

Monitoring of international normalized ratios

Comparison of community nurses with family physicians

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Abstract

Objective To determine whether community-based, nurse-led monitoring of the international normalized ratio (INR) in patients requiring long-term warfarin therapy was comparable to traditional physician monitoring.

Design A retrospective cohort analysis of patients taking long-term warfarin therapy.

Setting The study used data gathered from 3 family medicine clinics in a primary care network in Edmonton, Alta.

Participants Medical records of patients currently taking warfarin were examined.

Intervention Implementation of nurse-led monitoring in a primary care network in place of standard family physician INR monitoring.

Main outcome measures The degree of INR control before and after the implementation of nurse-run INR monitoring was assessed. The average proportion of time spent outside of therapeutic INR ranges, as well as the average number of days between successive INR readings, was calculated and compared. The degree of control placed patients into either a good-control group (out of range $\leq 25\%$ of the time) or a moderate-control group (out of range $> 25\%$ of the time) and these groups were compared.

Results Before nurse monitoring, INR values were out of range 20.4% of the time; after nurse monitoring they were out of range 19.2% of the time ($P = .115$); the time between sequential INR readings also did not differ before and after implementation of nurse monitoring (23.9 vs 21.6 days, $P = .789$).

Conclusion Nurse-led monitoring of INR is as effective as traditional physician monitoring. Advantages of nurse-led monitoring might include freeing family physicians to see more patients or to spend less time at work. It might also represent potential cost savings.

EDITOR'S KEY POINTS

- Given warfarin's narrow therapeutic index, it requires extensive monitoring through measurement of the international normalized ratio (INR) to prevent hemorrhagic or thrombotic complications. This has traditionally been managed by community family physicians, requiring appointments or telephone calls to discuss INR values and adjustments to dosing.
- Current literature shows dedicated tertiary anticoagulation clinics, compared with usual physician care, maintain patients in the therapeutic INR range a greater proportion of time, achieve target INR values for a higher proportion of patient visits, have a higher proportion of INRs within the therapeutic range, and show a lower percentage of high-risk INR values.
- This study aimed to examine the efficacy of a nurse-run, community-based anticoagulation program, and found that it was as effective as traditional physician monitoring. With physician-led monitoring patients in this study exhibited very good control compared with populations reported in the literature, and the nurse-led monitoring maintained this level of control. An improvement in INR might be possible under nurse-managed anticoagulation monitoring if a patient population's initial average time out of range is greater than that observed in this study.

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Monitoring du rapport international normalisé

Comparaison entre infirmières communautaires et médecins de famille

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Résumé

Objectif Déterminer si le monitoring du rapport international normalisé (RIN) effectué chez des patients nécessitant un traitement de warfarine à long terme par les infirmières œuvrant dans une communauté rurale se compare au monitoring traditionnel effectué par un médecin.

Type d'étude Analyse de cohorte rétrospective de patients recevant un traitement de warfarine de longue durée.

Contexte L'étude s'est servie de données provenant de 3 cliniques de médecine familiale faisant partie d'un réseau de soins primaires à Edmonton, Alberta.

Participants On a examiné les dossiers médicaux des patients qui recevaient actuellement de la warfarine.

Intervention Mise en place d'un monitoring effectué par une infirmière dans un réseau de soins primaires en remplacement du médecin de famille habituel qui le faisait.

Principaux paramètres à l'étude On a évalué le degré de contrôle du RNI avant et après la mise en place du monitoring du RIN par l'infirmière. On a calculé et comparé la proportion moyenne du temps où le RIN était en-dehors de la zone thérapeutique de même que le nombre moyen de jours entre les mesures successives du RIN. Le degré de contrôle plaçait les patients dans 2 groupes: un avec bon contrôle (hors de la zone $\leq 25\%$ du temps) et l'autre avec un contrôle modéré (hors de la zone 25% du temps) pour ensuite comparer ces groupes.

Résultats Avant le monitoring de l'infirmière, les valeurs de RIN étaient hors de la zone $20,4\%$ du temps; après le monitoring infirmier, elles étaient hors de la zone $19,2\%$ du temps ($P=,115$); les intervalles entre les mesures séquentielle du RIN étaient aussi semblables avant et après la mise en place du monitoring infirmier ($23,9$ vs $21,6$ jours, $P=,789$).

Conclusion Le monitoring du RIN par une infirmière est aussi efficace que le monitoring habituel du médecin. En libérant le médecin de famille, le monitoring infirmier pourrait lui permettre de voir plus de patients ou de réduire son temps de travail. Il pourrait aussi entraîner une éventuelle réduction des coûts.

POINTS DE REPÈRE DU RÉDACTEUR

- L'indice thérapeutique de la warfarine étant étroit, il faut un monitoring serré en mesurant le rapport international normalisé (RIN) pour prévenir les complications hémorragiques ou thrombotiques. Traditionnellement, cette tâche était réservée au médecin de famille communautaire, ce qui nécessitait des rendez-vous ou des appels téléphoniques pour discuter des valeurs de RIN observées et des ajustements de dose.
- La littérature disponible montre que si on les compare aux soins habituels d'un médecin, les cliniques tertiaires d'anticoagulation sérieuses maintiennent les patients à l'intérieur de la zone thérapeutique dans une plus grande proportion du temps, obtiennent des valeurs cibles de RIN pour une plus grande proportion de visites de patients, ont une plus grande proportion de RIN à l'intérieur de la zone thérapeutique et obtiennent un pourcentage plus faible de valeurs de RIN à haut risque.
- Cette étude voulait vérifier l'efficacité d'un programme d'anticoagulation en milieu communautaire dirigé par une infirmière; les résultats indiquent que le programme est aussi efficace qu'un monitoring traditionnel effectué par un médecin. Avec le monitoring effectué par le médecin, les patients de cette étude ont obtenu un très bon contrôle, en comparaison des groupes rapportés dans la littérature, et le monitoring fait par l'infirmière maintenait un même niveau de contrôle. Une amélioration des RNI pourrait être possible avec un monitoring effectué par une infirmière lorsque pour un groupe de patients, le temps passé hors de la zone thérapeutique est supérieur à celui observé dans la présente étude.

Cet article a fait l'objet d'une révision par des pairs.
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Warfarin is an anticoagulation agent commonly used for thromboembolism prophylaxis in conditions such as atrial fibrillation or previous venous thromboembolism, and in patients with prosthetic heart valves. Given its narrow therapeutic index, it requires extensive monitoring through measurement of the international normalized ratio (INR) to prevent hemorrhagic or thrombotic complications. Anticoagulation therapy has traditionally been managed by community family physicians, requiring appointments or telephone calls to discuss INR values and adjustments to dosing. However, alternative models of monitoring are becoming more common, including dedicated nurse-led¹⁻³ or pharmacist-led⁴⁻⁷ anticoagulation clinics. Recent meta-analyses^{8,9} show that traditional family physician-led anticoagulation monitoring is less effective at keeping patients within the target INR range than either of these alternative models. Family physician monitoring maintains patients in the therapeutic range 53%⁹ to 57%⁸ of the time.

Current literature shows dedicated anticoagulation clinics, compared with usual physician care, maintain patients in the therapeutic INR range a greater proportion of time,^{2,4,5,10,11} achieve target INR values for a higher proportion of patient visits,¹ have a higher proportion of INRs within the therapeutic range,^{12,13} and show a lower percentage of high-risk INR values.^{5,10,11} Further, emerging evidence from studies^{4,5,14} and economic model estimates^{15,16} examining anticoagulation clinics suggest a potential for health care cost savings. These anticoagulation clinics, however, have always been a part of large tertiary care centres.^{1,11}

In the Edmonton-Oliver Primary Care Network (EO PCN) in Edmonton, Alta, a nurse-run INR monitoring program has been established in the community and available to patients since 2007. In the nurse-run program, designated INR nurses housed inside the EO PCN interpret patients' INR values as they are received from the laboratory. Patients are contacted with these values. Dose and lifestyle adjustment algorithms allow the INR nurses to provide instructions about changes in warfarin dose or monitoring frequency, if required. Changes are later reported to patients' physicians. In essence, INR nurses offer patients evidence-based, protocol-directed counseling with respect to minor dose adjustments overseen by physicians while providing ongoing one-on-one contact that family physicians do not generally have the extra time for. Moreover, personalized support with the management of INR levels has been shown to equate to greater patient satisfaction¹¹ and increased adherence to treatment.¹⁴

The purpose of this study was to examine the efficacy of the nurse-run, community-based anticoagulation program in the EO PCN by comparing the INR values for patients while under physician monitoring to INR values

when being monitored by dedicated nurses. To our knowledge, this is the first study to assess the quality of a community-based, rather than a tertiary care centre-based, anticoagulation program. We assumed transferability of results from tertiary care anticoagulation clinics and thus hypothesized that the EO PCN nurse-run INR monitoring program would prove to be at least as effective as physician-managed INR monitoring in maintaining patients in therapeutic INR ranges.

METHODS

Electronic medical records (EMRs) for 3 clinics within the EO PCN were searched to identify patients currently taking warfarin. Queries to the EMR software searched for active prescriptions of *warfarin* and *Coumadin*. In addition, the INR nurses maintain active rosters of patients being monitored. The EMR queries and nurse rosters helped compile the complete list of patients. Consent to view the medical records was obtained from physicians within the EO PCN before the search, after ethics approval was received from the Human Research Ethics Board at the University of Alberta.

Figure 1 outlines the study design. Dates of blood tests and their corresponding INR values were collected for each patient; all INR values available from January 1, 2005, to July 1, 2010, were included. Deceased patients and those not taking warfarin at the time of data collection were excluded. The number of medications, number of patients taking specific medications, number of medical conditions, and patient age were also collected. The nurse-run monitoring program was implemented in the EO PCN over the course of 2 years (2007-2008); thus, collected data were dichotomized into either before nurse monitoring (ie, a family physician monitored the patient's INR) or after nurse monitoring (ie, a nurse in the program monitored the patient's INR). The level of INR control and the time between consecutive INR values was compared between the groups.

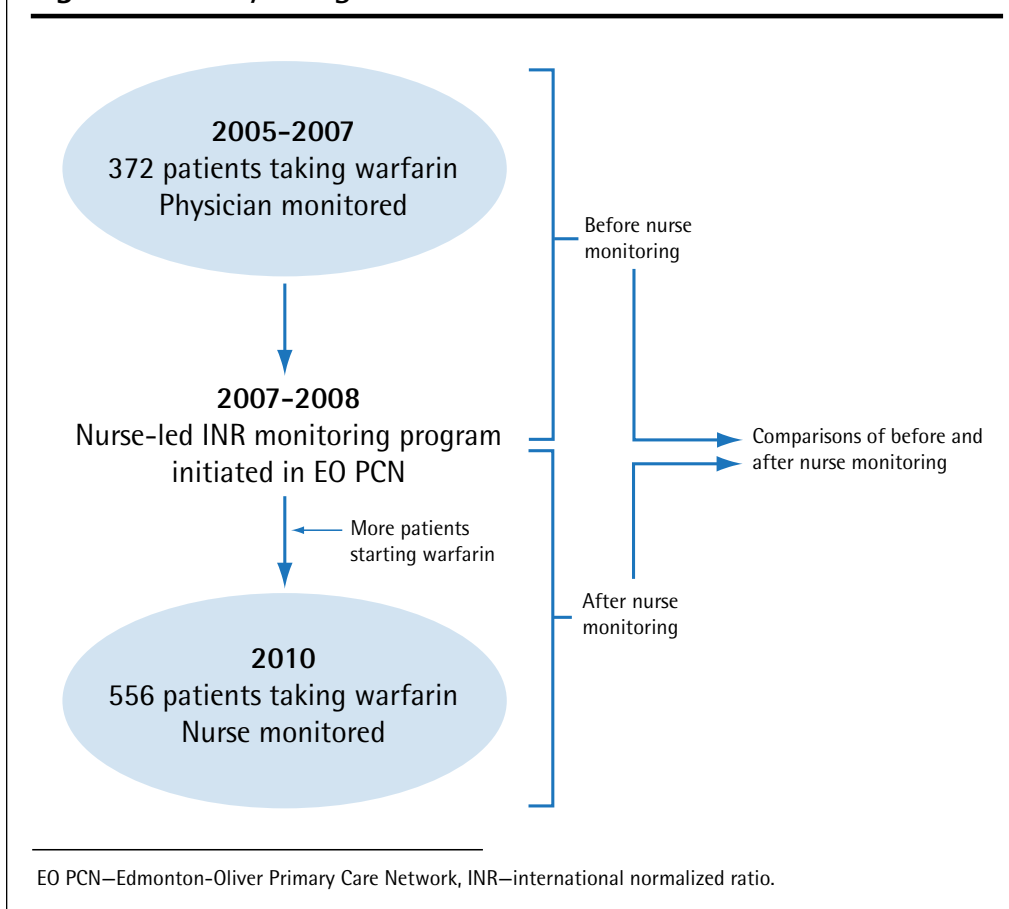
The degree of INR control was assessed based on collected INR dates and values. A normal INR value falls between 0.8 and 1.2, but for patients with medical conditions that increase the risk of thromboembolism, anticoagulation therapy with warfarin is indicated to achieve an INR value of 2.0 to 3.0 (for atrial fibrillation, history of deep vein thromboses or pulmonary emboli, etc) or 2.5 to 3.5 (for mechanical heart valves).¹⁷ The cutoffs used in this study for being in or out of range were 1.8 to 3.2 and 2.3 or 3.7, respectively (0.2 above or below target ranges). These expanded ranges have been shown to be more appropriate for the assessment of clinically significant INR control.¹¹ The total number of days a patient was out of therapeutic INR range was calculated based on a previously validated formula that assumes

a linear change in INR values exists between testing dates.¹⁷ The proportion of time spent outside the therapeutic range was calculated for each patient, as was the average number of days between INR collections. The proportion of time a patient's INR was out of the therapeutic range placed them into 1 of 2 categories. A cutoff for a good-control (GC) group and a moderate-control (MC) group was set at 25% of the time out of range: GC was out of range 25% of the time or less. This cutoff was chosen based on the lowest reported value of time out of range (24%) in our review of the literature.¹¹

The average proportion of time spent out of the therapeutic range for each group (GC, MC) and the mean time between consecutive INR col-

lections were compared. Nonparametric analysis was performed based on the distribution of the data. The Mann-Whitney *U* test was used for comparisons before and after implementation of nurse monitoring for the proportion of time out of the therapeutic range and the average intervals between INR collections, and for the comparison of demographic information (age, number of medications, number of comorbidities). Whether the observed distribution of GC and MC before and after nurse monitoring varied was determined by χ^2 tests. Warfarin indications between GC and MC groups were compared using a Kruskal-Wallis test.

Figure 1. Study design



RESULTS

In total, 556 patients were taking warfarin and had documented INR values that were monitored in the nurse-run INR monitoring program, and 372 patients had documented INR data both before and after the initiation of the nurse-run INR program.

Table 1 summarizes the number, sex, and age data for the patients included in the study at the time of data

collection, as well as the descriptive data for GC and MC and the indications for taking warfarin. The patients with GC were 7 years older than patients with MC ($P < .05$), although there was no difference in the number of medications patients were taking or the number of comorbidities present between GC and MC groups. The distribution of warfarin indications was significantly different between the GC and MC groups ($P < .05$).

Figure 2 shows the average proportion of time spent out of therapeutic INR range before and after nurse monitoring, and **Figure 3** shows the average number of days between INR tests for both time intervals. No significant differences were observed before and after nurse monitoring for these measures. **Table 2** shows the proportion of patients in either the GC or MC groups before and after nurse monitoring; no significant differences existed.

Before nurse monitoring, patients spent an average of 20.4% of monitored time outside of the therapeutic INR range, whereas after implementation of nurse monitoring, patients were out of the therapeutic range an average of 19.2% of the time. This difference was not statistically significant ($P = .115$), nor was the difference

Table 1. Demographic characteristics of all patients, good-control patients, and moderate-control patients and the documented indications for warfarin therapy in the nurse-monitored group: Boldface indicates that the distribution of warfarin indications in the moderate-control group is different from that in the good-control group ($P < .05$, Kruskal-Wallis test).

DEMOGRAPHIC CHARACTERISTICS	ALL PATIENTS (N = 556)	GOOD CONTROL (N = 414)	MODERATE CONTROL (N = 142)
Mean (SD) age, y	74 (13.0)	76 (12.0)	69 (14.0)*
Mean (SD) no. of medications	8.5 (4.1)	8.5 (3.9)	8.6 (4.4)
Mean (SD) no. of comorbidities	5.8 (2.5)	5.9 (2.5)	5.4 (2.4)
Men, n (%)	284 (51.1)	210 (50.7)	74 (52.1)
Women, n (%)	272 (48.9)	204 (49.3)	68 (47.9)
Warfarin indication, n (%)			
• Atrial fibrillation	386 (69.4)	306 (73.9)	80 (56.3)
• DVT, PE, or hypercoagulation disorder	106 (19.1)	73 (17.6)	33 (23.2)
• Mechanical valve	24 (4.3)	10 (2.4)	14 (9.9)
• CVA or TIA	11 (2.0)	5 (1.2)	6 (4.2)
• Other [†]	29 (5.2)	20 (4.8)	9 (6.3)

CVA—cerebrovascular accident, DVT—deep vein thrombosis, PE—pulmonary embolism, SD—standard deviation, TIA—transient ischemic attack.

*Significantly different ($P < .05$) compared with good control (Mann-Whitney U test).

[†]Other includes ventricular wall aneurysm, arrhythmia, apical thrombus, etc.

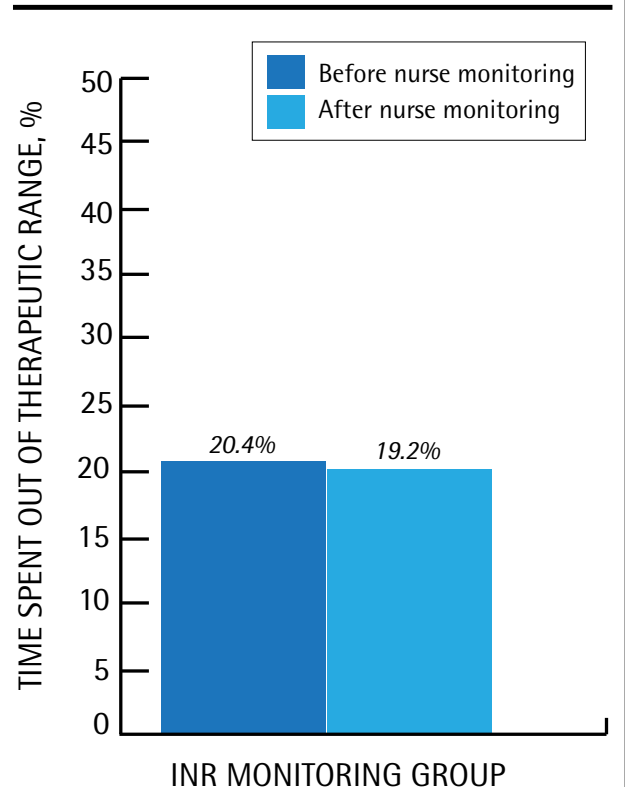
in the average time between INR visits (23.9 days vs 21.6 days, $P = .789$).

No correlation was found between the proportion of time out of range and the average interval between tests for patients either before or after the nurse-run anticoagulation program was implemented.

DISCUSSION

The results of this study show that the community-based, nurse-run INR monitoring program in the EO PCN is as effective as physician-managed care. The change in the amount of time patients spent outside of the therapeutic INR range before and after nurse monitoring was not significant. Before nurse monitoring, patients exhibited very good control compared with populations reported in the literature.^{4,8-11} The lowest average time out of range reported in our literature review was 24%,¹¹ and most (73.7%) patients in our study were at or below this level with physician management. A certain maximum possible degree of control across a patient population might exist, and thus no improvements in INR

Figure 2. Proportion of time patients spent out of the therapeutic range before and after nurse monitoring was introduced: The difference was not significant ($P = .115$).

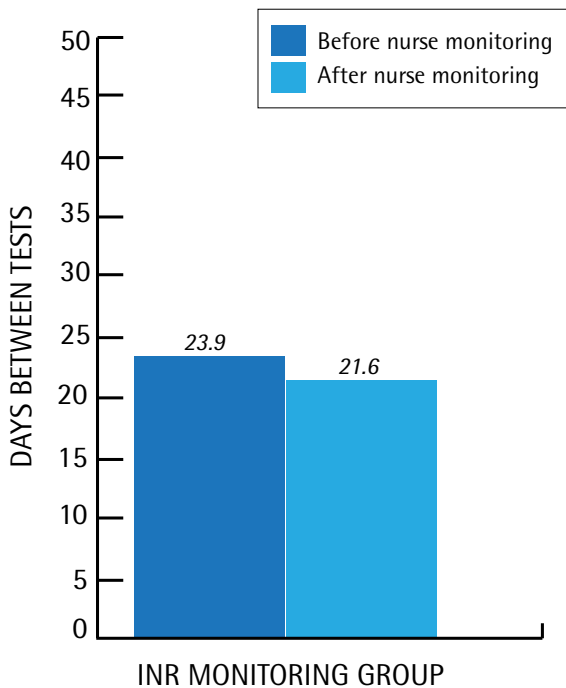


INR—international normalized ratio.

control were observed with nurse monitoring. A larger improvement might be possible under nurse-managed anticoagulation monitoring when a patient population's initial average time out of range is greater than that observed in this study. Furthermore, the average interval of time between testing dates was not different before and after nurse monitoring. This lends support for nurse-run monitoring of INR to be deemed comparable to physician monitoring. The proportion of people who were in the GC group did not change either.

The demographic data for patients in either the GC or MC groups were not different with respect to the number of medications they were taking or the number of comorbidities present, but the patients in the GC group were an average of 7 years older than patients in the MC group. This suggests that, in our population, older patients are more likely to maintain INRs in the therapeutic range. This has been demonstrated in other settings, where age older than 70 years is a predictor of stable INR values.¹⁸

Figure 3: Average number of days between consecutive INR tests before and after nurse monitoring was introduced: The difference was not significant ($P = .789$).



INR—international normalized ratio.

Table 2. Proportion of patients with good control and moderate control before and after nurse monitoring: The difference was not significant ($P = .924$, χ^2 test).

TIME PERIOD	GOOD CONTROL, %	MODERATE CONTROL, %
Before nurse monitoring	73.7	26.3
After nurse monitoring	74.3	25.7

Community-based, nurse-run monitoring, shown here to be equivalent to physician monitoring, has potential advantages for community practices. Chiquette et al showed that pharmacist-led anticoagulation clinics equated to a considerable decrease in health care costs.⁵ Our study did not directly examine the cost difference between nurse and physician monitoring, but the frequency of INR monitoring was not different between physician- and nurse-run monitoring and therefore no apparent increase in cost from testing resulted. Recent data from the United States showed anticoagulation offered by nurses operating under a model similar to that in the EO PCN led to an average yearly net cost savings

of \$241 400 per 100 patients.¹⁴ The savings were attributed to fewer trips to the emergency department for anticoagulation-related complications and less severe complications when they presented. Cost analysis in a community-based, nurse-run monitoring program in Canada has yet to be performed, but such results are encouraging for the role of nurse-run INR management. Perhaps most important, nurse-run monitoring allows physicians to allocate time previously used for INR follow-up and monitoring to other tasks, including seeing more patients or reducing time at work.

Limitations

This study has some limitations. First, it was a retrospective comparison, rather than a randomized controlled trial. Second, in examining patient demographic information, such as medications, age, and comorbidities, only the patient’s values at the time of data collection were considered, as it was not possible to track changes in these values over the entire study period for each patient. Third, we included all INR values, including those recorded in the time immediately following the initiation of warfarin. The initial titration period of warfarin levels is known to be a time where values can be expected to be out of the therapeutic range. Because start-up INR data are included both before and after nurse monitoring, we do not expect any bias in the results owing to these out-of-range INR values.

Conclusion

Our results are the first to show that a community-based, nurse-run anticoagulation monitoring program is as effective as traditional physician monitoring. Results seen in tertiary care anticoagulation clinics, which have been shown to be as good as or superior to results of physician monitoring,^{4,10,11,13} were demonstrated here in a community setting. Further analysis with respect to cost is warranted to more solidly link the nurse-managed program to considerable cost savings in a community setting, but the potential for economic benefit is a reasonable consideration. Further, the demonstrated effectiveness of nurse-run INR monitoring could equate to a reduced workload for family physicians. These attributes, coupled with the evidence of improved patient satisfaction and adherence, support a transition toward community-based, nurse-monitored anticoagulation care.

Mr Levine is a medical student at the University of Alberta in Edmonton. Dr Shao is a family physician in Vancouver, BC. Dr Klein is Associate Professor in the Department of Family Medicine at the University of Alberta.

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Contributors

Mr Levine collected and analyzed the data, contributed to interpretation of the data, and wrote the initial and final drafts of the manuscript. Dr Shao reviewed

the literature and wrote the summary of reviewed literature that formed the introduction to the manuscript, and reviewed and edited the manuscript during the writing process. Dr Klein initiated the project by developing the research question and hypothesis; he also oversaw data collection, directed analysis, and edited versions of the manuscript.

Competing interests

None declared

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