

# Quality Improvement Program Improves Time in Therapeutic Range for Hemodialysis Recipients Taking Warfarin



Daniel Blum<sup>1</sup>, William Beaubien-Souligny<sup>2</sup>, Marisa Battistella<sup>3</sup>, Eric Tseng<sup>4</sup>, Ziv Harel<sup>5</sup>, Jaspreet Nijjar<sup>6</sup>, Elena Nazvitch<sup>6</sup>, Samuel A. Silver<sup>7</sup> and Ron Wald<sup>5</sup>

<sup>1</sup>Division of Nephrology, Jewish General Hospital, Montreal, Quebec, Canada; <sup>2</sup>Division of Nephrology, Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada; <sup>3</sup>University of Toronto, Toronto, Ontario, Canada; <sup>4</sup>Division of Hematology, St. Michael's Hospital, Toronto, Ontario, Canada; <sup>5</sup>Division of Nephrology, St. Michael's Hospital, Toronto, Ontario, Canada; <sup>6</sup>Department of Pharmacy, St. Michael's Hospital, Toronto, Ontario, Canada; and <sup>7</sup>Division of Nephrology, Kingston Health Sciences Centre, Queen's University, Kingston, Ontario, Canada

**Introduction:** Studies have shown that achieving a time in therapeutic range (TTR) for warfarin of greater than 60% is associated with a lower risk of bleeding. However, many patients on hemodialysis (HD) do not achieve this target.

**Methods:** We audited TTR achievement at the in-center HD unit of our hospital in 2017 and found that only 40% of patients had achieved a TTR >60%. We aimed to improve the percentage of HD patients achieving target TTR within 2 years. We reported each patient's individualized trend in quarterly TTR to their primary warfarin prescriber as an audit-feedback report. These reports were generated, disseminated, and subsequently improved following a series of plan-do-study-act cycles. We then used statistical process control to assess for changes in the percentage of HD patients achieving target TTR over time.

**Results:** In the primary analysis, 28 patients were included in the baseline period, and 46 were included in the intervention period. At baseline, the percentage of patients achieving a TTR >60% varied between 33% and 45% (mean ± SD, 40% ± 5%); post-intervention, this metric improved and varied between 52% and 71% (mean ± SD, 61% ± 8%). In time-series analysis, there was evidence of statistically significant variation between the 2 periods and evidence of sustained improvement.

**Conclusions:** A quality improvement program consisting of an audit-feedback report that raises awareness of the quality gap in TTR achievement can result in substantial improvement in the safe and efficacious administration of warfarin to patients receiving maintenance hemodialysis.

*Kidney Int Rep* (2020) 5, 159–164; <https://doi.org/10.1016/j.ekir.2019.10.011>

KEYWORDS: hemodialysis; quality improvement; time in therapeutic range; warfarin

© 2019 International Society of Nephrology. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Warfarin is widely prescribed to patients on HD for a myriad of indications. As the only oral anticoagulant approved in Canada for patients with advanced chronic kidney disease, warfarin is the standard of care for patients with end-stage kidney disease for the treatment and prevention of venous thromboembolism, and the prevention of thromboembolic events in patients with mechanical heart valves or atrial fibrillation.<sup>1–5</sup>

In the nondialysis atrial fibrillation population, the literature suggests that consistent maintenance of the international normalized ratio (INR) in the appropriate

therapeutic range, specifically a TTR of greater than 60%, is associated with an improvement in stroke prevention and mitigation of bleeding risk.<sup>6</sup> However, only a handful of studies has investigated TTR in the HD population.<sup>7–11</sup> In each of these studies, TTR achievement was consistently poor.

Despite the widespread problem of low TTR achievement in the HD population, only 2 studies have examined strategies to improve warfarin control in patients receiving HD, and both were unsuccessful.<sup>8,12</sup> To date, no study has described the implementation of sequential interventions as an initiative to improve the quality of warfarin control in patients receiving HD.

An audit of our local data revealed a large-quality gap in managing patients taking warfarin in our HD unit, with an average of only 40% ± 5% of patients achieving a quarterly TTR >60%. This prompted the implementation of a quality improvement initiative to

**Correspondence:** Daniel Blum, Jewish General Hospital, 3755 Cote Sainte Catherine, D-070, Montreal, Quebec H3T 1E2, Canada. E-mail: [daniel.blum@mcgill.ca](mailto:daniel.blum@mcgill.ca)

Received 2 August 2019; revised 4 October 2019; accepted 28 October 2019; published online 6 November 2019

sustainably improve the proportion of dialysis patients in our HD unit on chronic warfarin anticoagulation who achieve a quarterly TTR >60%, within a period of 2 years.

## METHODS

### Context

Our HD unit is located within an urban academic teaching hospital in Toronto, Canada. Our HD unit provides maintenance dialysis to approximately 250 outpatients each month across 8 shifts: thrice-weekly conventional HD is administered on 6 shifts and the other 2 are devoted to long-duration in-center nocturnal HD. The care of each patient, including warfarin dose adjustment, was managed by a team comprising 1 of 4 nurse practitioners and 1 of 9 nephrologists. Local practice was to measure INR on a weekly basis, typically before the first dialysis session of the week, for all patients receiving warfarin. Additional measures of INR were occasionally requested when deemed to be clinically necessary by the primary prescriber (either a nurse practitioner or a nephrologist). Warfarin was adjusted according to clinician judgment without a specific protocol or algorithm. All INR measures drawn for each HD patient were captured within our local dialysis facility electronic health record and were extractable along with corresponding time-stamps and patient identifiers at quarterly intervals.

### Generation of TTR

We audited our in-center HD unit to assess whether a quality gap in TTR achievement existed at our institution. The population of interest included all patients who had received warfarin for at least 3 months during the 12-month period from October 1, 2016, through September 30, 2017. INRs for each patient during discrete 13-week intervals (quarters, Q1 [January–March], Q2 [April–June], Q3 [July–September], Q4 [October–December]) were used to generate up to 4 quarterly TTRs using the Rosendaal method.<sup>13</sup> The Rosendaal method of calculating TTR is widely accepted as a surrogate for efficacy and safety<sup>13</sup> and the quality standard is a TTR >60%.<sup>6</sup> Our audit revealed that an average of 40% ± 5% of patients achieved a quarterly TTR >60% during this 12-month baseline period.

The TTR for each patient in each quarter was calculated using an Excel template that was programmed to calculate TTR by the Rosendaal method using linear interpolation (Supplementary Table S1).<sup>13</sup> The template requires input of INR values with corresponding blood-draw dates. All data entry was performed by one of the authors (DB). Target INR lower and upper limits were set to 1.999 and 3.001, except for the rare cases of patients with a mechanical valve in which the target limits were reset to

2.499 and 3.501. We excluded quarters in which warfarin was initiated, quarters in which warfarin initiation was within the last 4 weeks of the preceding quarter, quarters in which patients were admitted to hospital, and quarters in which warfarin was intentionally interrupted for any reason. In quarters in which patients were either admitted to hospital or warfarin was intentionally interrupted, a value of “n/a” was included in the TTR report. For all other quarters, TTR was calculated and reported as a percentage in the TTR report.

### Intervention

We interviewed local nephrologists, nurse practitioners, pharmacists, and nurses to create a process map for the system of warfarin prescription for our HD patients. From the information gathered, we hypothesized that the root causes of poor TTR achievement in our HD unit were (i) lack of TTR awareness on the part of patients and providers leading to overestimation of the safety of the current management strategy, and (ii) labile INR as a result of nonstandardized dosing changes. In addition, we discovered that there was no standardized reassessment of ongoing warfarin prescription; therefore, once warfarin was initiated for any indication, it was often continued until a clinical event (for example, a bleed) prompted its reassessment. Consequently, we proposed that a reassessment of ongoing warfarin prescription should be regularly performed to avoid inappropriate exposure to warfarin (see Table 1).

In October 2017 we audited our local practice and generated data on local TTR achievement at the HD unit level. The initial audit results were then disclosed to warfarin prescribers as a group. We subsequently planned a series of targeted interventions. As our first planned intervention, we reported each patient’s individualized trend in quarterly TTR to their warfarin prescriber in an audit and feedback report that also prompted the prescriber to reassess the need for ongoing warfarin anticoagulation. The template’s first iteration prompted the prescriber to choose from 1 of 3 options: (i) stop warfarin, (ii) continue warfarin and reassess next quarter, or (iii)

**Table 1.** Common proximal causes of poor time in therapeutic range (TTR) achievement in our unit based on stakeholder interviews, and recommendations for improvement

Reason for poor TTR achievement	Recommendation for improvement
Lack of TTR awareness on the part of patients and providers	Audit and feedback reporting of time in therapeutic range, with patient engagement
Labile international normalized ratio as a result of nonstandardized warfarin dosing changes	Standardized warfarin dosing algorithms, and verbal and/or written reminders following warfarin dose changes
Lack of standardized reassessment of ongoing warfarin prescription	Standardized quarterly reassessment of risk and benefit of ongoing anticoagulation with warfarin

continue warfarin and reassess in 1 year. Based on user feedback and review with engaged stakeholders, the template underwent 4 revisions over time. Additions to the initial template included a new prompt to “consider strategies to improve TTR,” “time with INR supra-therapeutic above 4” (to inform whether poor TTR achievement was related to “missing high” or “missing low”), a brief list of specific strategies that had been shown to work locally to improve recent TTR in our population (including written and verbal reminders and the use of prescription algorithms), the indication for ongoing warfarin prescription and risk scores (CHADS2<sup>14</sup> and HASBLED<sup>15</sup>) for patients with atrial fibrillation receiving warfarin. We also added “adherence to a prespecified algorithm” as an improvement strategy; we proposed the C.A.R.E. warfarin dosing algorithm<sup>16</sup> because it was already being used successfully by one local prescriber. This algorithm is also used to guide warfarin dosing in HD recipients participating in the ongoing RENAL-AF trial ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02942407) NCT02942407). An example of the most recently revised TTR score report is shown in [Supplementary Figure S1](#).

### Study of the Intervention and Measures

Our primary outcome measure was the percentage of HD patients with quarterly TTR >60%. Given that quarterly TTR is calculated from a 3-month dataset, there is an expected lag-time of 3 to 6 months between rollout of the intervention and ascertainment of its potential effect.

Secondary measures to assess audit-feedback adherence included the percentage of HD patients with a completed feedback report, and the number of patients stopping warfarin at the time of audit-feedback. The percentage of HD patients with a completed feedback report was selected as our lead process indicator because it was inexpensive, reliable, easy to measure, and pertinent as a surrogate marker for patients having had their warfarin prescription reassessed by their prescriber.

As a balancing measure, we captured prescriber satisfaction based on qualitative feedback from an anonymous electronic survey sent to the 4 nurse practitioners who were the primary warfarin prescribers.

### Analysis

In the primary analysis, we generated a statistical process control (SPC) p-chart for the primary outcome measure. SPC charts are statistical tools that depict data over time and are traditionally used for time-series analysis in quality improvement.<sup>17–19</sup> On an SPC chart, the center line represents the baseline average.<sup>17–19</sup> Upper and lower control limits are generated for each data point and represent 3 SDs from the mean at each point in time<sup>17–19</sup>; the control limits may vary over time depending on the sample size. The SPC p-chart is used when the dependent

variable is a categorical variable and is represented as a percentage of the total.<sup>17–19</sup> A statistically significant change in the dependent variable over time has occurred when a signal of special cause variation is present on an SPC chart.<sup>17–19</sup> Traditional signals of special cause variation in health care data include the following: (i) shift (6 consecutive points either consistently higher or lower than the prior mean), (ii) trend (5 consecutive points either increasing or decreasing in the same direction), (iii) out-of-control (1 point beyond 3 SD), and (iv) 2-out-of-3 pattern (2 of 3 consecutive points beyond 2 SD).<sup>17–19</sup> An additional signal of special cause variation includes the presence of 4 of 5 consecutive points beyond 1 SD.<sup>20</sup> In our primary analysis, the center line is calculated based on data from the 12-month baseline period and fixed thereafter.

In our first additional analysis, we used a paired Student's *t* test to complement the SPC approach described previously. Only patients who were on warfarin in both periods were considered in this analysis. Data obtained during and after the first quarter of 2018 were considered post-intervention.

In our second additional analysis, we repeated the primary analysis using broader inclusion criteria for the generation of TTR. This analysis was done to account for potential bias due to our baseline strategy for TTR generation. Specifically, patients who were hospitalized may have been more prone to poorer TTR achievement; therefore, our exclusion of these patients' TTRs from our primary analysis may have inflated the proportion of patients achieving a goal TTR, thus biasing our results toward finding a signal for improvement. See the [Supplemental Methods](#) for more details.

QIMacros software (Denver, CO) and SPSS software version 25 (IBM, Armonk, NY) were used to complete the analyses.

### Patient and Public Involvement

Patients were not involved in the conception of the improvement program, nor the design of the interventions.

### Ethical Consideration

This initiative was formally reviewed by institutional authorities at St. Michael's Hospital, Toronto, Canada, and deemed to neither require Research Ethics Board approval nor written informed consent from participants. This article was written in accordance with the Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) publication guidelines.<sup>21</sup>

## RESULTS

### Primary Analysis

Data on TTR achievement was generated for 28 patients during the baseline period (Q4 2016–Q3 2017), and 46

patients following audit-feedback (Q1 2018–Q1 2019). Audit results from the baseline period were disclosed in Q4 2017, which was considered a period of transition. Targeted audit-feedback began in Q1 2018 for 31 patients, and their baseline characteristics are detailed in Table 2. Most patients included in the baseline period were also included in the intervention period. Following audit-feedback, the primary outcome measure improved, and the increase was sustained based on the SPC chart (Figure 1). When considering the time-series as 2 distinct periods, the preintervention mean  $\pm$  SD of 40%  $\pm$  5% (28 patients, 4 data points over time) improved to a post-intervention mean  $\pm$  SD of 61%  $\pm$  8% (46 patients, 5 data points over time) (Supplementary Figure S2). Evidence of statistically significant improvement was present on the SPC chart depicted in Figure 1 in various ways: (i) out-of-control points in Q3 2018 and Q1 2019, (ii) 2-out-of-3 points beyond 2 SD between Q1 and Q3 2018 and again between Q3 2018 and Q1 2019, and (iii) 5 consecutive points beyond 1 SD between Q1 and Q4 2018. Adherence during the intervention period was high, with 97% to 100% of audit-feedback reports completed at each interval. No patients had warfarin stopped as a result of the TTR score reports.

**Table 2.** Baseline characteristics for the patients included in the first quarter of the intervention period

Number of patients	31
Age, yr (mean $\pm$ SD)	68.0 $\pm$ 11.8
Sex, n (%)	
Male	13 (42)
Female	18 (58)
Race, n (%)	
Caucasian	11 (35)
Black	6 (19)
Other/unknown	14 (45)
Access type, n (%)	
Central venous catheter	18 (58)
Arteriovenous fistula	8 (26)
Arteriovenous graft	5 (16)
Cause of end-stage kidney disease, n (%)	
Diabetes	12 (39)
Hypertension	3 (10)
Glomerulonephritis	12 (39)
Other/unknown	4 (13)
Comorbidities, n (%)	
Heart failure	9 (29)
Diabetes	13 (42)
Hypertension	27 (78)
Stroke/transient ischemic attack	8 (26)
Warfarin indications, n (%) <sup>a</sup>	
Atrial fibrillation	16 (52)
Venous thromboembolism	15 (48)
Mechanical cardiac valve	2 (6)
Access patency	3 (10)

<sup>a</sup>Five patients had dual indications for warfarin.

## Additional Analyses

Our first additional analysis compared TTR during the pre- and post-intervention periods and revealed a significant improvement in TTR with a mean increase (95% confidence interval) of 5% (0.6%–10.2%) ( $P = 0.029$ ) in the 25 patients on warfarin during both observation periods. See Supplementary Figure S3 for further detailed results.

Our second additional analysis, which used a more inclusive strategy for TTR generation, revealed a sustained improvement in the percentage of patients achieving a TTR >60% (Figure 2). Special cause variation was present because 5 consecutive data points lay above 1 SD. The results from this analysis were similar to those from the original analysis with stricter INR inclusion criteria.

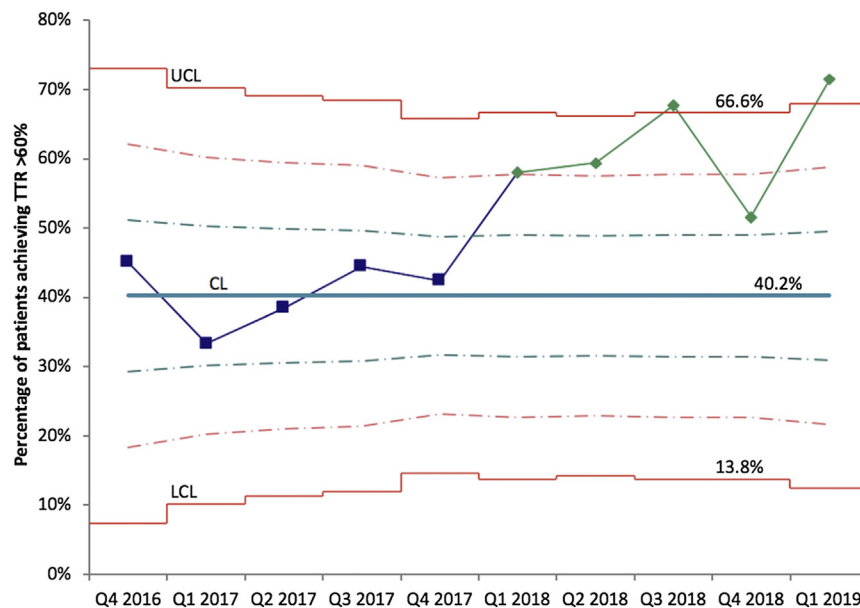
## Balancing Measure

Perceived prescriber satisfaction, as determined by anonymous electronic surveys sent to the 4 primary warfarin prescribers, increased as a result of our initiative: respondents reported they were either “very satisfied” or “a bit more satisfied” with their warfarin management in 2018 as compared with 2017. Respondents also provided positive feedback on our interventions, writing that their management was “more satisfying due to the report card of time in therapeutic range” and expressing that “uniform adoption of the algorithm available at the main desk would be very beneficial to all patients on warfarin.”

## DISCUSSION

An audit of TTR for warfarin achievement in our HD unit identified a significant quality gap. We subsequently developed a quality improvement program using an iterative audit-feedback report with the aim of improving TTR achievement at our hospital. The program was successful over a period of 12 months during which time the baseline mean  $\pm$  SD of 40%  $\pm$  5% improved significantly to a post-intervention mean  $\pm$  SD of 61%  $\pm$  8%.

The literature suggests a widespread problem of low TTR achievement among warfarin recipients in the HD population.<sup>7–11</sup> This is the first report to show improvement using a strategy of audit-feedback. In a prior report that examined strategies to improve warfarin control in HD patients, Lamontagne *et al.*<sup>8</sup> showed that uniform adoption of a warfarin dosing algorithm did not improve TTR but did reduce resource utilization. In another publication, Thomson *et al.*<sup>12</sup> showed that on-target anticoagulation was unchanged, but resource utilization was reduced, when local practice was shifted from physician-directed warfarin dosing to an electronic warfarin anticoagulation normogram implemented by HD nurses. In

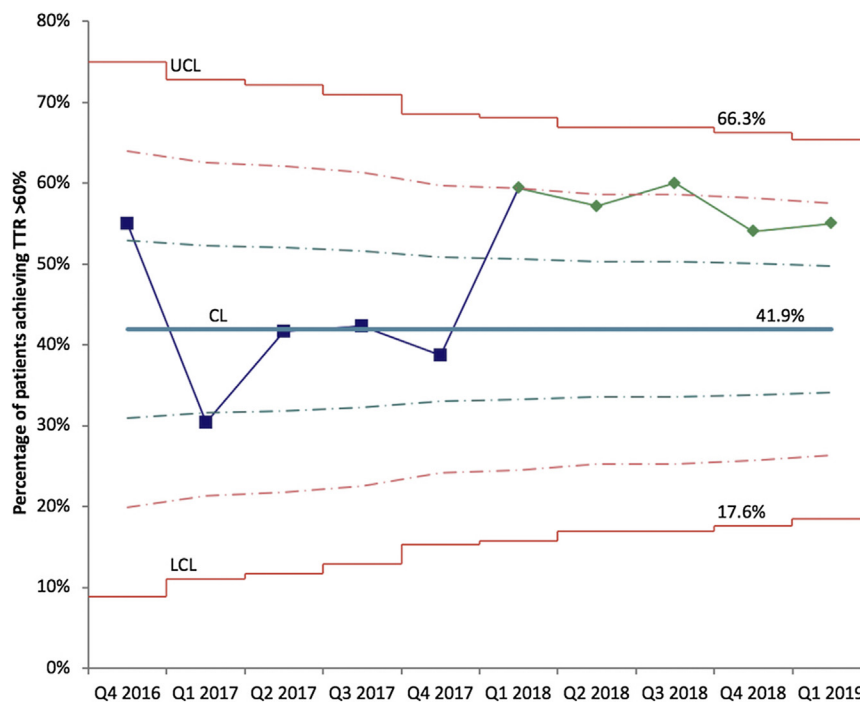


**Figure 1.** Percentage of hemodialysis patients prescribed chronic warfarin who achieved time in therapeutic range (TTR) >60%. Special cause variation is present in Q1 2018 through Q1 2019. CL, center line (mean); LCL, lower control limit (3 SDs below the mean); UCL, upper control limit (3 SDs above mean). Dashed blue lines represent 1 SD from the mean; dashed red lines represent 2 SDs from the mean.

contrast to these studies, our change strategy may have been successful because we used iterative plan-do-study-act cycles to target interventions to a series of root causes of poor TTR achievement in our local setting, rather than deploying a single intervention on warfarin dosing.

Strengths of our initiative included the use of a formal quality improvement approach with front-line engagement, consistent uptake of our interventions,

the incorporation of qualitative feedback into the intervention, and confirmation of our findings in prespecified additional analyses. We engaged all the key stakeholders in the warfarin prescription process by educating them about the deficiencies in the process and subsequently secured their complete commitment to the achievement of sustained improvement.



**Figure 2.** Percentage of hemodialysis patients prescribed chronic warfarin who achieved time in therapeutic range (TTR) >60% using broader inclusion criteria. Special cause variation is present in Q1 2018 through Q1 2019. CL, center line (mean); LCL, lower control limit (3 SDs below the mean); UCL, upper control limit (3 SDs above mean). Dashed blue lines represent 1 SD from the mean; dashed red lines represent 2 SDs from the mean.

Limitations of our initiative included the restriction to a single center and the relatively small number of warfarin recipients. Another limitation was that we could not verify adherence with some of the proposed strategies to improve TTR; specifically, we could not verify adherence to the C.A.R.E. warfarin dosing algorithm nor could we verify consistent provision of verbal and/or written reminders for patients. Finally, a larger study is needed to determine whether implementation of this initiative translates into a reduction in thromboembolic phenomena and/or a lower rate of bleeding.

In conclusion, we describe the implementation of a quality improvement initiative that led to a sustained improvement in the TTR for warfarin. Given the well-established relationship between TTR for warfarin and clinical outcomes, improving TTR achievement may translate into reduced bleeding risk and better protection against thrombosis. We encourage broader testing of our initiative to evaluate whether its adoption will affect clinical events.

## DISCLOSURE

All the authors declared no competing interests.

## SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

**Figure S1.** Most recently revised version of the time in therapeutic range (TTR) score report at St Michael's Hospital (SMH).

**Figure S2.** Percentage of hemodialysis patients prescribed chronic warfarin who achieve time in therapeutic range (TTR) >60%.

**Figure S3.** Results of the second additional analysis, a paired Student's *t* test.

**Supplementary Methods.** Specific methods for the second additional analysis.

SQUIRE 2.0 Checklist.

Supplementary File (Excel)

**Table S1.** Generation of time in therapeutic range.

## REFERENCES

- De Vriese AS, Caluwe R, Raggi P. The atrial fibrillation conundrum in dialysis patients. *Am Heart J*. 2016;174:111–119.
- Shah M, Tsadok MA, Jackevicius CA, et al. Warfarin use and the risk for stroke and bleeding in patients with atrial fibrillation undergoing dialysis. *Circulation*. 2014;129:1196–1203.
- Shen JI, Montez-Rath ME, Lenihan CR, et al. Outcomes after warfarin initiation in a cohort of hemodialysis patients with newly diagnosed atrial fibrillation. *Am J Kidney Dis*. 2015;66:677–688.
- Dahal K, Kunwar S, Rijal J, et al. Stroke, major bleeding, and mortality outcomes in warfarin users with atrial fibrillation and chronic kidney disease: a meta-analysis of observational studies. *Chest*. 2016;149:951–959.
- Harel Z, Chertow GM, Shah PS, et al. Warfarin and the risk of stroke and bleeding in patients with atrial fibrillation receiving dialysis: a systematic review and meta-analysis. *Can J Cardiol*. 2017;33:737–746.
- Connolly SJ, Pogue J, Eikelboom J, et al. Benefit of oral anticoagulant over antiplatelet therapy in atrial fibrillation depends on the quality of international normalized ratio control achieved by centers and countries as measured by time in therapeutic range. *Circulation*. 2008;118:2029–2037.
- Quinn LM, Richardson R, Cameron KJ, Battistella M. Evaluating time in therapeutic range for hemodialysis patients taking warfarin. *Clin Nephrol*. 2015;83:80–85.
- Lamontagne S, Basein T, Chang B, et al. A hemodialysis cohort study of protocol based anticoagulation management. *BMC Res Notes*. 2017;10:66.
- Genovesi S, Rossi E, Gallieni M, et al. Warfarin use, mortality, bleeding and stroke in haemodialysis patients with atrial fibrillation. *Nephrol Dial Transplant*. 2015;30:491–498.
- Yang F, Hellyer JA, Than C, et al. Warfarin utilization and anticoagulation control in patients with atrial fibrillation and chronic kidney disease. *Heart*. 2017;103:818–826.
- Bahbahani H, AlTurki A, Dawas A, Lipman ML. Warfarin anticoagulation in hemodialysis patients with atrial fibrillation: comparison of nephrologist-led and anticoagulation clinic-led management. *BMC Nephrol*. 2018;19:4.
- Thomson BK, MacRae JM, Barnieh L, et al. Evaluation of an electronic warfarin nomogram for anticoagulation of hemodialysis patients. *BMC Nephrol*. 2011;12:46.
- Rosendaal FR, Cannegieter SC, van der Meer FJ, et al. A method to determine the optimal intensity of oral anticoagulant therapy. *Thromb Haemost*. 1993;69:236–239.
- Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke. *JAMA*. 2001;285:2864–2870.
- Lip GY, Frison L, Halperin JL, et al. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation. *J Am Coll Cardiol*. 2011;57:173–180.
- C.A.R.E. Clinical Research Material. 2018. Available at: <http://careinternet.net/caregiver/warfarin.php>. Accessed October 4, 2019.
- Provost LP, Murray SK, eds. Chapter 3: understanding variation using run charts. In: *The Health Care Data Guide: Learning From Data for Improvement*. 1st ed. San Francisco, CA: John Wiley & Sons; 2011:67–106.
- Provost LP, Murray SK, eds. Chapter 4: learning from variation in data. In: *The Health Care Data Guide: Learning From Data for Improvement*. 1st ed. San Francisco, CA: John Wiley & Sons; 2011:107–148.
- Provost LP, Murray SK, eds. Chapter 5: understanding variation using Shewart charts. In: *The Health Care Data Guide: Learning From Data for Improvement*. 1st ed. San Francisco, CA: John Wiley & Sons; 2011:149–191.
- Wild CJ, Seber GAF. Chapter 13: Control charts. In: *Chance Encounters: A First Course in Data Analysis and Inference*. 1st ed. Wiley, 1999:1–32.
- Ogrinc G, Davies L, Goodman D, et al. SQUIRE 2.0 (Standards for Quality Improvement Reporting Excellence): revised publication guidelines from a detailed consensus process. *BMJ Qual Saf*. 2016;25:986–992.