Critical international normalized ratio results after hours

To call or not to call?

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Abstract

Objective To determine whether the timing of notification of critical international normalized ratio (INR) results (during or after clinic hours) altered the clinician's ability to affect same-day patient care.

Design Retrospective chart review.

Setting The Anticoagulation Management Service at the University of Alberta Hospital in Edmonton.

Participants A total of 276 patients with critical INR results (>5.0) separated by at least 30 days were identified to have 200 critical INR results reported during clinic hours and 200 reported after hours.

Main outcome measures Differences in the proportion of patients with critical INR results having same-day care altered (by changing warfarin dose, administering vitamin K, or referring for assessment) between those with results reported during clinic hours compared with those with results reported after clinic hours. Differences by highly critical INR results (>9.0 vs ≤9.0) and whether patients experienced thromboembolism or bleeding within 30 days were also assessed.

Results Same-day patient care was affected for 174 out of 200 (87.0%) critical INR results reported during clinic hours compared with 101 out of 200 (50.5%) reported after clinic hours ($P<.001$). The most common reason for not being able to intervene was that warfarin had already been taken. Warfarin dose alteration was the most frequent change (97.1% during clinic hours and 96.0% after hours). When patients with INRs greater than 9.0 were assessed separately, the ability to affect care increased for INRs reported both during and after clinic hours (92.9% and 63.6%, respectively), largely attributable to oral vitamin K use. Overall, thromboembolic and major bleeding event rates were low and were similar in both groups.

Conclusion Same-day care was less likely to be affected by critical INR results communicated after hours, most commonly because the patient had already taken their daily warfarin dose. However, after-hours care was still affected for 1 out of 2 patients, which is meaningful and supports current practice.

EDITOR'S KEY POINTS

- Sustaining on-call services requires health care resources and might affect patient safety. This retrospective chart review aimed to determine whether the timing of notification of critical international normalized ratio (INR) results affected the ability of clinicians to intervene and alter patient care on the same day.
- The data showed that clinicians were significantly ($P<.001$) less likely to affect care in managing critical INR results after hours (50.5%) compared with during clinic hours (87.0%).
- Strategies to improve after-hours management might include improved timing of INR testing and warfarin dosing, increased availability of vitamin K (eg, at the patient's home or a local pharmacy), and technology-based systems facilitating information sharing.
- Although long-standing laboratory policies mandate alerting clinicians about critical INR results regardless of the time of day, limited data support this practice, and these results provide a benchmark to guide future research and resource allocation.

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Résultats critiques du rapport international normalisé après les heures d'ouverture

Appeler ou ne pas appeler?

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Résumé

Objectif Déterminer si le moment du signalement de résultats critiques du rapport international normalisé (INR) (durant les heures d'ouverture de la clinique ou après) influençait la capacité des cliniciens de modifier le jour même les soins aux patients.

Conception Revue rétrospective des dossiers.

Contexte Le service de prise en charge de l'anticoagulation de l'Hôpital de l'Université de l'Alberta à Edmonton.

Participants Au total, 276 patients ayant reçu des résultats critiques de l'IRN (>5,0) à intervalle d'au moins 30 jours ont été identifiés de manière à avoir 200 signalements de résultats critiques de l'IRN durant les heures d'ouverture de la clinique et 200 après les heures.

Principaux paramètres à l'étude Les différences, dans la proportion de patients ayant reçu des résultats critiques de l'IRN dont les soins ont été modifiés le même jour (en changeant la dose de warfarine, en administrant de la vitamine K ou en demandant une consultation aux fins d'évaluation), entre ceux dont les résultats ont été signalés durant les heures de la clinique et ceux dont le rapport des résultats a eu lieu après les heures. On a aussi évalué les différences selon la gravité des résultats critiques (>9,0 c. ≤9,0), de même que la survenance d'épisodes de thrombo-embolie ou de saignements dans les 30 jours suivants.

Résultats Les soins aux patients ont été modifiés le jour même chez 174 personnes sur 200 (87,0%) lorsque les résultats critiques de l'IRN ont été transmis durant les heures de la clinique par rapport à 101 sur 200 (50,5%) quand les rapports ont été reçus en dehors des heures ($p<,001$). La raison la plus fréquente de l'incapacité d'intervenir était que la warfarine avait déjà été prise. Le changement de la dose de warfarine était la modification la plus fréquente (97,1% durant les heures de la clinique et 96,0% après les heures). Dans une analyse distincte concernant les patients dont l'IRN était supérieur à 9,0, on a constaté que la capacité de modifier les soins était plus élevée, tant durant qu'après les heures d'ouverture de la clinique (92,9% et 63,6% respectivement), cela étant en grande partie attribuable à l'utilisation de la vitamine K par voie orale. Dans l'ensemble, les taux d'incidents thrombo-emboliques et de saignements majeurs étaient faibles et semblables dans les 2 groupes.

Conclusion Il était moins probable que les soins soient modifiés le jour même quand les résultats critiques de l'IRN étaient communiqués en dehors des heures d'ouverture, le plus souvent parce que le patient avait déjà pris sa dose quotidienne de warfarine. Toutefois, même si les résultats étaient communiqués après les heures, les soins de 1 patient sur 2 avaient été modifiés, ce qui est significatif et appuie les pratiques actuelles.

POINTS DE REPÈRE DU RÉDACTEUR

- Le maintien de services de garde exige des ressources du secteur de la santé et pourrait nuire à la sécurité des patients. Cette revue rétrospective des dossiers visait à déterminer si le moment de la divulgation de résultats critiques du rapport international normalisé (INR) influençait la capacité des cliniciens d'intervenir et de modifier les soins aux patients le jour même.
- Les données ont démontré qu'il était significativement moins probable ($p<,001$) que les cliniciens modifient les soins dans la prise en charge de résultats critiques de l'INR lors d'un signalement après les heures (50,5%) par rapport à durant les heures d'ouverture de la clinique (87,0%).
- Les stratégies pour améliorer la prise en charge après les heures pourraient inclure le choix d'un meilleur moment pour les tests de l'INR et le dosage de la warfarine, une plus grande accessibilité à la vitamine K (*p. ex.* au domicile du patient ou dans une pharmacie locale) et des systèmes axés sur la technologie pour faciliter le partage de renseignements.
- Même si les politiques des laboratoires obligent depuis longtemps la divulgation au clinicien des résultats critiques de l'INR quelle que soit l'heure du jour, les données à l'appui de cette pratique sont peu nombreuses et ces résultats procurent un point de départ pour orienter à l'avenir la recherche et l'attribution des ressources.

Cet article a fait l'objet d'une révision par des pairs
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Clinicians managing patients taking warfarin therapy face the difficult challenge of balancing the risks of clotting and bleeding.[1] Decisions about warfarin dosing are guided by international normalized ratio (INR) results. Elevated INRs, especially those exceeding 4.5, are associated with increased risk of hemorrhage.[2,3] While guideline-mandated interventions for critical INR results have changed over time, most recent guidelines applicable to an ambulatory population not experiencing bleeding suggest holding 1 to 2 doses of warfarin without administering vitamin K for those with INRs between 4.5 and 10.0, and to hold warfarin and administer oral vitamin K for those with INRs exceeding 10.0.[2,4]

Regardless of the time of day, laboratories have policies in place to alert clinicians about critical INR results to enable prompt patient management. Despite this common practice, there are no published data to support that urgently communicating critical INR results allows clinicians to consistently alter patient care. Moreover, the on-call clinician faces barriers to altering warfarin therapy (such as contacting the patient and the inability to alter therapy that has already been administered), making care less likely to be affected compared with during regular office hours.

The Anticoagulation Management Service (AMS), a referral-based service located at the University of Alberta Hospital in Edmonton, manages approximately 750 patients at high risk of bleeding (eg, recent history of bleeding, concomitant medications enhancing anticoagulant effect) or thromboembolic events (eg, those with mechanical heart valves, atrial fibrillation with a $CHADS_2$ [congestive heart failure, hypertension, age ≥75, diabetes mellitus, and stroke or transient ischemic attack] score ≥3, active clots, or complex medical conditions or medications that affect anticoagulant control). The AMS continues to contact patients about all critical INR results, regardless of the time of day.[5,6] In contrast, same-day communication of critical INR results is not uniformly adopted by all AMSs, with one program contacting patients after hours only for INRs greater than 9.0 (written communication, Jennifer Lowerison, PharmD, Clinical Practice Leader and Program Liaison for the Calgary Zone AMS, May 2014). Because the practice of communicating critical INR results has resource implications and could affect patient safety and quality of life, we sought to evaluate whether the timing of notification (either during clinic hours or after hours) affects the ability of the clinician to intervene and alter patient care on the same day.

METHODS

Study design

We performed a retrospective chart review of critical INR results (defined as an INR >5.0) for patients taking warfarin, irrespective of indication, managed by the University of Alberta Hospital AMS. Consecutive eligible critical INR results were identified beginning in December 2013 and working backward using the AMS database, after-hours call log, and AMS patient charts. After 200 eligible events were identified for the after-hours group, critical INR results during clinic hours were identified by systematically matching events on an annual basis to ensure both groups had equal numbers from a temporal perspective. Multiple critical INR results per individual patient were included if they were at least 30 days apart. Critical INR results not communicated to the AMS on the same day were excluded.

All records were reviewed by 1 investigator (D.K.) to ensure consistency of data collection. Data were collected and managed using a secure, Web-based application tool, REDCap (Research Electronic Data Capture), hosted at the University of Alberta.[7] Data presented herein reflect the entire data set, and no additional data are available. Approval was received from the University of Alberta Health Research Ethics Board.

Outcomes

The primary outcome was the proportion of critical INR results (INR >5.0) reported after hours compared with those reported during clinic hours that resulted in a same-day effect on care by AMS staff. *Effect on care* was defined as any of holding warfarin, reducing the warfarin dose, prescribing oral vitamin K, or AMS staff referring the patient to another health care professional (eg, emergency department). *Same day* refers to the 24-hour clock for all days of the week, beginning and ending at midnight. *During clinic hours* included Monday through Friday from 9:00 AM to 5:30 PM, while *after hours* captured all times outside this range, including weekends and statutory holidays. To provide further insight into the primary results, first we assessed our primary outcome by only including the first critical INR result for each patient. Second, we eliminated those critical INR results belonging to patients who took their warfarin in the morning. Secondary outcomes evaluated the primary outcome stratified by highly critical INR results (INRs of 5.1 to 9.0 vs >9.0). We used the cut point of an INR greater than 9.0 (as opposed to the guideline-based cut point of INR >10.0) because our laboratories use this as an upper margin to report critical INR values. Additionally, each component of the primary outcome between the 2 groups was compared. Last, we tracked the incidence, location, and outcome of thromboembolism or major bleeding occurring within 30 days of incident critical INR results.

Sample size and data analysis

There were no published data to provide clear estimates of the rates of being able to alter therapy for those with critical INR results during or after clinic hours, leaving

us to rely on anecdotal estimates. We anticipated that in our control group (during clinic hours), care would be affected the same day 95% of the time, while for the after-hours group it was anticipated that, at best, an 85% threshold would be achieved. With this, a sample size of 188 critical INR values for each group would have 90% power to detect a 15% difference in the ability to affect same-day patient care ($\alpha = .05$).[8] We adjusted this sample size to 200 in each group in order to account for those patients who had already taken their dose of warfarin, precluding our ability to alter care.

To assess for differences in our primary end point, we performed a χ^2 test treating each critical INR result as a discrete event. Using the same test, 2 analyses were done to provide further insight into the primary results (first critical INR result for each patient, eliminating those critical INR results belonging to patients taking warfarin in the morning). Statistical analyses were not performed on our secondary outcomes. Secondary outcomes consisted of individual components of the primary composite end point. The secondary outcomes had few events, and our study was not powered to detect differences between groups for the those outcomes.

RESULTS

There were 572 critical INR records screened to reach our sample size of 400 critical INR results after exclusions (**Figure 1**). The critical INR results belonged to 276 individual patients: 128 patients with results during clinic hours and 148 patients with results after hours. A total of 30 patients had critical INR events included both during and after clinic hours.

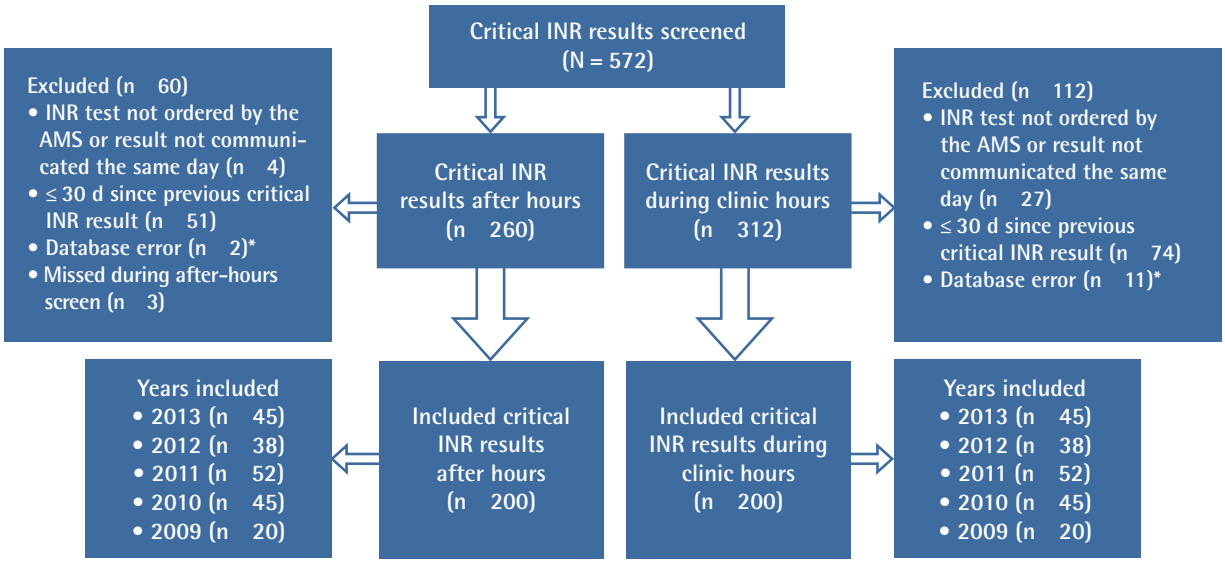
The most common indication for anticoagulation was a mechanical heart valve (46.4%), and most patients had a target INR range of 2.0 to 3.0 (56.2%). Nearly half (49.3%) had a history of more than 1 critical INR result. Most (82.6%) patients took their warfarin in the evening (**Table 1**).

Same-day patient care was affected during clinic hours for 174 critical INR results (87.0%) compared with 101 events (50.5%) after hours ($P < .001$) (**Table 2**).

The results remained consistent when the analysis was confined to only the first critical INR result per patient, and were slightly increased in both arms when those critical INRs belonging to subjects taking morning doses were eliminated. The most common same-day intervention was altering the dose, either by holding warfarin or reducing the dose (97.1% of critical INR results during hours and 96.0% after hours). When patients with an INR greater than 9.0 were analyzed separately, the ability to affect same-day care increased both during clinic hours and after hours, attributable to the use of oral vitamin K (of those receiving same-day care, 76.9% of cases during clinic hours and 71.4% of cases after hours received vitamin K) (**Table 2**).

Thromboembolic and major bleeding events occurred following 5 critical INR results (2.5%) reported during

Figure 1. Identification of critical INR results included in the study



INR—international normalized ratio.
*Database errors included data entry errors and misclassification of when INR was reported.

Table 1. Patient characteristics: *N* = 276.

CHARACTERISTIC	VALUE
Male sex, n (%)	157 (56.9)
Median (IQR) age, y*	60 (47-68)
Time of warfarin administration, n (%)	
• Morning	42 (15.2)
• Evening	228 (82.6)
• Not stated	6 (2.2)
Target INR range, n (%)	
• 2.0-3.0	155 (56.2)
• 2.5-3.5	110 (39.9)
• Other	11 (4.0)
History of > 1 critical INR result, n (%)	136 (49.3)
Antiplatelet therapy, n (%)†	132 (47.8)
Indication for anticoagulation, n (%)‡	
• Mechanical heart valve	128 (46.4)
-Aortic	62 (48.4)
-Mitral	51 (39.8)
-Aortic and mitral	15 (11.7)
• Venous thromboembolism	65 (23.6)
• Atrial fibrillation	64 (23.2)
Concurrent medical conditions, n (%)‡	
• Atrial fibrillation	116 (42.0)
• Hypertension	112 (40.6)
• Heart failure	83 (30.1)
• Coronary artery disease	70 (25.4)
• Stroke or TIA	67 (24.3)
• Diabetes (type 1 or 2)	49 (17.8)
• Thyroid disorder	41 (14.9)
• Renal dysfunction§	30 (10.9)

INR—international normalized ratio, IQR—interquartile range, TIA—transient ischemic attack.
*At the time of the most recent critical INR result included in the study.
†Includes 1 patient taking dual antiplatelet therapy.
‡Indications and concurrent conditions with < 10% occurrence are not reported.
§Defined as dialysis or serum creatinine level > 200 µmol/L.

clinic hours and 7 critical INR results (3.5%) reported after hours (**Tables 2** and **3**). The adverse event rates at 30 days were similar between the 2 groups.

DISCUSSION

The results of this study provide baseline information about front-line clinicians' ability to affect same-day patient care for critical INR results received either during or after clinic hours. There was a statistically significant difference in the ability to alter patient care the same day between the 2 groups, with greater ability to do so when results were reported during clinic hours. Altering the warfarin dose (holding or reducing warfarin) was the most common strategy employed. When the INR was greater than 9.0, there was an increase in the ability to intervene in care the same day for both groups, attributable to an increased use of oral vitamin K (consistent with current guideline recommendations). Overall, the incidences of thromboembolism and bleeding requiring an emergency department visit or hospitalization were low and similar in both groups. This was a finding we anticipated, given that our study was not powered to detect differences in either of these outcomes.

Our data reflect a realistic view of daily operations for critical INR result management among an ambulatory group of patients, both during and after clinic hours. We found that patients having 1 critical INR are likely to have another (reported in 49.3% of our cohort). From a clinical standpoint, there might be patient factors that influence the independence of critical INR results belonging to the same patient and appearing in both groups. However, regardless of how our primary end point was analyzed (using all critical INR events versus using the first critical INR event for a patient), the results remain unchanged. This suggests that those having multiple critical INRs do not have care affected any differently with subsequent reports.

While some variability in the practices of AMSs now exists within Alberta, it remains prudent to assess the consequences on care delivery and subsequent patient outcomes, then inform system-related processes of care. While no differences in patient outcomes were evident in our study, it was not powered to detect such a difference. We found care to be affected in 1 out of 2 patients having a critical INR result reported after hours, and the clinical significance of such a finding can only be determined with larger-scale studies. The challenges of effectively managing patients with critical INR results after hours are widely applicable to any clinician managing any critical laboratory value in this setting. These include the ability to establish contact with the patient, to alter therapy that might have already been taken, to access medical information about an individual patient, and to access medications for reversal or treatment options after hours (eg, oral vitamin K for highly critical INR results).

Limitations

As a retrospective chart review, we relied on the documentation in the AMS clinic charts being accurate and complete to determine our end points of interest. Overall, the interventions and ability to alter care were well documented, as determining whether or not a patient followed through with instructions is necessary to determine subsequent warfarin management plans.

Table 2. Comparison of the ability to affect care for critical INR results communicated during clinical hours and after hours

OUTCOME	TIMING OF INR RESULT NOTIFICATION	
	DURING CLINIC HOURS	AFTER HOURS
Notification of result led to same-day care, n/N (%)*		
• All critical INR results	174/200 (87.0)	101/200 (50.5)
• Only first critical INR result assessed per patient	108/128 (84.4)	72/148 (48.6)
• Excluding patients taking warfarin in the morning and those for whom timing was unknown	162/171 (94.7)	94/164 (57.3)
Same-day care implemented, n/N (%)†		
• Hold warfarin	153/174 (87.9)	80/101 (79.2)
• Reduce warfarin dose	16/174 (9.2)	17/101 (16.8)
• Administer oral vitamin K	21/174 (12.1)	6/101 (5.9)
• Refer to health care provider or ED	3/174 (1.7)	1/101 (1.0)
Notification of result led to same-day care based on severity of INR, n/N (%)		
• INR 5.1-9.0	161/186 (86.6)	94/189 (49.7)
• INR >9.0	13/14 (92.9)	7/11 (63.6)
Incidence of thromboembolism, n/N (%)‡	1/200 (0.5)	1/200 (0.5)
Incidence of bleeding, n/N (%)‡	4/200 (2.0)	6/200 (3.0)

ED—emergency department, INR—international normalized ratio.
*The differences between after-hours notification and notification during clinic hours are significant ($P<.001$).
†More than 1 strategy to alter care is possible, except both holding and reducing warfarin.
‡Includes 7 critical INR results without event-related outcomes for 30 d either owing to transfer of care to patients' general practitioners or warfarin discontinuation.

Table 3. Major bleeding and thromboembolic events

TIMING OF INR RESULT	AGE, Y	SEX	INDICATION FOR ANTICOAGULATION	TARGET INR	CARE SOUGHT	TIME FROM CRITICAL INR RESULT TO EVENT	EVENT	INR CLOSEST TO EVENT	OUTCOME
During clinic hours	75	Male	VTE	2.0-3.0	Hospitalized	29 d	DVT	1.5	Nonfatal
	26	Female	VTE	2.0-3.0	Emergency department	Same day	GI bleeding	5.6	Nonfatal
	45	Male	Superior mesenteric vein thrombosis	2.2-3.2	Hospitalized	21 d	GI bleeding	1.6	Nonfatal
	51	Female	Mechanical mitral valve	2.5-3.5	Emergency department	18 d	Bleeding, large bruises to arms and legs	2.8	Nonfatal
	74	Male	Atrial fibrillation	2.0-3.0	Hospitalized	1 d	GI bleeding	10.0	Nonfatal
After hours	85	Female	Atrial fibrillation	2.0-3.0	Hospitalized	15 d	Stroke	1.4	Fatal
	27	Male	LV dysfunction	2.0-3.0	Emergency department	1 d	Genitourinary bleeding	9.1	Nonfatal
	58	Female	Atrial fibrillation	2.0-3.0	Hospitalized	16 d	GI bleeding	2.0	Nonfatal
	67	Male	DVT, portal vein	2.5-3.0	Hospitalized	Same day	Bleeding, fell and bruised ribs	7.0	Nonfatal
	40	Male	VTE	2.0-3.0	Emergency department	2 d	Genitourinary bleeding	1.8	Nonfatal
	80	Male	Atrial fibrillation	2.0-3.0	Hospitalized	2 d	GI bleeding	5.3	Nonfatal
	66	Male	VTE	2.0-3.0	Hospitalized	30 d	Retroperitoneal bleeding	1.5	Nonfatal

DVT—deep-vein thrombosis, GI—gastrointestinal, INR—international normalized ratio, LV—left ventricular, VTE—venous thromboembolism.

However, there are still limitations to adequately defining and determining if thromboembolism or major bleeding occurred based on chart documentation, without confirmation of clinical criteria (eg, decline in hemoglobin). To ensure consistency of completing the data collection, there was 1 trained data abstractor (D.K.). We recognize that staffing, individual practitioner practices, and guidelines for care might change over time, and we attempted to limit this effect by temporally matching the groups on an annual basis. Our study was based out of an AMS that targets patients at higher risk of thromboembolism or bleeding, and our results therefore might not be generalizable to other community-based practices. However, they do serve as a benchmark for differences in care delivery depending on the timing of notification of a critical result.

Conclusion

While the ability to affect same-day patient care during clinic hours was high, the ability to alter care when notified after hours was lower than anticipated. Nonetheless, being able to change care for 1 in 2 patients with critical INR results is arguably still meaningful; interrupting further warfarin ingestion when the INR is already critically elevated might mitigate the severity of INR elevations and lower the risk of subsequent symptomatic hemorrhage when applied to large numbers of patients. Strategies to address barriers to affecting same-day patient care when notified after hours might include proactively educating patients to administer warfarin as late as possible on days when INR testing is done to enable clinicians to alter warfarin dosing (provided this does not impair adherence), and having patients keep some vitamin K at home. Ongoing collaboration among various stakeholders, including laboratory physicians and front-line clinicians, in concert with information technology–based systems is necessary to optimize care delivery. Our findings serve as a benchmark to provide estimates about the ability to affect care for patients with critical results based on the timing of notification, and might serve to guide future resource allocation for after-hours access and services. Further research is necessary to determine the effects on patient outcomes.

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Contributors

Ms Korn and **Dr Bungard** were responsible for the conception and design of this research project and manuscript. **Ms George-Phillips** and **Dr McMurtry** helped with the design of the research. **Ms Korn** was responsible for the acquisition, analysis, and interpretation of the data and for drafting the work. **Ms George-Phillips** and **Drs Bungard** and **McMurtry** were responsible for critically revising the manuscript for important intellectual content. All authors approved the final version submitted for publication.

Competing interests

None declared

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