

Assess the Impact of the Pharmacist on Enhancing Pharmacological Thrombo-Prophylactic Prescriptions in Patients with Renal Impairment

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ABSTRACT

Patients with chronic kidney disease (CKD), irrespective of the extent of renal impairment, are acknowledged to have an elevated risk for venous thromboembolism (VTE) and stroke; yet, study findings on the association between CKD and the heightened risk of VTE and stroke have been inconclusive. Venous thromboembolism (VTE) predominantly arises during hospitalization for significant surgical procedures or trauma, however it may potentially manifest several months post-surgery. The quantity of anticoagulants approved for the prevention and treatment of thromboembolic disorders has risen. Irrespective of the anticoagulants employed, prior studies indicated that improper utilization in patients with renal impairment elevates the risk of hemorrhage. An interventional study was done to evaluate the proper utilization of anticoagulants in patients with renal impairment within healthcare institutions in Najaf Province. Intervention consists of lectures, brochures, rollups and buck lists about updated guideline of safe anticoagulant use in patients with renal impairment. The study included two patients' groups according to receiving intervention or not. the appropriateness of intervention was assessed at 3 periods preintervention, 4 weeks after-intervention and 12 weeks after intervention according to CHAD-VASC scoring system for stroke risk and PADUA scoring system for VTE risk. Results shown that at baseline there were no significance difference between two groups according to Chi-square analysis with respect to inappropriate prescribing of anticoagulants. after 4 weeks of intervention the is significant decline in percentage of patients receiving inappropriate anticoagulants (9%) in comparison to patients not received intervention (23.5%). After 12 weeks of intervention the is significant decline in percentage of patients receiving inappropriate anticoagulants (2.5%) in comparison to patients not received intervention (21.5%). The results also shown that inappropriate prescribing has been improved dramatically after 12 weeks in comparison to 4 weeks of intervention. This study demonstrated that appropriate prescribing of anticoagulants in CKD patients significantly improved following the intervention and Prolonged monitoring is advised to evaluate the enduring effects of this intervention.

Keywords: Chronic Kidney Disease, Stroke, Venous Thromboembolism, Pharmacological Thromboprophylaxis

I. INTRODUCTION

Chronic renal disease is defined as kidney impairment or reduced kidney function persisting for at least three months, irrespective of the cause. Kidney damage generally signifies pathological irregularities in the native or transplanted kidney, detected via imaging, biopsy, or inferred from clinical indicators such as increased albuminuria, particularly an albumin-to-creatinine ratio (ACR)

surpassing 30 mg/g (3.4 mg/mMol), or alterations in urinary sediment. Impaired kidney function indicates a reduced glomerular filtration rate (GFR), typically calculated (eGFR) from serum creatinine concentrations.¹ Chronic renal disease is associated with hypercoagulability and blood platelets disorder, potentially increasing the risk of atherosclerotic heart disease. Despite the same processes of arterial and venous cardiovascular

disorders, research regarding the impact of renal illness on the risk of blood clotting disorders (developing VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is limited.² Several essential factors relate to the role of avoiding strokes in individuals with renal insufficiency. Patients having kidney disease have a markedly increased risk of stroke, which is imperative for several clinicians to recognize. Although subclinical cerebrovascular disease and stroke risk factors are common in ESRD patients, the data indicating a heightened risk of clinical stroke is inconclusive. The only research evaluating the incidence of stroke in dialysis patients relative to the general population.³ Given that all direct oral anticoagulants (DOACs) are partially excreted by the kidneys, the simultaneous presence of chronic kidney disease (CKD) and atrial fibrillation (AF) poses a distinct challenge in clinical practice due to the heightened risk of thromboembolic and hemorrhagic complications, particularly in patients with advanced renal disease. Current observational data indicate that in those who have severe persistent renal disease (an eGFR of 15–29 mL/min/1.73 m²), reduced dosage regimens of rivaroxaban, apixaban, and edoxaban exhibit a favorable effectiveness and safety profile in comparison to warfarin. Consequently, the 2020 AF ESC recommendations and the 2021 EHRA practical guide advocate for the prudent application of Factor Xa inhibitors in patients with severe ongoing kidney disease.⁴ The incidence of venous blood clots including thrombosis of deep veins and pulmonary edema in hospitalized medical patients without sufficient prophylaxis varies between 5% and 15%. One to three Specific healthcare people, especially those with tumor, ischemic cardiovascular disease, and kidney problems face an increased risk of thromboembolic events. A reduced level of glomerular filtration increases the likelihood of venous thromboembolism. The incidence of pulmonary embolism in patients on hemodialysis is approximately three times higher than in individuals without renal impairment. In addition to the risk of venous thromboembolism, persons with renal impairment (RI) face an increased likelihood of hemorrhage. Seven Thus, a delicate balance between the risks of venous

thromboembolism and bleeding requires physicians to implement a careful and prudent approach in the use of anticoagulants for the prevention of venous thromboembolism in patients with renal impairment. Patients are evaluated for thromboprophylaxis based on the PADUA score system.⁵ The underutilization and inappropriate use of anticoagulants in this population persist as significant concerns, despite the availability of pharmacological prophylaxis. Clinical chemists are essential in optimizing thromboprophylaxis through patient risk assessment, adherence to evidence-based guidelines, and the education of healthcare professionals. Pharmacist-led interventions have demonstrated improvements in the appropriateness of anticoagulant use, enhanced patient safety, in addition a decrease in the risk venous thromboembolism in those individuals with renal impairment.⁶ Individuals with persistent renal disorder exhibit an increased susceptibility to venous thromboembolism (VTE), especially while hospitalized. Nonetheless, owing to intricate renal dosage and hemorrhagic apprehensions, pharmacological thromboprophylaxis is frequently underutilized or inaccurately given. In this setting, clinical chemists have demonstrated their value as an important part of the healthcare system. Their role in evaluating anticoagulant utilization, directing suitable prescribing practices, and instructing personnel has demonstrated enhancement in prophylactic results and a decrease in problems. Research has shown that pharmacist-led interventions substantially enhance anticoagulant utilization in high-risk groups, particularly in patients with renal impairment.⁷ Patients with atrial fibrillation (AF) and chronic kidney disease (CKD) are predisposed to a heightened CHA₂DS₂-VASc score for stroke risk, remaining at significant risk even with a score of 0–1; thus, this scoring method is advised for assessing the necessity of anticoagulation therapy.⁸

Inclusion criteria:

Nephrologists operate at the nephrology ward at Al-Najaf Educational Hospital. All relevant patients with atrial fibrillation, hospitalized or surgical, who have persistent kidney failure.

II. RESEARCH METODOLOGY

Design: interventional quasi-experimental study with a control group. The investigation commenced in early January 2025 and concluded in early May 2025. **Participants:** physicians employed in nephrology departments. **Intervention:** The educational lecture encompasses the latest recommendations for thromboprophylaxis in those people with chronic renal impairment to avert stroke beside venous thromboembolism, in accordance with recent guidelines. The intervention also included brochures, roll-ups, and checklists to enhance awareness among nephrologists. The questionnaire was administered again at two intervals Four weeks and twelve weeks following the intervention.

Ethical considerations

This research obtained ethical approval from two educational institutions. Initial approval granted through Medical The ethical board of the Faculty of Medicine, Kufa University 17/10/2024, reference number: MEC-79. The Scientific Committee of Researches of Al-Najaf Health Directorate granted a second approval in September 2024 (Reg No: 4430). Furthermore, verbal consent was acquired from the participating physicians after elucidating the study's goal. **Study Population and Sampling.** The study targeted physicians employed at one of three healthcare institutions: Al-Hakeem Hospital, Al-Sadder Medical District, and Al-Najaf Educational Hospital. The three institutes employed 40 nephrologists in their respective departments. The overall sample quantity was calculated using a statistical expert utilizing IBM SPSS Sample Strength version 24, according to the subsequent equation: $n = ((Z\alpha/2 + Z\beta)^2 \times (\sigma_1^2 + \sigma_2^2)) / (\mu_1 - \mu_2)^2$ where: $Z_{\alpha/2}$ denotes the Z-value associated with the designated significance threshold (alpha). Z_{β} denotes the Z-value associated with the designated power (1 – beta). σ_1 and σ_2 are the standard deviations of the two groups. μ_1 and μ_2 denote the means of the two groups. By employing the previously given equation and substituting the values of each variable, the computed total of physicians was 40. The physicians were assigned to a cohort of 20 in the group receiving an intervention and 20 in the

nonintervention group, which were not given the intervention. Each group, intervention and control, comprises 200 patients

Study Questionnaire

A questionnaire was utilized to assess the knowledge of participating physicians concerning pharmaceutical thromboprophylaxis in individuals who have renal impairment. In absence prior analogous studies, the researcher developed the questionnaire following an extensive review of the topic matter. It comprised 53 questions divided into four sections: demographics, knowledge, practice, and impediments, all articulated in the English language. The questionnaire structure was verified and gained final permission based on the expert document from the Kufa Faculty of Pharmacy in 2024. Demographics encompass participant data such as participant ID, age, gender, degree, experience, expected weekly encounter instances, and prior medical educational activities. The knowledge segment of the questionnaire comprised four sections: A, B, C, and D, which included questions pertaining to pharmaceutical thromboprophylaxis in patients with renal impairment. Each question presents five options: Definitely approve, are neutral, disapprove, and strongly disapprove. Section A encounters five questions regarding the comprehension in hazards for stroke and thromboembolism among those with renal impairment, including those undergoing dialysis. Section B has seven inquiries regarding the indications for thromboprophylaxis for persons having impaired kidney function to avert stroke as well as venous thromboembolism, including individuals undergoing dialysis. The third component comprises three sections: A, B, and C, which encompass enquiries pertaining to the prescribing practices of pharmacological thromboprophylaxis in patients with renal impairment. Every question presents five options: often, often, sometimes, seldom, and never. Section A has eight questions about the prescription of thromboprophylaxis agents for patients with renal impairment to prevent stroke and venous thromboembolism, as well as for patients undergoing dialysis. Section B has seven questions pertaining to the dose of thromboprophylaxis in patients with renal impairment to avoid stroke and venous

thromboembolism, as well as in patients undergoing dialysis. Section C comprises seven questions concerning the length of thromboprophylaxis prescription in patients with renal impairment to avert stroke and venous thromboembolism, including those undergoing dialysis. The final section of the questionnaire addressed barriers to prescribing, comprising seven specific barriers along with an open-ended question for elaboration on these barriers. The questionnaire underwent validity testing by five qualified academic professionals prior to distribution, comprising a clinical pharmacy expert, three specialists in pharmacology and therapeutics, and a biostatistics expert. The modified questionnaire was distributed to 40 physicians for pilot research, yielding a Cronbach alpha score of 0.9, signifying strong internal consistency and readability.

Statistical analysis

The analysis was conducted using Microsoft Excel 2019 and version 24 of the SPSS software for social sciences. Frequencies, percentages, means, and standard deviations were utilized to represent categorical data. The Friedman test, pairwise comparison, and Pearson Chi-square have been conducted. Categorical data were presented through frequencies, percentages, means, and standard deviations. The Friedman

test was utilized to assess knowledge differences among the three phases of the study: beginning, for a period of four weeks after the program, and twelve weeks later thereafter. Pairwise comparisons were conducted to evaluate each phase pair. The association and discrepancies in knowledge were assessed using the Chi-square test. The mean difference was determined by reducing the mean value prior to the intervention from that post-intervention to compare the mean scores before and after the intervention. The percentage change was calculated by dividing the final value by the pre-intervention mean score and multiplying by 100%. The effect size was determined using the z-value from the Wilcoxon test that contrasts two means (Effect size (r) = $Z/\sqrt{N}$). Cohen (1988) categorized effect size values into three classifications: around 0.2 represents a modest influence, around 0.5 suggests a moderate influence, and 0.8 or higher shows a substantial influence.⁹

III. RESULTS AND DISCUSSIONS

Sociodemographic characteristics of participant patients at baseline phase:

The initial demographics for those participating in the control and intervention categories (n = 200 each) are shown in Table 1 to guarantee comparability before the intervention.

Table 1 demonstrates Sociodemographic characteristics of the participant individuals in the intervention and control groups at starting phas

.Variables		Group		Total no.	P
		Intervention (n=200) No. (%)	Control (n=200) No. (%)		
Age (years) Mean±SD		68.7±17.3	73.3±15.6		0.005
Sex	Female	97(48.5%)	100(50%)	197(49.3%)	0.8
	Male	103(51.5%)	100(50%)	203(50.7%)	
AF		89(44.5%)	97(48.5%)	186(46.5%)	0.4
(DVT)		61(30.5%)	51(25.5%)	112(28%)	0.3
Dialysis		50(25%)	52(26%)	102(25.5%)	0.8
High risk receives PTX (appropriate prescription)		102(52.3%)	110(55.8%)	212(54.1%)	0.2
High risk not receive PTX (inappropriate prescription)		19(9.7%)	24(12.2%)	43(10.9%)	
Low risk receives PTX (inappropriate prescription)		34(17.5%)	20(10.2%)	54(13.8%)	
Low risk not receive PTX (appropriate prescription)		40(20.5%)	43(21.8%)	83(21.2%)	
PTX contraindications		5(2.5%)	3(1.5%)	8(2%)	

Distribution of Age

The average age was 68.7 ± 17.3 years in the intervention group and 73.3 ± 15.6 years in the case of the control category, a statistically significant distinction was observed ($p = 0.005$). This indicates that the control group consisted of relatively older individuals, potentially affecting their baseline risk for venous thromboembolism (VTE) or stroke. Age is a significant risk factor in tools such as CHADS-VASc and Padua scores; therefore, this difference must be taken into account when interpreting outcomes.¹⁰

Distribution of Gender

The gender distribution was equitable, with females constituting 48.5% of the participants in the intervention arm and 50% of the control group ($p = 0.8$), indicating no significant disparity. This equilibrium mitigates gender-related confounding in treatment efficacy. The prevalence of atrial fibrillation (AF) was 44.5% in the groups receiving the intervention team and 48.5% in the nonintervention group ($p = 0.4$), demonstrating no statistically significant difference. History of deep vein thrombosis (DVT) was noted in 30.5% of intervention individuals, in contrast to 52.5% in control individuals. The statistical gap was not analyzed statistically in Table 1. The prevalence of dialysis was 25% in one group and 26% in the other ($p = 0.8$), signifying similar exposure to renal replacement treatment across the groups. The results demonstrate that both groups were equivalent at baseline for gender, atrial fibrillation, and dialysis status. The elder control group may require modifications in multivariate analysis to address potential bias in clinical outcomes, particularly concerning bleeding or thromboembolic risk.¹¹

The proportion of high-risk patients receiving appropriate PTX was 52.3% in the team receiving the intervention compared to 55.8% in the nonintervention team ($p = 0.2$). Although somewhat elevated in the case of the control group, the deviation lacked statistical significance, indicating that both groups adhered to the rules with similar consistency in this subset. Inadequate

Management Within High-Risk Populations Undertreatment—high-risk patients not receiving PTX—was significantly more prevalent in the nonintervention arm (12.2%) compared to the intervention population (9.7%). Although not statistically significant, this change indicates that the intervention may help reduce clinical inertia or oversight. The percentage of patients with low risk who received PTX erroneously was 17.5% in the targeted population compared to 10.2% in the untreated class. This unexpected result suggests a potential overprescription within the intervention group, maybe due to a conservative or risk-averse prescribing approach post-intervention, or misclassification of risk. appropriate the withholding of PTX in low-risk patients demonstrated comparable non-prescription rates between groups (20% vs. 21.5%), showing consistency in clinical judgment. Two percent of patients in each cohort exhibited documented contraindications to PTX (2.5% versus 1.5%). Another investigation demonstrated analogous results.⁵

Sociodemographic characteristics of participant patients 4 weeks post-intervention phase:

A statistically significant disparity in mean age was observed between the groups: Intervention group: 61.9 ± 13.3 years. Control group: 71.7 ± 16.1 years ($p = 0.0001$). This disparity is clinically significant, as age is a principal determinant of thromboembolic risk, as reflected in the CHADS-VASc and Padua scores. The gender distribution was essentially equal, with females constituting 48% of the team receiving the lecture and 48.5% of the non-interventional team ($p = 0.9$), signifying well-matched cohorts by sex. Coexisting medical conditions Atrial Fibrillation (AF) prevalence was comparable between groups (43% vs. 47.5%, $p = 0.4$). History of DVT: 30% in The group participating in the lecture had a rate of 26.5%, in contrast to the unaffected category ($p = 0.3$). Dialysis status: Equally distributed among groups (26.5% vs. 26%, $p = 0.9$). These commonalities validate the clinical comparability of the groups at the time of analysis.¹²

Table 2: Sociodemographic characteristics of participant patients in intervention and control group at 4 weeks post-intervention

Variables		Group		Total no.	P
		Intervention (n=200) No. (%)	Control (n=200) No. (%)		
Age (years) Mean± SD		61.9±13.3	71.7±16.1		0.0001
Gender	Female	96(48%)	97(48.5%)	193(48.3%)	0.9
	Male	104(52%)	103(51.5%)	207(51.7%)	
AF		86(43%)	95(47.5%)	181(45.3%)	0.4
(DVT)		60(30%)	53(26.5%)	113(28.2%)	0.4
Dialysis		53(26.5%)	52(26%)	105(26.3%)	0.9
High risk receives PTX (appropriate prescription)		117(59.1%)	104(53.1%)	221(56.1%)	0.0001
High risk not receive PTX (inappropriate prescription)		8(4%)	19(9.7%)	27(6.9%)	
Low risk receives PTX (inappropriate prescription)		10(5.1%)	28(14.3%)	38(9.6%)	
Low risk not receive PTX (appropriate prescription)		63(31.8%)	45(23%)	108(27.4%)	
PTX contraindications		2(1%)	4(2%)	6(1.5%)	

A significant difference is evident in the appropriateness of PTX prescribing for high-risk patients, with 117 (58.5%) in the participant sample receiving PTX compared to 104 (52%) in the untreated category ($p = 0.0001$), indicating improved prescription accuracy following the intervention. The inappropriate undertreatment of high-risk patients was reduced in the treated group (4%) compared to the nonintervention collection (9.7%). Overtreatment of low-risk patients: 5.1% in the targeted cohort versus 14.3% in the placebo population. The percentage of low-risk patients who correctly did not receive PTX

was higher in the treatment sample (31.8% versus 23%). findings demonstrate that intervention significantly improved adherence to risk-based anticoagulant prescribing, hence reducing both under-treatment and over-treatment. This corresponds with previous studies highlighting the effectiveness of pharmacist-led or clinician educational interventions in enhancing guideline-based medication usage among those at greatest risk, including patients with ongoing kidney failure. Additional investigations demonstrated comparable outcomes.¹³

Table 3: Sociodemographic characteristics of participant patients in intervention and control group at 12 weeks post-intervention

Variables		Group		Total no.	P
		Intervention (n=200) No. (%)	Control (n=200) No. (%)		
Age (years) Mean± SD		62±13.5	68.8±15.8		0.0001
Gender	Female	97(48.5%)	99(49.5%)	196(49%)	0.8
	Male	103(51.5%)	101(50.5%)	204(51%)	
AF		74(37%)	93(46.5%)	167(41.8%)	0.05
(DVT)		72(36%)	53(26.5%)	125(31.3%)	0.04
Dialysis		54(27%)	53(26.5%)	107(26.8%)	0.9
High risk receives PTX (appropriate prescription)		120(60.9%)	113(58%)	233(59.4%)	0.0001

High risk not receive PTX (inappropriate prescription)	2(1.1%)	18(9.2%)	20(5.1%)	
Low risk receives PTX (inappropriate prescription)	3(1.5%)	25(12.8%)	28(7.2%)	
Low risk not receive PTX (appropriate prescription)	72(36.5%)	39(20%)	111(28.3%)	
PTX contraindications	3(1.5%)	5(2.5%)	8(2%)	

With $p = 0.0001$, the overall mean ages in the experimental category (62.1 ± 13.5 years) was considerably younger than that in the untreated category (68.8 ± 15.8 years), implying that age still influences the baseline thromboembolic risk. With female representation around 49% overall, gender was balanced between groups ($p = 0.8$), therefore eliminating gender bias in the interpretation of intervention results. Clinical Features With no statistically significant differences, AF and DVT were evenly distributed (AF: 37% vs. 45%, DVT: 36% vs. 25.5%). Dialysis patients accounted for over 27% of the sample for both groups, therefore supporting clinical comparability.¹⁴

The intervention group exhibited a statistically significant enhancement in PTX prescribing ($p = 0.0001$): High-risk patients receiving appropriate PTX were more prevalent among those who received the program (60.9%) compared un-received ones (58%). Inappropriate undertreatment prescriptions (high risk, no PTX) were dramatically smaller among intervention participants at 1% in contrast to 9.2% in untreated team. Participants who received the study exhibited a significant reduction in overtreatment of low-risk patients, with rates of 1.5% compared to 12.8% in the control group. Low-risk patients not receiving PTX appropriately were more prevalent in the intervention group, with rates of 36.5% compared to 20%. The data indicate that the intervention led to improved accuracy in guideline-based prescribing decisions, thereby reducing both the overuse and underuse of anticoagulants. This finding corroborates existing literature that suggests structured clinical interventions, including education and risk score implementation, enhance the appropriateness of thromboprophylaxis in patients with chronic conditions.⁵

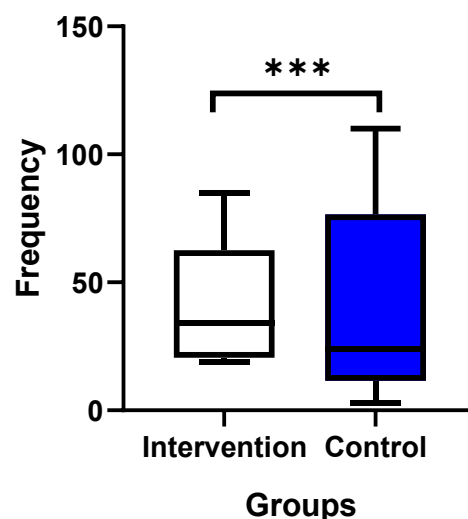


Figure 1: Bar chart shows Comparison of appropriate Thromboprophylaxis Prescription in patients with renal impairment Between Intervention and Control Groups at base line interval (before Intervention).

Figure 1 illustrates a comparison of the frequencies of appropriate thromboprophylaxis prescriptions between the two groups of patients throughout the baseline period. A box graph demonstrates a much higher median frequency of appropriate prescriptions in the population receiving the intervention compared to the nonintervention group of people, with a difference achieving statistical significance. ($***p < 0.001$). This study indicates a pre-existing disparity across groups, possibly due to differences in institutional processes or foundational physician knowledge. The extensive interquartile range (IQR) in the control group indicates significant variability in prescribing practices. The results underscore the necessity of standardizing thromboprophylaxis protocols, especially for patients with renal impairment who face heightened risks of thromboembolism and hemorrhage. Timely recognition of these gaps serves as a vital benchmark to assess the ensuing effects of educational or therapeutic interventions.¹⁵

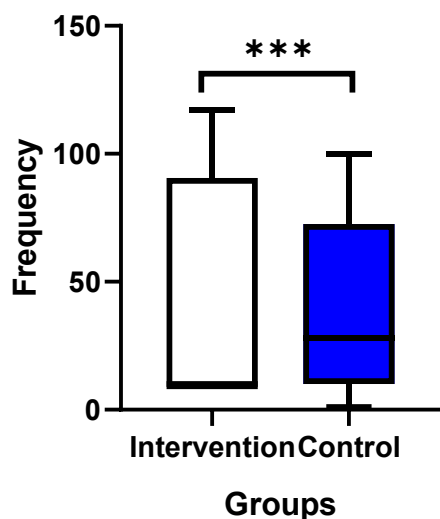


Figure 2: Bar chart shows Comparison of appropriate Thromboprophylaxis Prescription in patients with renal impairment Between two categories of individuals the four weeks following Intervention.

The incidence of suitable thromboprophylaxis prescriptions between the two-participating people at four weeks post-intervention. The boxplot demonstrates a statistically significant enhancement in the individuals who revived the study ($***p < 0.001$), showing that the educational or clinical intervention substantially influenced physician prescription behavior.¹⁶

The intervention group exhibited a higher median frequency and a narrower interquartile range, indicating enhanced appropriateness and greater consistency among clinicians. This result corresponds with prior data highlighting those structured interventions, especially those with pharmacist-led or interdisciplinary teaching, can markedly improve adherence to guidelines in high-risk groups, such as individuals with renal impairment. In contrast, the control group exhibited diminished prescription appropriateness, underscoring the need for focused treatments.¹⁷

The intervention group had a markedly elevated median frequency ($****p < 0.0001$), signifying a persistent beneficial impact of the educational technique.⁵ This indicates that the intervention resulted in sustained enhancements in prescribing practices among physicians managing patients with renal impairment. Conversely, the control group exhibited comparatively lower and more variable prescribing patterns, highlighting the lack of a

standardized intervention. These findings corroborate data that underscores the enduring advantages of clinician education and guideline-driven decision assistance in enhancing thromboprophylaxis use.¹⁸

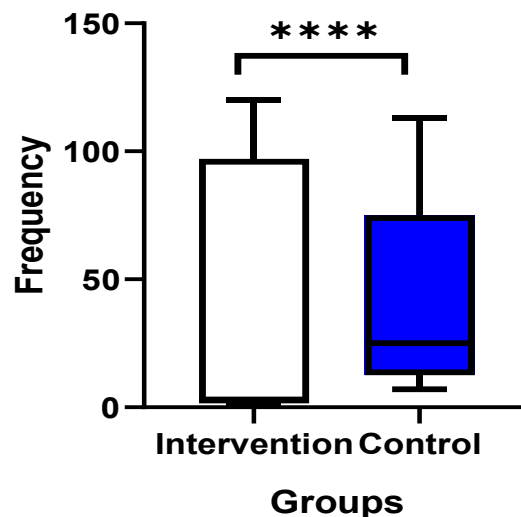


Figure 3: Bar chart shows Comparison of appropriate Thromboprophylaxis Prescription in patients with renal impairment Between Intervention and Control Groups at 12 after Intervention.

IV. CONCLUSION

The findings demonstrated a statistically significant improvement in the group that received the intervention compared to the controls grouping at all three evaluated time spent points: the beginning, four weeks later, and all twelve weeks after an intervention. Physicians who participated in the program demonstrated a higher frequency of appropriate thromboprophylaxis prescriptions, with sustained improvement over time. The findings demonstrate the effectiveness of structured educational programs in improving adherence to healthcare protocols and promoting patient safety. Given the increased risk of thromboembolic and hemorrhagic events in patients with renal impairment, such therapies are critical. The study indicates that targeted physician training can improve anticoagulant use and reduce preventable outcomes in high-risk populations.

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