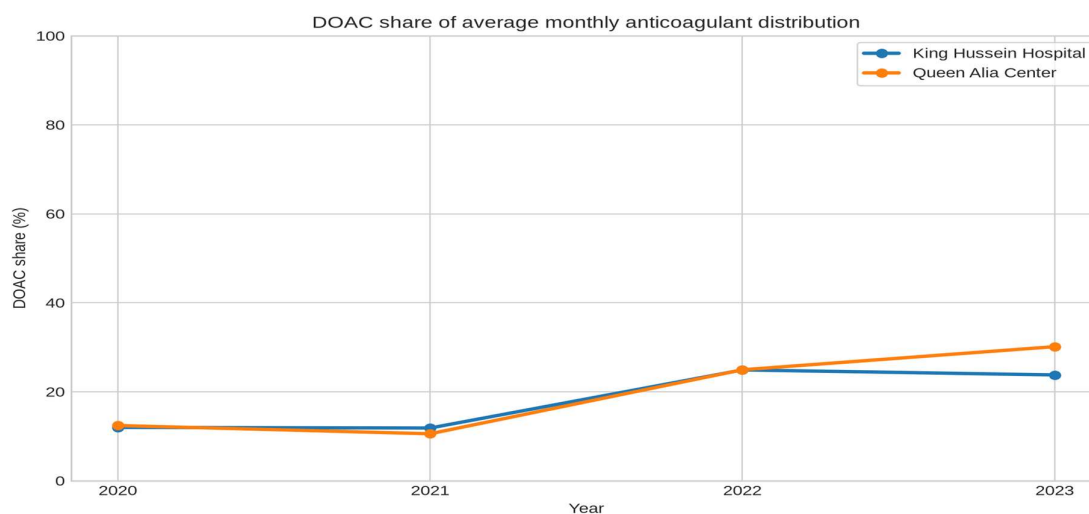


Figure 1: The denominator is the sum of the four listed products in each hospital-year. The 2021 denominator excludes rivaroxaban because no value was supplied for that cell.

4.2 Warfarin persistence and apparent displacement: Warfarin distribution decreased between 2020 and 2023 at King Hussein Hospital, from 29,361 to 24,984 average monthly units, corresponding to a reduction of 14.9%. At Queen Alia Center, it fell from 39,174 to 24,900, a decrease

of 36.4%. In contrast, the total of the listed DOACs increased from 3,998 to 7,794 at King Hussein Hospital and from 5,549 to 10,739 at Queen Alia Center. The distributed anticoagulants therefore showed a shift in composition towards DOACs, although warfarin remained the largest category (Table 2).

Table 2: Warfarin persistence and apparent displacement

HOSPITAL	WARFARIN 2020	WARFARIN 2023	CHANGE	LISTED DOACS 2020	LISTED DOACS 2023	CHANGE
KING HUSSEIN HOSPITAL	29,361	24,984	-14.9%	3,998	7,794	+94.9%
QUEEN ALIA CENTER	39,174	24,900	-36.4%	5,549	10,739	+93.5%

The rise in DOAC distribution alongside the decline in warfarin distribution generally aligns

with the international trend towards switching to DOACs in clinical practice ^[3-5]. However, this

pattern should not be taken as a blanket substitution for therapy. In 2023, warfarin was still the majority of the distribution at both King Hussein Hospital and Queen Alia Center, accounting for 76.2% and 69.9%, respectively. There may be clinical, local-practice, availability, or cost reasons why some patients continue to be treated with warfarin, but none of these can be tested using the supplied table. The literature has also demonstrated that drug-class preference should not be the only consideration in choosing between warfarin and DOACs; patient characteristics and monitoring quality must also be considered^[1,2,4].

4.3 Product-specific patterns and apparent hospital profiles: Detail can be added to the overall pattern by reading the data year by year. A comparison of the DOAC shares of King Hussein Hospital and Queen Alia Center in 2020 shows similarities within the range of 12.0%–12.4% between the two hospitals, although Queen Alia Center had the higher total distribution of listed DOACs. Queen Alia Center had the highest volume of the leading DOAC, dabigatran (3,103 units), while King Hussein Hospital distributed more dabigatran than apixaban or rivaroxaban. The first year therefore shows a similar composition at different absolute scales.

In 2021, the total listed distribution decreased at the King Hussein Hospital from 33,359 in 2020 to 29,758 and at the Queen Alia Center it's decreased from 44,723 in 2020 to 36,394 in 2021. The shares performance of the King Hussein Hospital got minimal impact, while the shares of Queen Alia Center decreased. It was difficult to ascertain if the drop was caused by decreased

demand, a product that was not distributed, a data entry error or another reason as rivaroxaban was not recorded for this year. The most defensible interpretation would be that the numbers of apixaban, dabigatran, and other products listed did not explain the overall decrease in total listed distribution.

This all drastically reversed in 2022. The total number of DOAC units issued to King Hussein Hospital was 8,210 and that issued to Queen Alia Center was 8,900. Their proportion of DOAC was almost equal (24.9%) but different as King Hussein Hospital had 2137 units of rivaroxaban vs. 1212 units of rivaroxaban for Queen Alia Center. Similarity on the class level, thus, didn't suggest similarity on the product level.

In 2023 the hospitals split once again. The apixaban value of King Hussein Hospital (4,066 units) was highest, and the values of dabigatran (3,967 units) and rivaroxaban (3,872 units) were highest in Queens Alia Center. The overall totals at Queen Alia Center and King Hussein Hospital respectively were 10,739 and 7,794. The former led to a ratio of 0.431 and the latter to 0.312 ratios between DOAC and warfarin. These are not therapeutic-equivalence ratios, it is only ratios of distribution.

The 4-year averages of the observations showed the highest average quantities of warfarin at both hospitals. Dabigatran was the most commonly collected DOAC at both locations, with apixaban as the next most common. Rivaroxaban's average was the lowest at King Hussein Hospital and higher at Queen Alia Center, but the former is restricted due to the absence of the data for 2021 (Table 3).

Table 3: The average use of APIXABAN, DABIGATRAN, RIVAROXABAN, and WARFERIN in study hospitals

HOSPITAL	APIXABAN AVERAGE	DABIGATRAN AVERAGE	RIVAROXABAN AVERAGE*	WARFARIN AVERAGE
KING HUSSEIN HOSPITAL	2,418.8	2,724.5	984.3	26,334.3
QUEEN ALIA CENTER	2,509.5	3,339.3	1,877.7	30,855.0

*Rivaroxaban averages use the three years with supplied values: 2020, 2022, and 2023.

In 2023, the hospital profiles became distinct. At King Hussein Hospital, apixaban was the leading DOAC at 4,066 units, followed by dabigatran (3,223) and rivaroxaban (505). At Queen Alia Center, dabigatran was marginally higher than rivaroxaban in absolute terms, with 3,967 and 3,872 units, respectively; the two products were close

relative to the center's total DOAC distribution. The safest conservative conclusion is that an apixaban–dabigatran DOAC profile was more represented at King Hussein Hospital in 2023, whereas rivaroxaban was more represented at Queen Alia Center (Figure 2).

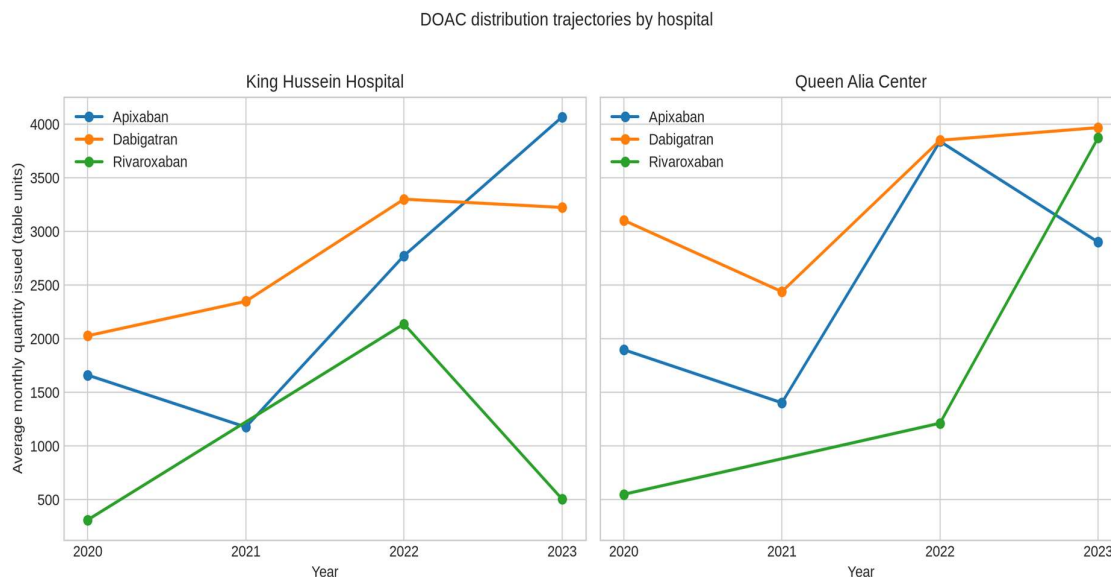


Figure 2: Rivaroxaban is not plotted for 2021 because the source table contains no value for that year.

4.4 Shortage-aware interpretation: To make up for some periods of stock shortage the average monthly quantities were used, the authors note. This effect is not present in every month but it is an effect that is a good fit to be displayed in the issue-level series as this is not a monthly effect. No months, however, are indicated in the table with shortages and those shortages are not indicated with respect to duration of shortages, the quantity requested, the quantity not supplied, emergency substitutions or balances in the warehouse. Thus the data reflect distribution under the specified supply conditions and not reflect underlying clinical demand.

That's key for the 2021 rivaroxaban gap. The computed percentage of DOAC share if the blank is counted as zero would result in a lower DOAC share and potentially suggest there was no rivaroxaban distributed. This would put an assumption into the study design, which wasn't supported by the study. The safest way to play is then to leave it missing. Future JRMS analysis should maintain counts for requested, issued, backordered and "on hand" quantities at a monthly level, to better understand if apparent decreases in quantity are due to changes in demand or supply.

4.5 Implications for planning and interpretation of physician preference: The findings yield three planning implications. First, warfarin should not be de-emphasized simply because the DOAC share has increased. Second, DOAC procurement plans should be applied at the hospital level rather than through a single network-wide mix: the DOAC share at Queen Alia Center in 2023 was 30.1%, compared with 23.8% at King Hussein Hospital. Third, hospitals should be monitored by product

within the DOAC portfolio because the facilities did not show the same trend lines.

The data cannot be used to conclude that any particular physician favored one medicine. The most defensible claim is that the distribution profiles of the two hospitals differed. Prescriber-level attribution would require prescription or dispensing information linked to physician identifiers. Likewise, the data cannot determine whether a product was selected because of guideline-concordant clinical considerations, formulary policy, patient ability to pay, provider familiarity, or availability. This conservative view is consistent with evidence that real-world anticoagulant use varies across health-care settings and that adherence or prescribing appropriateness cannot be inferred from distribution alone [1,5,6].

4.6 Sensitivity considerations, limitations, and planning implications: The direction of several comparisons is reasonably clear. The 2020–2023 comparison shows reduced warfarin distribution and increased DOAC distribution in both hospitals, with warfarin remaining the largest category in every complete hospital-year. The change in DOAC share is more affected by the missing rivaroxaban value in 2021. If that value were known, the 2021 denominator and DOAC total would need to be recalculated, and the apparent increase in DOAC share from 2021 to 2022 could be greater or smaller.

There are several caveats to the study. The data are aggregate and do not have a denominator that could be used to calculate per-patient results. The values represent quantities issued, not quantities administered or ingested. The table does not list indication, dose, medicine strength, treatment

duration, prescriber, patient characteristics, medicine requisitions or returns, back-orders, or inventory balances. Because there is no direct stock-out variable, stock-out frequency and unmet demand cannot be measured. Finally, only four annual observations are available for this period, which is not sufficient for inferential time-series modelling. These constraints are consistent with drug-utilization studies that recognize the different stages of medicine use, from recommendation to initiation, adherence, and persistence [6].

The study restrictions do not diminish its value, but they limit it. The analysis can detect differences in the location and supply of medicines and changes in the supply mix at two sites. It cannot show which drug was clinically preferred, how many more patients may have been treated at one hospital, whether a shortage caused fewer patients to be treated, or whether a particular treatment was clinically appropriate. An increase in tablets issued could reflect increased use, restocking of orders, or a change in ordering practice. A decline, on the other hand, could be due to decreased demand, a stock limitation, substitution, or a data issue.

The results lead to some planning implications. As the transition continues, procurement and monitoring assistance for warfarin continues to be relevant, even though the medication is widely distributed, but with a different intensity – an excess of focus on DOAC growth could lead to a neglect of the need for warfarin. Accompanying this proportional upward trend in DOAC distribution in recent years is, however, a proportional increase after 2021, suggesting that the annual forecast approach should not be based solely on the LRM. Forecasting with product-specific approach should be preferred as the trend of the three DOAC products does not match.

An average number of issues per product, the percentage of issues containing DOACs, the ratio of DOAC issues to warfarin issues, data completeness, and the number of issues requested vs. issues issued could be included in a JRMS monitoring dashboard. Recall that if there are more requests than issues then there may be demand that went unrefilled or it may be that a gap was there because replenishment was light in the presence of strong demand. The monthly requisitions, issues, returns, back-orders and stock on hand balance, therefore, should be incorporated into future data collection efforts. These fields would be useful in differentiating unmet demand from the inventory corrections and aid in interpretation of sustained utilization.

When the results can inform clinical governance, this does not endorse anyone overhauling the use of one drug over another. Each facility's local formularies, prescriber programs, renal-function data and availability logs could be

examined to explore the product divergence for 2023. This audit is based on guidelines recommending personalized decision making about the choice of the right anti-coagulant [4] and evidence that many cases of potentially inappropriate DOAC use may relate to the dose, duration, administration and interaction with other medications [1]. The distribution series may point the direction for the search, but not give the explanation.

In another study, the distribution series could be associated with just prescription or patient data and then associated with both in future steps. Firstly, the lost cell for rivaroxaban 2021 should be reconciled and the unit strength and details of the tablets should be checked in the products. Second, monthly requisitions and inventory events should be added. Third, issues should be linked to prescriptions, indications, dosing schedules, and patient numbers. Fourth, adherence, persistence, safety, and appropriateness could be evaluated. This would maintain a current baseline without over-interpreting the distribution data.

It is not possible to conclude from the data which medicine individual doctors preferred. The most defensible statement is that the two hospitals exhibited different average distribution profiles. Prescription records and physician or prescriber identifiers would be needed for physician-level attribution. Likewise, the information does not indicate whether a product was selected because of guideline-concordant factors, formulary policy, cost, prescriber familiarity, or availability. This conservative view is consistent with evidence that distribution alone is not evidence of use or prescribing appropriateness [1-6].

5. Conclusions:

Throughout 2020–2023, warfarin continued to be the most prevalent oral anticoagulant distributed through JRMS main medical stores to the two study facilities, while its share decreased as the distribution of listed DOACs increased. The DOAC share at King Hussein Hospital rose from 12.0% to 23.8%, whereas the share at Queen Alia Center rose from 12.4% to 30.1%. The most significant change is that from 2021. Distribution of DOACs increased over time, particularly at Queen Alia Center, with the number of apixaban and dabigatran distributed over time being higher at King Hussein Hospital compared with the other centers.

The findings and implications are related to distribution and apparent medicine mix reported at the hospital level only and do not necessarily represent actual medicine mix received, physician selection of medicine, adherence or clinical appropriateness. The results of the causal interpretation are restricted due to the lack of information on denominators among patients, stock-out reports, and the lack of information on 2021

observation with rivaroxaban. In spite of this the study gives an excellent point-of-reference for JRMS pharmaceutical planning. Future studies should correlate issues from the warehouse, monthly stock, order size, number of prescriptions, volume of medication dispensed, number of patient visits, drug

class and medication strength aspects with the physicians' information. For this linkage, more specific assessment of demand, shortages, substitution, appropriateness of use, and clinical factors related to DOAC use, would be possible.

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