INCREASING THE PERCENTAGE OF WARFARIN-TREATED PATIENTS WITH GOOD TTR CONTROL IN SULTAN ISMAIL HEALTH CLINIC

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Abstract

Time in therapeutic range (TTR) for warfarin measures the percentage of time the patient's International Normalised Ratio (INR) is within the therapeutic range, reflecting the quality of anticoagulation control. Poor TTR control increases patients' risk of thromboembolic events, bleeding, hospitalisations, and mortality. A pre-remedial study revealed that only 58.8% of patients in Sultan Ismail Health Clinic achieved good TTR control (TTR>60%). This study aimed to increase the percentage of patients with good TTR control to 65% within six months, which is the standard set in the Quality Assurance Programme Indicators Manual 2023. In this quality improvement study, patients' INR levels were collected via Chemolims to assess TTR control, while questionnaires were disseminated to doctors, pharmacists, and patients to study the contributing factors. The contributing factors identified were incomplete patient history-taking by prescribers (80.0%), lack of pharmacist counselling (50.0%), non-compliance with the warfarin diet (60.0%), and dosage regimen (20.0%). In Cycle 1, the Warfarin checklist (Warf-Check) was developed to streamline the process of taking patients' history and the Express Warfarin Calculator (E-Warf) was introduced to expedite the calculation of dosage adjustments. Warfarin extended counselling (Warf-EC) was established to provide more focused counselling sessions for high-risk warfarin patients. Educational sessions were conducted for doctors and pharmacists to enhance their knowledge. In Cycle 2, the Klinik Warfarin Protocol (K-WARF) was developed to guide the management of warfarin therapy. Post-interventional results showed that the percentage of patients achieving good TTR control increased from 58.8% to 68.6% in Cycle 1, and improved to 69.3% in Cycle 2. The Achievable Benefit Not Achieved decreased from 6.2% to -3.6% in Cycle 1 and to -4.3% in Cycle 2. The average number of visits for INR monitoring per patient decreased from six to three visits within six months. We plan to expand our strategies and promote our K-WARF protocol nationwide.

KEYWORDS: Warfarin, time in therapeutic range, international normalised ratio, quality improvement study

Problem

Warfarin, a vitamin K antagonist, is commonly used as an anticoagulant in patients with atrial fibrillation, atrial or mitral valve replacement, venous thromboembolism, or antiphospholipid syndrome. Patients receiving warfarin therapy require routine International Normalised Ratio (INR) blood monitoring to ensure their INRs are within the therapeutic range. To monitor the quality of anticoagulation control, Time in Therapeutic Range (TTR) is preferred as it measures the percentage of time the patient's INR is within the therapeutic range. The minimum TTR that international guidelines have adopted to define good INR control typically ranges from 60% to 70% (1-3).

However, achieving these target standards in clinical practice remains a challenge. A verification study conducted in Sultan Ismail Health Clinic (KKSI) from September 2022 to February 2023 revealed that only 58.8% of warfarin-treated patients achieved good TTR control (TTR >60%), highlighting a notable gap in meeting recommended international benchmarks for safe anticoagulation management.

Maintaining optimal anticoagulation control is particularly crucial for primary care facilities like KKSI in the Johor Bahru district. Serving a population of 143,113 with daily patient visits ranging from 1,200 to 1,500, KKSI operates diverse departments such as the outpatient, maternal and child health, pharmacy, laboratory, dental services, dietetic services, and physiotherapy staffed by three Family Medicine Specialists, 26 medical officers, 20 pharmacists, and allied health staff.

Among its outpatient services covers acute care, chronic disease clinics, and specialised wellness program. Currently, KKSI manages 128 active patients on warfarin therapy. INR monitoring for patient on warfarin therapy is handled by a multidisciplinary workflow where laboratory staff conduct point-of-care testing (POCT) every Friday. Following the testing, medical officers adjust dosage regimens, and pharmacists provide individualised counselling alongside prescription refills.

To bridge this clinical gap and align patient outcomes with national standards, this quality improvement project aimed to increase the percentage of warfarin-treated patients with good TTR control at KKSI from 58.8% to 65% within six months, following the target set in the Manual for Quality Assurance Program Indicators 2023 (4).

Background

Warfarin remains the most commonly used anticoagulant to prevent thromboembolic events despite the emergence of direct oral anticoagulants (DOACs) due to its availability and cost. Due to its narrow therapeutic index, it is important to ensure the patients' INR is maintained within their therapeutic range. A good TTR control ensures the safety and efficacy of the warfarin therapy. However, several Asian studies have shown that the mean TTR achievements were generally lower. For example, in a study in Korea, the TTR was 49.1%, while in Singapore it was reported to be slightly higher at 58.0% (4,5). A retrospective observational study carried out in a cardiology referral centre in Selangor, Malaysia, revealed that the mean TTR was 60.6% over 5 years. During the study period, only slightly more than half of the patients (57.6%) achieved good INR control (TTR>60%) (6).

Patients with poor INR control experienced a higher risk of ischaemic strokes or thromboembolic events and had higher mortality risks associated with intracranial bleeding, strokes, and cardiovascular events (7-9). A British study has shown that a 10% increase in time when INR is deranged is linked with a 29% increase in mortality risk and a 12% increase in the risk of suffering from strokes or thromboembolic events. Poor INR is also associated with an increased hospitalisation rate (10). Increased hospitalisation and strokes or thromboembolic events would, in turn, lead to an increase in healthcare costs. Several factors may contribute to the poor INR control among patients treated with warfarin. A study conducted by Alphonsa and colleagues (11) reported that 50% of the patients had a poor knowledge level. Most patients (62.9%) on oral anticoagulation therapy were unaware of their INR targets, and only 30% of them had their INRs within range. Poor knowledge level in most patients

taking warfarin was also documented in other studies (12-14). The lack of knowledge regarding their condition and warfarin treatment may lead to intentional non-compliance.

A doctor's knowledge of oral anticoagulant therapy is also crucial in ensuring optimal therapeutic effect. Despite that, a few studies in China have reported that the doctors' knowledge of oral anticoagulants is inadequate, and huge gaps exist between regions, hospitals, and departments. Multiple studies in China showed that less than 50% of patients on oral anticoagulants were prescribed an appropriate dose according to recommended guidelines (15). According to the China National Stroke Registry, out of 96 nonvalvular atrial fibrillation patients with stroke who were taking warfarin, only one was admitted with an INR between 2 and 3 (16). A single-centre study in 2020 from Fuwai Yunnan Cardiovascular Hospital showed that the prevalence of inappropriate anticoagulant prescriptions was 46.3% (17).

To address this problem, the involvement of pharmacists in the management of patients treated with warfarin has been practised in both local and international healthcare settings. In pharmacist-led warfarin clinics, patients who receive more comprehensive counselling have achieved better INR control (18,19). A study in Kajang Hospital, Malaysia, showed that the TTR was significantly higher in the Warfarin Medication Therapy Adherence Clinic (MTAC) (66.6%), compared to usual medical care patients (45.5%) (20). The Warfarin MTAC is a pharmacist-led clinic where pharmacists take an active role in managing and monitoring warfarin patients. During each INR follow-up visit, pharmacists assess the patient's overall anticoagulation control and provide individualised counselling. They are responsible for making dosage adjustments, monitoring drug-drug or drug-food interactions, counselling on compliance, and detecting adverse events (21-22).

In addition, the provision of educational interventions for patients by pharmacists has also shown positive results in improving patient knowledge and their INR control (13,23). These materials can range from physical information booklets, DVDs as visual aids, and self-monitoring diaries. Besides patients, the MTAC pharmacists concurrently conduct periodic training, guidance, and establish a local network for sharing clinical decision-making. Such efforts are necessary to improve medical staff knowledge and to strengthen their clinical management ability (15).

A scoping review by Omer et al. (24) has shown that 81.6% of the studies on Vitamin K Antagonists (VKAs) reported at least one statistically significant positive outcome from pharmacist-led education on VKAs. Specifically, 31 out of 38 studies on VKAs demonstrated significant improvements in patient knowledge, INR control, TTR, and medication adherence. Even though the role of pharmacists in patient education on VKAs has been widely studied globally, a significant gap persists in the local literature. While pharmacists are identified as a key part of the solution, their own baseline knowledge and competency in managing complex warfarin therapy have not been systematically evaluated, particularly outside of specialised clinic settings like MTACs. The existing research assumes pharmacists are already fully equipped to bridge the knowledge gaps of both patients and other clinicians. Consequently, there is a lack of studies investigating the effectiveness of a targeted educational program designed specifically to standardise and enhance pharmacists' clinical skills in this critical area.

Measurement

This quality improvement study adopted a universal sampling approach. The indicator used was the percentage of warfarin-treated patients with good TTR, and it was calculated as follows:

$$\text{Percentage of warfarin-treated patients with good TTR control} = \frac{\text{Number of warfarin-treated patients with good TTR}}{\text{Total number of warfarin-treated patients}} \times 100$$

The study was conducted in two phases: Cycle 1 from March 2023 to August 2023 and Cycle 2 from September 2023 to February 2024. This study included all active warfarin-treated patients with valid prescriptions and ongoing doctors' appointments in KKSI throughout the study

period. However, patients who collected their medicines using the Integrated Drug Delivery Service (SPUB) were excluded. The SPUB is a medication supply system through which patients can have their medicines refilled at other healthcare facilities within the Ministry of Health via prescription referrals. These SPUB patients were excluded because they do not undergo INR monitoring at KKSI, and their warfarin dosage regimens are maintained according to the original prescription throughout the supply period. In addition, patients who missed their INR appointments or switched to alternative oral anticoagulants were excluded.

TTR for each patient was calculated using the Rosendaal method based on their INR results from each visit, retrieved from Chemolims, a laboratory review system (25). By determining each patient's TTR, the percentage of warfarin-treated patients with good TTR can be calculated. The standard was set as 65%, which was aligned with the Quality Assurance Programme (QAP) Indicators Manual 2023 standard (4).

Self-administered questionnaires were additionally used to collect data regarding factors contributing to the problem. The questionnaires (Appendix 1) were distributed among all doctors (n=26) and pharmacists (n=20) to assess their knowledge level in managing warfarin-treated patients, as well as to the patients (Appendix 2) (n=30) to assess their understanding of warfarin treatment. Furthermore, all warfarin prescriptions received by the pharmacy during 12-15 February 2023 (n=30) were reviewed to check the appropriateness of the warfarin dosing regimen.

Data collected from September 2022 to February 2023 in the verification phase showed that only 58.8% of the patients treated with warfarin achieved good TTR control. The Achievable Benefit Not Achieved (ABNA) was 6.2%.

Initial Assessment of the Problem

The factors contributing to the low percentage of warfarin-treated patients with good TTR were analysed using a problem analysis chart as depicted in Figure 1.

The existing process of care (Figure 2) was reviewed to determine the critical steps involved in ensuring better INR control. During each visit for INR monitoring, doctors will review patients' INR results and identify possible factors affecting their INRs. They will then make appropriate dose adjustments based on guidelines. When patients go to the pharmacy for a medicine refill, pharmacists screen the warfarin prescriptions to ensure the dose regimens are appropriate based on the patients' current INR and target ranges. They will make interventions if the dose adjustments are inappropriate. Pharmacists will then dispense warfarin and counsel the patients.

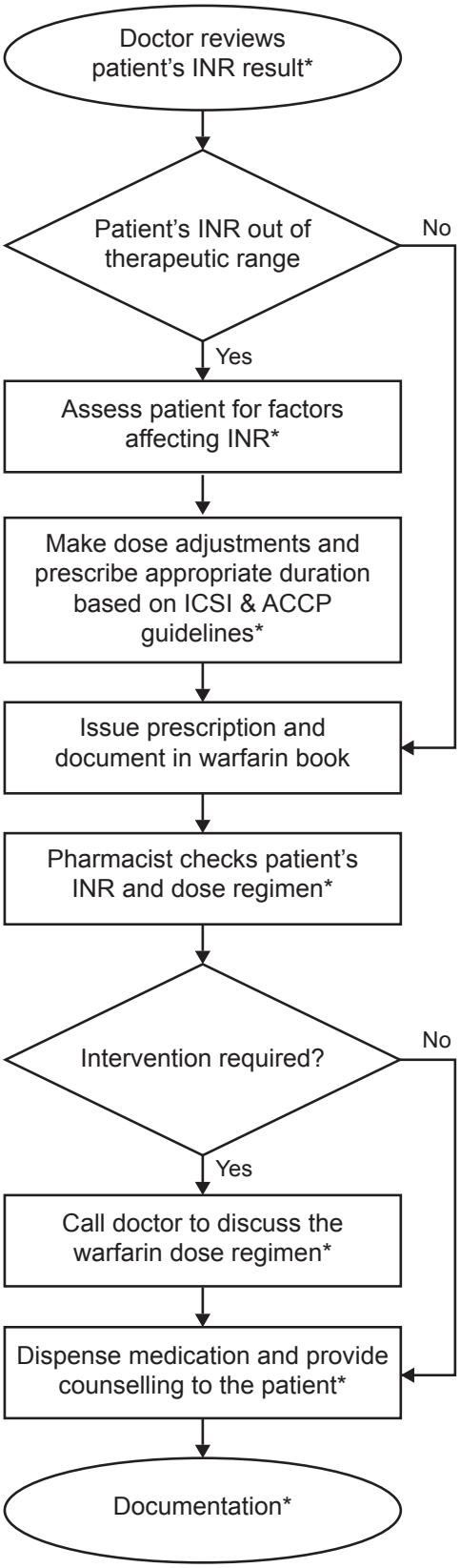
Upon reviewing this process of care, we identified two main contributing factors: inappropriate dose adjustment and duration prescribed by prescribers, and inadequate pharmacist counselling. Analysis of all the warfarin prescriptions collected over one week (12-15 February 2023) during the verification study has shown that only 70.0% (n=21) of patients seen by the doctor had their warfarin indication and INR target appropriately documented. Moreover, a comprehensive history assessing all factors influencing INR was obtained in only 20.0% (n=6) of patients. Dose adjustments adhered to the Institute for Clinical Systems Improvement (ICSI) guideline (26) in 50.0% (n=15) of cases, whereas 70.0% (n=21) of patients received treatment durations consistent with the American College of Chest Physicians (ACCP) guideline (27). Pharmacist review was conducted in 60.0% (n=18) of patients who underwent dose adjustments and had treatment durations prescribed. Additionally, counselling records in the Pharmacy Information System (PhIS) revealed that only half of the patients received counselling on factors affecting INR, with corresponding assessments of their understanding and medication compliance. Notably, no follow-up appointments were scheduled for patients whose INR values fell outside the therapeutic range.

A self-administered questionnaire among 30 warfarin patients identified lack of patient engagement as another contributing factor. Based on the questionnaire findings, 60.0% (n=18) of them were not compliant

with the warfarin diet, and 20.0% (n=6) of them were not compliant with the warfarin dosage regimen. Additionally, 70.0% (n=21) reported that the waiting time for doctor consultations and medication refills was long. These highlighted that it was possible to improve patients' compliance with the warfarin regimen by implementing suitable strategies. The pre-test (Appendix 3) revealed that only 19.2% (n=5) of doctors and 30.0% (n=6) of pharmacists demonstrated adequate knowledge (scoring ≥7) in managing patients on warfarin.



Figure 1: Problem analysis chart of the low percentage of warfarin-treated patients with good TTR control in KKSI



* indicates critical steps

ICSI = Institute for Clinical Systems Improvement
ACCP = American College of Chest Physicians

Figure 2: Flow chart of the process of care of doctors' consultation sessions and management of warfarin-treated patients in the pharmacy

Strategy

In this study, four strategies were introduced in Cycle 1 (March to August 2023). All these strategies were reinforced in Cycle 2 (September 2023 to February 2024), along with the development of the *Klinik Warfarin* (K-WARF) Protocol (28).

During Cycle 1, the first strategy was the implementation of a warfarin checklist (Warf-Check). Warf-Check was developed for doctors to provide a structured and standardised patient history taking. The two-page checklist was formulated in a table form, which allowed a clear and concise presentation of information. The first page gathered general information such as the indication of warfarin, target range, dose regimen, and compliance, while the second page included all the possible factors affecting the patient's INR. This checklist guides the doctors to interview patients when reviewing their INR results. Subsequently, the information documented by the doctors on the checklist can be passed on to the pharmacists, who then counsel patients based on the factors identified by the doctors. Overall, this checklist has eased communication between doctors and pharmacists and has been time-saving.

Secondly, an express warfarin dose calculator (E-Warf) was introduced in March 2023 to assist doctors in calculating warfarin dose adjustments. This calculator is a Microsoft Excel file with pre-included formulas that help to simplify the dose adjustment and calculation process. The recommended dose adjustments and regimens are based on the Anticoagulation MTAC (AC-MTAC) Protocol (24). By just entering the patient's current INR value and dose, this calculator instantly suggests a new warfarin dose regimen with an estimated INR value based on the percentage of weekly dose increase/decrease required. Using E-Warf has accelerated the calculation process and shortened the consultation time by five minutes.

Thirdly, warfarin extended counselling (Warf-EC) was established to focus on high-risk warfarin-treated patients. Before this quality improvement study, all of the warfarin-treated patients were counselled over the counter, and there were no proper follow-up appointments. With this patient-focused intervention, patients who had two consecutive INRs out of the therapeutic range or those with extreme INRs (INR<1.5 or INR>4) were sent to the counselling room for extended counselling. The pharmacist-in-charge reviewed the factors affecting the patients' INR and provided relevant counselling to the patients. The pharmacist also ensured that the doctors' dose adjustments were appropriate, and interventions were made if necessary. In addition, patients were followed up during their subsequent visits for INR monitoring until their INRs were stable (within range for two consecutive visits). This strategy allowed more comprehensive care to be delivered to the patients to improve their understanding and compliance.

The fourth remedial strategy was focused on improving the knowledge level of doctors and pharmacists. Three face-to-face educational sessions were conducted by trained pharmacists to enhance their knowledge of warfarin dose adjustment and patient counselling. The topics delivered include pharmacological action of warfarin, warfarin-food interactions, warfarin-drug interactions, and guideline-based dosage adjustment. The teaching materials were prepared based on the anticoagulant MTAC training modules developed by the warfarin MTAC Task Force, Pharmaceutical Services Division, Ministry of Health. After the one-hour educational sessions, all participants were given the same set of questions as the pre-test to reassess their level of understanding. Comparison between pre-test and post-test showed improvement in their knowledge level.

In Cycle 2, all strategies introduced in Cycle 1 were continued with some reinforcements. To improve accessibility to the E-Warf, we upgraded it to online mode, in which it can be accessed easily by scanning the QR code. QR codes for the E-Warf calculator were generated and pasted on the desks in consultation rooms and pharmacists' stations. Moreover, another CME session was held in January 2024 to introduce Warf-Check and E-Warf to new doctors and pharmacists. It allowed doctors and pharmacists to refresh their knowledge on warfarin management.

In addition, the *Klinik Warfarin* (K-WARF) Protocol was developed by

our team in Cycle 2. K-WARF Protocol is a documented protocol summarising the overall work process that was developed by pharmacists in collaboration with Family Medicine Specialists in managing warfarin-treated patients in KKSI. The protocol highlights the new standard operating procedures of the Warfarin Clinic that include the process of reviewing patients, prescribing, screening, intervention, counselling, and documentation (26). This protocol enables the standardisation and sustainability of our project.

Results

Following the implementation of the above strategies, the percentage of warfarin-treated patients with good TTR increased from 58.8% to 68.6% in Cycle 1, then to 69.3% in Cycle 2, which was both better than our standard of 65%. The ABNA was successfully reduced from 6.2% to -3.6% and finally to -4.3% (Figure 3).

All criteria in the Model of Good Care (MOGC) had improved following interventions (Table 1). For instance, the implementation of the warfarin checklist ensured that 100% of the patients were interviewed on all the possible factors affecting INR results before dose adjustment. However, there was a decline in the percentage of appropriate dose adjustments and duration of warfarin based on recommended guidelines, possibly due to a high turnover rate among doctors.

Doctors' (n=26) and pharmacists' (n=20) knowledge levels in managing warfarin-treated patients also improved after attending educational sessions. Analysis of post-test results showed that the percentage of doctors with excellent knowledge (score 10 out of 10) has increased from 0% to 42.3% (n=11) in Cycle 1 and further increased to 46.1% (n=12) in Cycle 2. Likewise, the same improvement trend was observed for pharmacists. In Cycle 2, only 14 pharmacists answered the post-test, as some of them had transferred to other health facilities. The percentage of pharmacists with excellent knowledge has improved from 0% to 35.0% (n=7) in Cycle 1 and 57.1% (n=8) in Cycle 2. Improved knowledge levels have enabled them to manage warfarin-treated patients with higher competency.

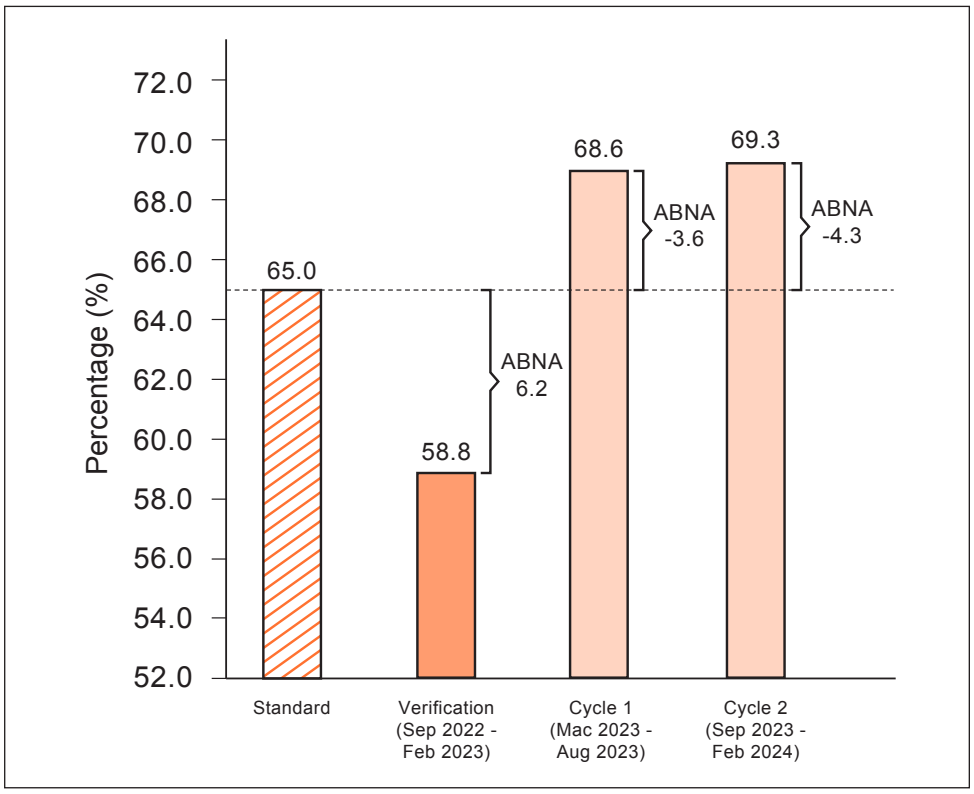


Figure 3: Percentage of warfarin-treated patients with good TTR in KKSI

Concurrently, we managed to improve patients' compliance levels with warfarin dose and diet following the establishment of warfarin extended counselling. The percentage of patients with good adherence to warfarin dose increased from 80.0% to 88.5% in Cycle 1 and 94.1% in Cycle 2. The percentage of patients with good compliance to the warfarin diet had also doubled from 40.0% in the verification study to 82.4% in Cycle 2. With a better understanding of the importance of compliance with warfarin and warfarin diet, patients were more cooperative in adhering to warfarin treatment and diet consistency to ensure good TTR control.

Another important result was that the average number of visits for INR monitoring per patient was reduced from six visits as documented in the pre-remedial study to three visits per half a year post Cycle 1. The number of visits was the same post Cycle 2. Fewer patient visits also implied less clinic workload and a reduction in the cost of INR monitoring.

Table 1: MOGC to increase the percentage of warfarin-treated patients with good TTR in KKSI post-intervention (Cycle 1 and Cycle 2)

No.	Proses	Criteria	Standard	Verification (n=30)	Cycle 1 (n=102)	Cycle 2 (n=111)
1.	The doctor reviews patient's INR result	Check warfarin indication	100%	70.0%	100%	100%
		Check INR target	100%	70.0%	100%	100%
2.	Assess the patient for factors affecting INR	History taking for all factors which may affect INR	100%	20.0%	100%	100%
3.	Make dose adjustments and prescribe appropriate duration based on ICSI and ACCP guidelines	Make dose adjustments based on ICSI guidelines	100%	50.0%	80.4%	75.7%
		Prescribe appropriate duration based on ACCP guidelines	100%	70.0%	90.2%	90.1%
4.	Pharmacist checks patient's INR and dose regimen	Ensure the correct INR targets and indications are written on the prescription	100%	100%	100%	100%
		Ensure the dose adjustment and duration prescribed are appropriate based on guidelines	100%	60.0%	100%	100%
5.	Call the doctor to discuss the warfarin dose regimen	Discuss with prescribers if the dose adjustment or duration prescribed is inappropriate	100%	80.0%	100%	100%

6. Dispense medication and provide counselling to the patient	Counsel patients on relevant factors that affect their INRs	100%	50.0%	100%	100%
	Assess the patient's understanding and compliance	100%	50.0%	100%	100%
	Ensure patients who require additional counselling are referred to the counselling room	100%	0.0%	100%	100%
7. Documentation	Document the counselling session	100%	50.0%	100%	100%
	Arrange for a follow-up appointment	100%	0.0%	100%	100%

Lessons and Limitations

The implementation of all the remedial strategies had led to a successful improvement in TTR control among our warfarin-treated patients. The strength of this study was that it showed the potential of pharmacists' involvement in the management of warfarin-treated patients even in a health clinic setting. Currently, the warfarin MTAC run by pharmacists is mostly available in hospital settings, and may not be feasible in health clinic settings. Multidisciplinary collaboration between doctors, pharmacists, and laboratory staff, as portrayed in our study, showed a positive impact on patients' treatment outcomes. These strategies can be applied to other health clinics in Malaysia to improve the safety and efficacy of warfarin treatment.

In this study, we also learnt that patient empowerment was crucial to achieving better treatment outcomes. With proper education and guidance, patients could recognise the importance of compliance with warfarin treatment and diet and be more empowered in their treatment.

Despite the success, our study had several limitations. Our quality improvement study only calculated TTR based on patients' INR within a six-month period, which might be insufficient to present the full anticoagulation profile of the patients. Additionally, although we showed that the number of visits for INR monitoring had reduced, there was no cost analysis study on the total amount of spending saved on INR testing.

Conclusion and the Next Steps

The percentage of warfarin-treated patients with good TTR increased to 68.6% in Cycle 1 following the implementation of strategies and further improved to 69.3% in Cycle 2 with strategy reinforcement. To date, we had presented our study at the Johor State Health Department Pharmacy Practice Meeting and the National Family Medicine Scientific Conference 2024. In February 2024, a standardisation letter was also issued, mandating the implementation of this QA project across all primary health clinics in the Johor Bahru district to ensure a standardised approach to improving the safety and quality of care for patients receiving warfarin therapy (Appendix 4). Our remedial strategies in this study had great potential to be adopted and adapted by other health clinics in Johor state.

Recognising the improvements and benefits of our study, we plan to publish our protocol online and to upgrade our E-Warf to a mobile application so that our strategies can reach out to more health facilities throughout Malaysia. With that, beneficial treatment outcomes in terms of warfarin efficacy and patient safety can be achieved nationwide. From here, we also plan to continue our study for more study cycles and focus on the cost aspect to study the long-term benefit of improving patients' TTR.

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Conflict of Interest

The authors declare that there was no conflict of interest.

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References

1. Camm AJ, Lip GYH, De Caterina R, Savelieva I, Atar D, Hohnloser SH, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation—developed with the special contribution of the European Heart Rhythm Association. Europace. 2012;14(10):1385–1413. doi:10.1093/europace/eus305.

2. Atrial fibrillation: diagnosis and management [Internet]. National Institute for Health and Care Excellence (NICE); 2021 Jun 30 [cited 2023 Oct 3]. Available from: http://www.nice.org.uk/guidance/cg180/resources/guidance-atrial-fibrillation-the-management-of-atrial-fibrillation-pdf

3. Thrombosis Canada [Internet]. Thrombosiscanada.ca. 2025 [cited 2025 May 6]. Available from: http://thrombosiscanada.ca/clinicalguides/#.

4. Hong KS, Kim YK, Bae HJ, Nam HS, Kwon SU, Bang OY, et al. Quality of anticoagulation with warfarin in Korean patients with atrial fibrillation and prior stroke: A multicenter retrospective observational study. J Clin Neurol. 2017;13(3):273–80.

5. Bernaitis N, Ching CK, Chen L, Hon JS, Teo SC, Davey AK, et al. The Sex, Age, Medical History, Treatment, Tobacco Use, Race Risk (SAMe-TT_2R_2) score predicts warfarin control in a Singaporean population. J Stroke Cerebrovasc Dis. 2017;26(1):64–9.

6. Lee SL, Ong TJ, Mazlan-Kepli W, Mageswaran A, Tan KH, Abd-Malek AM, et al. Patients' time in therapeutic range on warfarin among atrial fibrillation patients in Warfarin Medication Therapy Adherence Clinic. World J Cardiol. 2021 Sep 26;13(9):483–92.

7. Krittayaphong R, Chantrarat T, Rojjarekampai R, Jittham P, Sairat P, Lip GYH. Poor time in therapeutic range control is associated with adverse clinical outcomes in patients with non-valvular atrial fibrillation: a report from the nationwide COOL-AF registry. J Clin Med. 2020 Jun 2;9(6):1698.

8. White HD. Comparison of outcomes among patients randomized to warfarin therapy according to anticoagulant control. Arch Intern Med. 2007 Feb 12;167(3):239–45.

9. Haas S, Ten Cate H, Accetta G, Angchaisuksiri P, Bassand JP, Camm AJ, et al. Quality of vitamin K antagonist control and 1-year outcomes in patients with atrial fibrillation: a global perspective from the GARFIELD-AF registry. PLoS One. 2016 Oct 28;11(10):e0164076.

10. Jones M, McEwan P, Morgan CL, Peters JR, Goodfellow J, Currie CJ. Evaluation of the pattern of treatment, level of anticoagulation control, and outcome of treatment with warfarin in patients with non-valvular atrial fibrillation: a record linkage study in a large British population. Heart. 2005 Apr 1;91(4):472–7.

11. Alphonsa A, Sharma KK, Sharma G, Bhatia R. Knowledge regarding oral anticoagulation therapy among patients with stroke and those at high risk of thromboembolic events. J Stroke Cerebrovasc Dis. 2015 Mar 1;24(3):668–72.

12. Li X, Sun S, Wang Q, Chen B, Zhao Z, Xu X. Assessment of patients' warfarin knowledge and anticoagulation control at a joint physician- and pharmacist-managed clinic in China. Patient Preference and Adherence. 2018 May;Volume 12:783–91.

13. Lane DA, Ponsford J, Shelley A, Sirpal A, Lip GYH. Patient knowledge and perceptions of atrial fibrillation and anticoagulant therapy: effects of an educational intervention programme. Int J Cardiol. 2006 Jun;110(3):354–8.

14. Shrestha S, Sapkota B, Kumpakha A, Acharya U, Sharma R. Evaluation of patients' knowledge on warfarin in outpatient pharmacy of a tertiary care cardiac center. BMC Res Notes. 2015 Sep 10;8:429.

15. Shang L, Zhang Y, Zhao Y, Tang B, Hou Y. Contemporary oral anticoagulant therapy of patients with atrial fibrillation in China: status, obstacles, and strategies for improvement. BioSci Trends. 2022;16(5):317–29.

16. Wang C, Yang Z, Wang C, Wang Y, Zhao X, Liu L, et al. Significant underuse of warfarin in patients with nonvalvular atrial fibrillation: results from the China National Stroke Registry. J Stroke Cerebrovasc Dis. 2014 May 1;23(5):1157–63.Qian Y, Zhang J, Li J, Weng Z. A retrospective study on the evaluation of the appropriateness of oral anticoagulant therapy for patients with atrial fibrillation. PLoS One. 2021; 16:e0259199.

17. Young S, Bishop L, Twells L, Dillon C, Hawboldt J, O'Shea P. Comparison of pharmacist-managed anticoagulation with usual medical care in a family medicine clinic. BMC Fam Pract. 2011 Aug 17;12(1):88.

18. Alghadeer SM, Alzahrani AA, Alalayet WY, Alkharashi AA, Alarifi MN. Anticoagulation control of warfarin in pharmacist-led clinics versus physician-led clinics: a prospective observational study. Risk Manag Healthc Policy. 2020 Aug;13:1175–9.

19. Shafie S, Choy EL, Hui W, Noor S. Assessment of the clinical outcomes of warfarin therapy in two models of anticoagulation services [Internet]. [cited 2023 Oct 3]. Available from: https://research.pharmacy.gov.my/system/files/PRR3.1pp.18-25.pdf

20. Hasan SS, Shamala R, Syed IA, Basariah N, Chong DWK, Mei TK, et al. Factors affecting warfarin-related knowledge and INR control of patients attending physician- and pharmacist-managed anticoagulation clinics. J Pharm Pract. 2011 Aug 15;24(5):485–93.

21. Aidit S, Soh YC, Yap CS, Khan TM, Neoh CF, Shaharuddin S, et al. Effect of standardized warfarin treatment protocol on anticoagulant effect: comparison of a warfarin medication therapy adherence clinic with usual medical care. Front Pharmacol. 2017 Nov 9;8:637.

22. Clarkesmith DE, Pattison HM, Lip GYH, Lane DA. Educational intervention improves anticoagulation control in atrial fibrillation patients: the TREAT randomised trial. PLoS One. 2013 Sep 9;8(9):e74037.

23. Omer AAA, Kusuma IY, Csupor D, Doró P. Outcomes of pharmacist-led patient education on oral anticoagulant therapy: a scoping review. Res Social Adm Pharm. 2025 Feb 19. doi:10.1016/j.sapharm.2025.02.009.

24. Anticoagulation MTAC (AC-MTAC) Protocol. 2nd edition (2020). Pharmaceutical Services Programme, Ministry of Health Malaysia [Internet]. [cited 2023 Oct 3] Available from: https://pharmacy.moh.gov.my/sites/default/files/document-upload/acmtac-protocol-2019-revised_1.pdf

25. Rosendaal FR, Cannegieter SC, van der Meer FJ, Briët E. A method to determine the optimal intensity of oral anticoagulant therapy. Thromb Haemost. 1993;69(3):236-9.

26. Institute for Clinical Systems Improvement. Antithrombotic Therapy Supplement [Internet]. Bloomington (MN): ICSI; 2013 [cited 2023 Oct 3]. Available from: www.icsi.org2

27. Wigle P, Hein B, Bernheisel CR. Anticoagulation: updated guidelines for outpatient management. Am Fam Physician. 2019;100(7):426-34.

28. Klinik Warfarin (K-WARF) Protocol. 2nd edition (2024). Sultan Ismail Health Clinic, Johor Bahru District Health Office [Internet]. [cited 2024 Oct 3] Available from: https://drive.google.com/file/d/1U2Ut7_kSBZFiEI2gjFRAOvANvcchcOhf/view?usp=drive_link

Appendix 1: Questionnaire for doctors and pharmacists

1. Year of practice
   a) Less than 5 years
   b) 5 to 10 years
   c) 10 years and above

2. How confident are you in interviewing warfarin-treated patients?
   1 2 3 4 5 6 7 8 9 10
   Low High confidence

3. How confident are you in doing dose adjustments for patients' warfarin regimens?

   1 2 3 4 5 6 7 8 9 10
   Low High confidence

4. What is the biggest challenge, in your opinion, when managing warfarin-treated patients?
   a) Time constraints, heavy patient load
   b) Uncooperative patients
   c) Language barrier and poor communication with patients
   d) Others please state:_____

5. Have you ever been to any courses/ seminars related to the management of warfarin-treated patients?
   a) Yes
   b) No

6. Would you like to attend courses related to the management of warfarin-treated patients?
   a) Yes
   b) No

7. Do you think educational sessions, e.g. CME will help to improve your knowledge and confidence level in managing warfarin-treated patients?
   a) Yes
   b) No

Appendix 2: Questionnaire for patients

1. Are you aware of your current warfarin dose, in mg?
   Yes No

2. Do you remember to take warfarin every day?
   Yes No

3. Are you aware that a change in vegetable intake (Vitamin K) may affect INR readings?
   Yes No

4. Do you keep your vitamin K intake constant?
   i) Yes, I follow a consistent warfarin diet every day
   ii) No, I find it hard to keep my vitamin K intake consistent
   iii) I follow most of the time, but there are days that I take more/less vitamin K food

5. Do you face any communication problems during a doctor's consultation?
   i) Yes, I do not understand BM/BI
   ii) No

6. Do you think you receive clear instructions and counselling from the pharmacist when the pharmacist dispenses the medication to you?
   Yes No
7. Do you think the waiting time to see a doctor and to receive medication is long?
   Yes No

8. Based on the consultation session just now, were you asked about:
   □ Current dose regimen
   □ Missed dose or compliance
   □ Diet pattern
   □ Changes in medicines or recent supplement/herbal medicine intake
   □ Change in physical activities
   □ Smoking or alcohol intake
   □ Body discomforts
   □ Others

Appendix 3: Pre-test & post-test knowledge questions for doctors and pharmacists

1. Warfarin is indicated in which of the following:
   A) Atrial fibrillation
   B) LV clot
   C) Antiphospholipid syndrome (APLS)
   D) All of the above

2. In which situation below would you expect a **decrease** in patient's INR result
   A) Patient A, who went hiking with friends last weekend
   B) Patient B, who has consumed papaya for past 2 days
   C) Patient C, who recently just completed a course of amoxicillin following dental surgery
   D) Patient D, who has just started on fish oil supplement last week
   E) None of the above

3. Which of the following drug interferes with warfarin and result in an **increase** in patient's INR
   A) Rifampicin
   B) Propylthiouracil
   C) Gemfibrozil
   D) Metformin

4. When calculating dosage adjustment, how many % of the total weekly dose change of warfarin is expected to result in a change of INR by 1
   A) 10
   B) 1
   C) 0.1
   D) 0.01

5. The following food/vegetable is expected to decrease patient's INR when consumed in large amounts, **except:**
   A) Kale
   B) Broccoli
   C) Cabbage
   D) Bell pepper
   E) None of the above

6. Patient A was a 55-year-old Chinese lady with a history of DVT and PE. Her INR was found to be 3.6 (target 2-3) today. She claimed no changes in diet or physical activities. She started taking tonic soup with ginseng weekly since a month ago. She noticed herself getting more energetic after started on the ginseng tonic soup. In fact, she enthusiastically informed you that she shall keep the ginseng tonic drink as her weekly routine. one day before warfarin clinic, she was also given Metronidazole 400mg TDS by O&G as her PAP smear showed signs of infection

   Choose the CORRECT statement below:

   i) Metronidazole decreases warfarin metabolism, leading to an increased risk of bleeding
   ii) Advise patient A to stop ginseng soup even though she intends to continue as her weekly routine
   iii) Withhold the warfarin dose until she completes the course of antibiotics
   iv) Advise on the consistency if she insists on taking the tonic soup with ginseng weekly

A) i only
B) i, ii
C) iv only
D) i, iv

7. Patient B was diagnosed with AF and his current INR was 1.7 with warfarin dose of 2.5mg OD. He claimed that he did not take any green leafy vegetables. Neither any supplement. During this visit, patient was diagnosed with hypothyroidism. Hence, he was newly added with levothyroxine 50mcg. Choose the **CORRECT** management(s) of this patient with the newly added medication?

   i) Explain the interaction of levothyroxine with warfarin
   ii) Advise to withhold levothyroxine until his INR is stable
   iii) Maintain patient on 2.5mg OD for this visit & repeat INR after 2 weeks
   iv) Watch out for bleeding symptoms due to increased risk of bleeding

   A) i only
   B) ii only
   C) iii and iv
   D) i, iii, iv

8. Which of the following combinations is FALSE?
   A) Acute alcohol intake + warfarin: increase INR
   B) Dong quai (Chinese herb) + warfarin: decrease INR
   C) Cranberry juice + warfarin: increase INR
   D) Green tea + warfarin: decrease INR

9. Warfarin tablets are available in the following strengths, except
   A) 1mg
   B) 2mg
   C) 3mg
   D) 4mg

10. Patient INR today was 4.1. His target INR is 2-3. Which of the following is the most appropriate management for this patient supposing all parameters are as usual/ no changes
    A) Maintain current dose and recheck INR in 1 week time
    B) Withold warfarin for 1 day and decreases 10% of weekly dose and recheck INR after 1 week
    C) Increase dose by 5% of weekly dose
    D) Decrease 5% of weekly dose and review INR after 2 weeks

Appendix 4: Memo of standardisation of the QA project across all facilities in Johor Bahru District Health Office

MEMO DALAMAN
PEJABAT KESIHATAN JOHOR BAHRU

☎ Telefon : 07 - 2224711/4818 ✉ Email : pkdjb@moh.gov.my

Ruj Kami : PKJB.QLAT/100-8/4/1 (84)		Tarikh: 27 Februari 2024
Kepada	**SEPERTI SENARAI EDARAN**	**Salinan kepada :** Unit Kualiti Dan Latihan
Daripada	**PEGAWAI KESIHATAN DAERAH**	
Perkara	**PENYERAGAMAN PROJEK QA"*INCREASING THE PERCENTAGE OF WAFARIN PATIENTS WITH GOOD TIME IN THERAPEUTIC RANGE (TTR)* IN KK SULTAN ISMAIL" DISEMUA FASILITI PEJABAT KESIHATAN DAERAH JOHOR BAHRU (PKDJB)**	

Tuan,

Saya dengan segala hormatnya merujuk perkara di atas.

2 Sukacita dimaklumkan bahawa Inovasi Projek QA "*Increasing The Percentage Of Wafarin Patients With Good Time In Therapeutic Range* (TTR) In KKSI" adalah projek QA yang dijalankan di KKSI adalah untuk meningkatkan kualiti rawatan warfarin dan menjamin keselamatan pesakit.

3 Mesyuarat Jawatankuasa Pemilihan Kategori Produk QA,KIK dan Inovasi yang terpilih mewakili PKDJB yang telah diadakan pada 4.2.2024 telah memutuskan untuk membuat penyeragaman p rojek QA ini ke semua Klinik-klinik Kesihatan Daerah Johor Bahru.

4 Pematuhan dan penyeliaan akan dibuat oleh Unit Kualiti dan Latihan dari masa ke semasa.

Sekian, terima kasih.

"MALAYSIA MADANI"

"BERKHIDMAT UNTUK NEGARA"

Saya yang menjalankan amanah

(DR. HAIDAR RIZAL BIN TOHA)
(No. Pendaftaran MMC:36541)
Pakar Perubatan Kesihatan Awam
Pegawai Kesihatan Daerah
Pejabat Kesihatan Daerah Johor Bahru

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