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# EMPoWARed: Edmonton pediatric warfarin self-management study

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ABSTRACT

*Background:* Patient self-management (PSM) in adults is safer and more cost effective than conventional management. Warfarin is a narrow therapeutic index drug with individual patient response to changes and frequently a long-term therapy. Children and their families are proposed to be able to effectively manage their child's warfarin therapy. Increased health related quality of life is highly associated with effective therapy in patients with chronic conditions.
*Objectives:* The aim of this study is to evaluate the safety and efficacy of PSM over time including HRQOL and variables that may influence PFU success at PSM.
*Patients/methods:* Children and their family units (PFUs) current performing patient self-testing/monitoring for ≥3 months were enrolled in this cohort study. PFUs participated in comprehensive education on warfarin testing and management followed by an apprenticeship. Socio-demographic, clinical, and laboratory data were collected to evaluate safety and efficacy and health related quality of life. Outcomes were compared between the first 6 months on PSM (phase 1) and the last 6 months data collected on PSM (phase 2).
*Results:* Forty-two patients performed PSM for a median of 2.7 years (range: 1.1–6.2 years). Time in therapeutic range was 90% and 92.9% ($p = 0.30$) in phases 1 and 2 respectively. All measures were strongly associated with improved heath related quality of life. PFUs socio-demographic status did not influence success at PSM. All PFUs maintained warfarin knowledge and INR testing competency. Warfarin dosing decision errors median 0 (range: 0–5, $p = 0.73$) and a median 0 (range 0–4, $p = 0.55$) per patient in phases 1 and 2 respectively. There were no adverse hemorrhagic or thrombotic events.
*Conclusions:* Empowering PFUs to self-manage warfarin results in increased knowledge and understanding of their health condition, improved commitment to their health care and adherence to medication regimens and is demonstrated to be sustainable over time.



## 1. Introduction

Improvement in patient self-efficacy via self-management strategies are demonstrated to result in behavior change, improved health status and health related quality of life (HRQOL) [1]. Self-management is the day-to-day management of a chronic condition, which is typically lifelong and ever changing. Indefinite duration warfarin therapy is frequently prescribed in children with chronic illnesses. Successful warfarin management is complex, requiring frequent international normalized ratio (INR) testing and warfarin dose adjustments, resulting in increased burden for the child (patient) and family/caregiver (patient-family unit (PFU)). Increased burden is associated with decreased HRQOL, which affects adherence [2].

Patient self-testing (PST) (INR is performed using a coagulometer and reported to the health team who make the warfarin dose adjustment) is considered to be a safe and effective method of INR testing [3, 4]. Among adults, patient self-management (PSM) of warfarin is demonstrated to improve outcomes, including reduction in major hemorrhage and thromboembolic complications, increased time in therapeutic range (TTR) and patient satisfaction [5, 6]. Several small pediatric warfarin self-management studies have demonstrated results similar to adult studies [3, 7–18].

Warfarin self-management (PSM) involves the PFU performing an INR using a coagulometer and then adjusting their warfarin dose to achieve and maintain a target INR. The EMPoWarMENT pilot study [19] randomized children to PST versus PSM and demonstrated that PFUs could successfully self-manage warfarin (non-inferior TTR and significant patient preference). In addition, PFUs described confidence in their abilities to make decisions and develop behaviors to successfully manage their warfarin therapy. The success of the EMPoWarMENT

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[19] study mandated the opportunity for PSM to be available to all PFUs. However, the sustainability of warfarin safety and efficacy and influence on PFU HRQOL with PSM has not been evaluated.

## 2. Objectives

The aim of this study is to evaluate the safety, efficacy and sustainability of PSM over time and the influence of PSM on HRQOL.

The primary outcome is INR time in therapeutic range (TTR). Secondary outcomes are two-fold and include safety and efficacy and PSM influence on HRQOL.

## 3. Methods

All patient-family unit (PFU) self-testers on warfarin for ≥3 months, who were fluent in English and demonstrated adherence to INR testing without requiring reminders more than 50% of the time to perform an INR test, were eligible to participate in the study.

This prospective cohort study enrolled eligible patients who were followed in the KIDCLOT program between May, 2008 and May, 2012 and who provided informed consent. Data was collected until August, 2014. The KIDCLOT program is a dedicated anticoagulation program at Stollery Children's Hospital, Edmonton, Alberta, Canada. Within the KIDCLOT program, the use of point of care (POC) INR meters for INR testing is standard of care.

### *3.1. Standard KIDCLOT warfarin management — patient self-testing*

Children who are prescribed warfarin therapy for various indications participate in warfarin and coagulometer education [20] and are discharged home on warfarin performing PST. [13] The coagulometer used in the KIDCLOT program is the CoaguChek XS (Roche Diagnostics, Geneva Switzerland). PFUs report their INR and any changes in DIME (**D**iet, **I**llness, **M**edication changes or **E**rrors (such as missed dose)), to the KIDCLOT provider. The KIDCLOT provider then makes a warfarin dose decision and sets the next INR testing date. Based on the EMPoWarMENT pilot study results [9], including PFU feedback, the decision was made to provide the opportunity for eligible patients to participate in PSM.

### *3.2. Intervention — patient self-management*

1) Initiation: group education
   Within one year of warfarin initiation, PFUs attend a group anticoagulation clinic appointment where they participate in comprehensive warfarin education as the commencement of PSM. The interactive classroom session (approximately 1.5 h) is followed by a brief focused individual assessment to assess and address outstanding patient needs. The education presented is child focused, and encourages participation of both the child and the caregiver to develop warfarin knowledge. Topics include:
   - 'Warfarin' what is it and how does it work, including indications.
   - Influence of **DIME** (**D**iet, **I**llness, **M**edication, **E**rror (missed doses)) on warfarin.
   - Maintaining target INR and its relationship to safety and efficacy of warfarin.
   - Patient behaviors and safety related to warfarin therapy.
   - INR reporting.
   - Recognition, reporting and management of adverse events.

2) Warfarin dose adjustments and INR testing frequency using a standardized algorithm (Table 1). Practical knowledge is taught using case scenarios and dose calculations, enabling the PFU to apply their knowledge and problem solving skills to optimize decision-making for warfarin dose adjustments when deviations from the algorithm are reasonable (i.e. missed dose).
3) Evaluation of INR testing competency using the coagulometer
   - Direct observation of PFU performing a POC INR test using the coagulometer with laboratory/meter INR comparisons is performed to demonstrate PFU competency (proper technique to perform an INR test).

4) Introduction to the kidclot.com website for web-based INR reporting.
   - The KIDCLOT© website was established as a tool for INR reporting using a secure sockets layer (SSL) address, www.kidclot.com. PFUs enter INR results into the website via computer or smart-phone. This reporting method is efficient, easily accessible, time-friendly and engaging while providing the opportunity to report on influences on warfarin therapy (DIME). Each PFU is assigned a secure identification (ID) and password to log into the site where they will enter their INR, current warfarin dose, any changes to DIME or warfarin dose, and set the next INR date. Patient and administrative staff have different levels of access; therefore no patient has access to data outside of their own profile. This security is consistent with national health privacy policies [21, 22]. The website is set up to provide reminder and out of range alerts.

5) KIDCLOT PAC QL
   - Children > 8 years and caregivers complete the KIDCLOT PAC QL and the Parent Proxy KIDCLOT PAC QL, respectively.
   - The KIDCLOT PAC QL is a valid and reliable inventory to measure the impact of anticoagulation on PFUs [23]. The inventory reports the impact of warfarin on the participant's life; therefore a higher score indicates a lower QOL.

6) Knowledge evaluation
   - PFUs complete a 25 question validated [23, 24] questionnaire evaluating knowledge of warfarin and POC INR testing. A score of >80% is acceptable. Any incorrect responses are reviewed with the PFU prior to leaving clinic to ensure PFUs have the required knowledge to begin PSM.

7) Apprenticeship of patient self-management
   - PFUs participate in a 3-month apprenticeship in warfarin management. During the apprenticeship, INRs are reported to KIDCLOT, as in PST, however also entered on-line into www.KIDCLOT.com.
   - When the INR is performed and reported, PFU's discuss their warfarin dose decision and rationale with the KIDCLOT provider. This discussion facilitates further practical teaching and learning to facilitate additional knowledge transfer on personalizing the algorithm based on the PFUs knowledge of the patient's historical warfarin response.
   - Once the 3-month apprenticeship is completed, PFUs proceed with PSM with yearly follow up.

8) Independent PSM
   - Evaluation of adherence occurs by reviewing website entries at least monthly to estimate adherence with performing INRs at appropriate intervals. Warfarin dose decisions are reviewed giving consideration to factors influencing individualized dosing, including DIME, and the value of the following INR.
   - KIDCLOT remains available for INR support, with the requirement that PFUs contact KIDCLOT if the INR is <1.6 and ≥5.
   - Out of range INRs are reviewed by KIDCLOT to ensure the dose decision made is consistent with the education provided and the dosing algorithm.

**Table 1**
Warfarin maintenance dose algorithm.

| INR 1.5–2.0 | INR 2.0–3.0 | INR 2.5–3.5 | **D**iet | **I**llness | **M**edication change | **E**rror-missed | Warfarin dose adjustment |
|---|---|---|---|---|---|---|---|
| | 1.0–1.4 | 1.0–1.4 | | | | | Contact the KIDCLOT Service (call locating) |
| | | 1.5–1.8 | | | | | ↑20% |
| 1.0–1.4 | 1.5–1.9 | 1.9–2.5 | | | | | ↑10% |
| 1.5–2.4 | 2.0–3.0 | 2.5–3.5 | | | | | YAHOO! No change |
| | 3.1–4.0 | 3. 5–4.0 | | | | | ↓10% |
| 2.5–3.5 | 4.1–4.9 | 4.1–4.9 | | | | | Take one dose at 50% less than last dose. Then restart at 10% less than your previous daily dose |
| >3.6 | >5.0 | >5.0 | | | | | No bleeding. → Hold 1 dose. Contact your KIDCLOT doctor or nurse. Evaluate **DIME** |

If any bleeding contact your warfarin doctor or nurse.
If you are within 0.2 of your therapeutic range for the first time, continue the same dose and recheck your INR in one week.

9) Patient self-management: yearly follow-up
In subsequent years following PSM initiation, PFUs participate in focus groups, complete the KIDCLOT PAC QL, website satisfaction questionnaire and knowledge questionnaire.

- Focus groups
Focus groups are held during group anticoagulation clinics to ensure patients have the opportunity to express their values, perceptions, concerns, and preferences. Eight open-ended questions are used to stimulate discussion from the participants. For example, "what are some positive things about PSM?" and "what are some concerns or fears of PSM?". Five research associates circulate during the focus group to clarify the question stems, further stimulate discussion and record responses. A wrap up question is used to explore any additional missing information. The responses from the focus groups are grouped into themes (categories) by two independent researchers and collated.
- KIDCLOT PAC QL
- Knowledge questionnaire that includes six questions such as "is the website easy to use?", "does using the website assist you to better manage your warfarin?", and "what is your preference for INR reporting — diary, phone, email, website?" In addition, there is a general comment section. Scores are reported as a mean score.
- Socioeconomic questionnaire that consists of 5 questions about the PFU's home setting including highest education level, income category, number of adults, and number of children.
- Direct observation of POC INR test to confirm competent technique.
- Individual clinic assessment that provides opportunity for discussion of patient-sensitive issues in addition to providing prescriptions for the following year.
For the purposes of this analysis, outcomes were compared between the first 6 months on independent PSM (phase 1) and the last 6 months of data collected on PSM (phase 2). Safety and efficacy were assessed by TTR, frequency of INR testing, adherence to the dosing algorithm (warfarin dose decision-making and INR retest date), warfarin knowledge scores, testing competency, total number of INRs (overall, <1.6 or ≥5), number of calls to KIDCLOT for support, and adverse events (major bleeding and thrombosis). Major bleeding events were defined as those requiring an emergency visit or admission to hospital. A thrombotic event was defined as any objectively confirmed thrombosis. HRQOL was measured using the PAC QL [24] and data from the focus groups. In addition, socio-demographic information and characteristics that may influence success at performing PSM were assessed, including highest family educational level, family income and number of children and adults in the home.

Data from patients requiring warfarin interruption for planned procedures was excluded from the analysis from time of initiation of warfarin reversal until return to target INR range. During this period, the KIDCLOT provider managed INRs. The University of Alberta Health Research Ethics Board approved this study.

## 4. Statistical analysis

The patients' and their families' baseline characteristics are reported descriptively. The TTR for each group and study phase was estimated using linear interpolation [25] between INR values. Outcomes were compared using paired t-test, Wilcoxon signed-rank test, or Kruskal–Wallis test as appropriate. A p value $< 0.05$ was considered statistically significant. Stata/SE 13 (Stata Corp, College Station, TX) was used for the statistical analysis.

## 5. Results

There were a total of 77 patients enrolled in the study from June, 2008 to August, 2014; 16 patients who were on PSM < 1 year and 19 patients who were young adults were excluded. The remaining 42 patients are reported in this study (see Tables 2 and 3). Median age at study enrollment was 6.0 years (range: 1.1–16.2). Baseline statistics and comparisons between the two study periods are reported in Tables 2 and 3, respectively. PFUs performed PSM for a median of 2.7 years (range: 1.1–6.2).

1) Time in therapeutic range
There was no statistically significant difference in median TTR between phase 1 (90.0%, range: 32.4–100) and phase 2 (92.9%, range: 12.0–100) ($p = 0.30$).
2) Frequency of INR testing
There was a statistically significant decrease in the median number of INR tests performed between phases 1 and 2; from 18.0 (frequency every 10.0 days) to 10.5 (frequency every 17.1 days) ($p < 0.0001$), respectively.

**Table 2**
Demographic data.

| | | |
|---|---|---|
| Median age | 6.0 years (range: 1.1–16.2) | |
| Median time on PSM | 2.7 years (range: 1–6.2) | |
| Diagnosis | N= | % |
| CHD | 30 | 72% |
| AHD | 6 | 14% |
| Other | 6 | 14% |
| **Indication for anticoagulation** | N= | % |
| Mechanical valve | 15 | 36% |
| Fontan | 15 | 36% |
| AHD | 4 | 9% |
| DVT/PE | 5 | 12% |
| Stroke | 3 | 7% |
| Discontinuation of warfarin | N= | |
| Transferred | 1 | 2% |
| Deceased | 5 | 12% |

**Table 3**
Outcome measures (median).

| | Phase 1 first 6 months | Phase 2 last 6 months | p |
|---|---|---|---|
| TTR | 90 | 92.9 | 0.30 |
| Knowledge score | 92 | 92 | 0.55 |
| Number of INR tests within 6 month period | 18 (every 10 days) | 10.5 (every 17 days) | <0.0001 |
| INR ≥ 5 | 0 (range: 0–2) | 0 (range: 0–2) | 0.16 |
| INRs < 1.6 | 1 (range: 0–7) | 0 (range: 0–2) | <0.0001 |
| Errors | 0 (range: 0–11) | 0 (range: 0–5) | 0.55 |
| Number of calls to KIDCLOT for support | O (range: 0–5) | 0 (range: 0–11) | 0.73 |

3) Warfarin dose decisions/adherence

- Warfarin dose decisions resulted in a median of 0 INRs ≥ 5 (range: 0–2, p = 0.16) in both phases; and a median of 1 INR ≤ 1.6 (range: 0–7) and 0 (range: 0–2) (p < 0.0001) per patient in phases 1 and 2, respectively.
- Frequency of INR test errors was a median of 0 (range: 0–5) (p = 0.73), and 0 (range: 0–4) (p = 0.55) per patient in phases 1 and 2, respectively.
- Calls for support were a median of 0 (range: 0–11) and 0 (range: 0–10) (p = 0.55) per patient in phases 1 and 2, respectively.

4) Adverse events
There were no clinically relevant adverse hemorrhagic or thrombotic events. No patient deaths were related to anticoagulation.

5) Focus groups
PFU comments reflected patient preference for PSM and overall improved warfarin related HRQOL following an initial period of anxiety. Focus group responses are grouped according to themes and presented in Table 4.

6) KIDCLOT PAC QL
A total of 39 and 18 KIDCLOT PAC QL© inventories of parent proxies and children/teens, respectively (pre- and post-PSM) were collected over the study period (total available for analysis with pre-/post-inventories). There was a significant difference in the mean scores for parent-proxy pre-PSM (29.28, SD: 12.4) and post-PSM (21.22, SD: 9.6) conditions (p = 0.002). Similarly, there was significant difference in the scores for children/teens pre-PSM (29.22, SD: 8.9) and post-PSM (19, SD: 10.7) (p = 0.001).

7) Knowledge evaluation and review of incorrect responses
Parents retained their knowledge of warfarin and INR testing over time with median knowledge scores of 92 (range: 88–100) and 92 (range: 88–100) (p = 0.54) in phases 1 and 2, respectively.

8) KIDCLOT website questionnaire
38 of 42 website users responded to the satisfaction survey. Results from the patient satisfaction survey found that 100% of respondents "liked" the website format, found it easy to use, convenient, and preferred the website to any other method of INR reporting. Ninety-five percent of patients reported that it assisted them to better manage their warfarin through INR alerts and ease of reporting. Patients reported the website to be a 'great improvement', 'the best thing ever' and 'outstanding' for INR reporting. Patients valued the ability to enter personal notes, and resource materials available on the website, and continued to feel supported by the KIDCLOT health care team. The KIDCLOT© health providers found the website to be an effective and efficient method for monitoring VKA therapy and for quality control for patients and health providers.

9) Assessment of POC INR testing competency
All patients were observed to be competent in INR testing on yearly assessments using the coagulometer.

**Table 4**
Focus group responses.

| | |
|---|---|
| Communication | "Able to call when INR off"; "if there is a concern — test INR call KIDCLOT" |
| | "It has become my responsibility as a patient to look after all of my own warfarin treatments such as communicating with INR doctor/nurse" |
| | "Way better than calling" |
| | "Inspires cooperation between us" |
| | "Schedule INR tests on calendar and educate parents/friends — related to ensuring child takes warfarin" |
| | "I do miss reminders to do the test, especially when we are so busy all the time" |
| | "Increases communication with parents and others regarding changes in diet, sickness, etc." |
| | "Still always have support if needed so takes the pressure off" |
| Relationships/emotional responses | "Fear of giving child power" |
| | "We become closer"; "more closer" |
| | "It has affected [relationships]. My friends have become more aware I am on warfarin" |
| | "Sometimes grumpy in the morning when having to test INR" |
| | "Shared responsibility for managing health" |
| | "Become more worried when INR was too low or high" |
| | "Anxiety about wrong dose" |
| | "Stressful at first because its new then settled in" |
| Autonomy | "Able to make decisions based on guidelines — knowing why INR level changes based on guidelines" |
| | "More empowered" |
| | "I like doing it for the knowledge. We haven't had to adjust more than once. So we still feel a little inexperienced" |
| | "XX is also more aware of where his range is and why he may need testing more often" |
| | "Everybody has a little more info" |
| | "It hasn't altered anything but just made everyone more aware" |
| | "Always become more altered when my INR was out of range, so it caused more stress" |
| | "XX has to do most of the testing by himself" |
| Lifestyle | "It is a good experience because it makes things more simpler" |
| | "Flexibility to work within your lifestyle"; "flexibility of testing"; "convenient and flexible" |
| | "Fear on how to transfer care when adult" |
| | "I preferred when Stollery pediatric thrombosis did the testing. Being a single parent working full time has made it difficult" |
| | "At first didn't think I would want to, I thought XX would want the protection of thrombosis (program), but it worked out well" |
| | "Not tied to hospital" |
| | "Way better for rural families" |
| | "Would not want to do it any other way"; "don't want PST" |
| | "Graduate into it" |
| | "Part of our routine" |
| | "It is a good experience because it makes things more simpler" |
| | "No disruptions" |
| Technology | "Technology an asset" |
| | "Computer entry — best system" |
| | "Having a POC machine is much easier than the lab"; "don't have to go to the lab" |
| | "Less trips to the hospital for testing. Her fear of getting needles has decreased" |
| | "Website — really beneficial" |
| | "Easy to monitor" |
| | "Hard to get strips. When they arrive they are almost expired. Expensive. Not using 24 strips a year"; "test strips expire too soon" |

10) Socio-economic influence on PSM
TTR did not differ across household income (Table 5) in either study phase. However, TTR did differ across education categories with families with higher household education having a larger

**Table 5**
Time in therapeutic range (TTR) by sociodemographic characteristics and study phase. Values are presented as median (range).

| | N | % time in therapeutic range (median, range) | | | p value* |
|---|---|---|---|---|---|
| | | Phase 1 | Phase 2 | Within-patient difference | |
| Family income [CAN$] | | | | | 0.37 |
| <30,000 | 4 | 96.7 (32.4, 100) | 85.8 (12, 100) | 3.3 (−88.0, 39.2) | |
| 30,000–60,000 | 6 | 84.4 (61.5, 100) | 97.3 (58.5, 100) | 7.0 (−23.3, 24.4) | |
| ≥60,000 | 23 | 87.3 (66.2, 98.5) | 95.1 (62.8, 100) | 7.3 (−29.5, 31.6) | |
| Not reported | 9 | 92.4 (79.6, 100) | 86.3 (61.7, 100) | −4.4 (−38.3, 20.4) | |
| Highest parental level of education | | | | | 0.03 |
| ≤Grade 8 | 3 | 93.5 (85.1, 100) | 77.0 (12.0, 100) | −8.0 (−88.0, 6.5) | |
| Grade 9 | 9 | 92.4 (32.4, 100) | 91.8 (58.5, 100) | 0 (−29.5, 39.2) | |
| Secondary school | 11 | 84.0 (61.5, 92.7) | 97.8 (65.6, 100) | 7.3 (−12.6, 31.6) | |
| University or college | 8 | 84.0 (75.6, 98.5) | 94.5 (86.9, 100) | 10.4 (−8.4, 24.4) | |
| Post-graduate | 4 | 82.0 (78.9, 100) | 98.6 (90.7, 100) | 12.4 (0, 20.4) | |
| Not reported | 7 | 92.7 (83.6, 100) | 79.2 (61.7, 100) | −12.0 (−38.3, 7.6) | |

* p values are for the difference in median TTR across categories.

increase in TTR from phase 1 to phase 2 compared to lower household education.

11) Individual clinic assessments were a mean of 7 min, as most patient questions had been addressed in the large group education session.

## 6. Discussion

PSM and PST in adults have been demonstrated to be safer than conventional management and are associated with consistently lower rates of thromboembolism [25–27]. This is the first study to evaluate the practicality and sustainability of warfarin PSM and demonstrates PSM to be a sustainable, safe and effective strategy for optimal warfarin management with increased HRQOL in children. Adherence, as defined in this study, through review of website entries, TTR as a reflection of dosing decisions and INR testing was greater than the norm for patients with chronic conditions [28].

Time in therapeutic range has been demonstrated to be the principle determinant of safety and efficacy of warfarin therapy [6]. Within this study, the TTR was stable at greater than or equal to 90% with no adverse events, demonstrating safe and effective warfarin therapy. Notably, one participant had a reported TTR of 12%, however on clinical assessment, by reviewing INR values in the memory of the coagulometer, it was apparent that the PFU had completed INRs and appropriately dose adjusted. The parent of the child stated that they felt it was unnecessary to report INRs, given their knowledge and experience related to their child receiving warfarin 10 years prior to entering into study.

Frequency of INR testing significantly decreased from 10 days to 17.1 days over the study period, which reflects PFU confidence in their warfarin knowledge and management.

mHealth technology describes the use of mobile devices for the collection and distribution of health data, remote delivery of care, and near real-time monitoring of patients and is transforming health delivery [29, 30]. PFUs valued the ability to enter personal notes, access to resource materials, and continued to feel supported by the KIDCLOT team. The KIDCLOT health providers found the website to be an effective and efficient method for supervising warfarin therapy. Written diary logs were available for PFUs without internet access, although all participants used the website.

PFUs (parents and children ≥ 8 years of age) independently completed the validated KIDCLOT knowledge retention test to ensure children and their caregivers' sustained adequate knowledge about their warfarin therapy. Theoretical knowledge was sustained with knowledge scores 91%. Significantly, within the classroom setting, PFUs would report increased knowledge and understanding of warfarin use in their child; however, given the structure of the test, practical knowledge that PFUs developed over time could not be captured. In addition, PFUs maintained competent INR testing technique and by 10 years of age, the child learned the skill of POC INR testing with proper technique. Warfarin is a narrow therapeutic index drug with individual patient response to changes [31]. Parents know their child best and have had an opportunity to increase their theoretical and practical knowledge over time; facilitating individualized dosing. Consequently, PFUs are encouraged to apply their knowledge and experience when making warfarin dose changes that may best reflect their child's response to warfarin. These dose adjustments may vary from the algorithm and thus PFUs report their rationale for their decision. Success of PSM may be related to household education level with decreased TTR over time in ≤Grade 8 education level. Further studies are needed to confirm this finding.

Quality of life (QOL) is the individual's perception of their position in life in the context of culture and value systems in which they live, and in relation to their goals, expectations standards and concerns [2]. Health related QOL (HRQOL) describes the influence of health and medical management on an individual's QOL and is the most influential factor in patient adherence when medical therapies are equal in safety and efficacy. Increased HRQOL is highly associated with effective therapy in patients with chronic conditions and is increased when patients participate in their health management [32–34]. Assessment of HRQOL is essential to develop appropriate therapeutic choices, generate research strategies, and adjust policies for improvement of healthcare adherence and outcomes. HRQOL is suggested to be the “gold-standard” measurement for patient relevant outcomes [35]. There was both a statistically significant improvement of HRQOL on children/teens and parent proxy measurements as well as a qualitative reported improvement for PFU's in terms of their warfarin management while on PSM. Focus groups revealed that although caregivers felt anxiety about the increased responsibility in managing their child's warfarin, a strong preference for PSM existed. One family decided to leave PSM due to anxiety but then returned to PSM practice after a few months, as PST was less flexible. Overall, PFU's preferred PSM over PST, felt empowered, engaged, there was an increased sense of freedom and investment in warfarin management and the burden of warfarin on participants lives declined. A previous study by Jones et al. [15] demonstrated that home INR testing (PST) improved HRQOL.

PSM better equips adolescents for transition to adult care. Self management of a chronic condition requires executive functioning (problem solving, planning and organizational skills) [36]. The brain develops from infancy through to young adulthood with executive functioning being the last to mature [37]. Better executive functioning is associated with better adherence behaviors [1]. PSM facilitates the early development of executive functioning skills related to warfarin therapy. Health team/parental mentoring, repetitive practice, problem solving, planning, organizational skills, and consequences of behaviors (missed doses) is practiced such that it becomes second nature; almost like the activities of daily living [33, 34, 38]. Within this study, 19 adolescents

participated and were transitioned seamlessly to adult care. These results will be reported separately.

This study is the first to evaluate the sustainability of PSM in the pediatric population and the first to examine HRQOL in pediatric PSM. Similarly, McCahon et al. [39] demonstrated improved QOL in adult self-management patients in comparison to controls. However, this study was unable to fully measure the growth of practical warfarin knowledge and improvement in self-efficacy that PFUs described during and at study closure. Although the assessments were numerous within this study, the interventions were to ensure a comprehensive evaluation of safety and sustainability of all patient important factors. When implementing warfarin PSM in the clinical setting, the important aspects to implement include educating PFUs, apprenticeship of PFUs and competency/proficiency assessment yearly.

Patient self-management is the most cost-effective option and should be offered to patients when feasible [40]. The costs associated with PST, including coagulometer, have been reported to be significantly less than laboratory monitoring over time [41]. Although no formal cost analysis was performed, with PSM there are further significant savings to the health care system as demonstrated in this study. One percent of INRs performed per patient per year enlisted health team support to the PFU resulting in substantial health cost savings per year while maintaining warfarin safety and efficacy [40].

Although the new direct oral anticoagulants (DOACs) are becoming increasingly used in adults, warfarin will currently remain the anticoagulant of choice for many patients [42]. Disadvantages that may preclude use of DOACs include lack of reversibility, cost, and absence of estimates of safety and efficacy in children [43]. As a result, warfarin continues to be the recommended oral anticoagulant in children [44].

This study was not without limitations. The relatively small sample size is reflective of the pediatric population. In addition, an experienced anticoagulation service to provide teaching and support was integral to the PSM approach in this study. The duration of follow-up varied from 1–6 years, given that PFUs were enrolled year 1 through 5.

## 7. Conclusions

Warfarin therapy in children is a chronic burden, which can persist throughout their lifetime. Interventions to improve self-efficacy are needed to create behavior change and improve health status and are both effective and sustainable. Empowering patients and their families to self manage warfarin results in increased knowledge and understanding of their health condition, improved commitment in their health care, adherence to medication regimens, and HRQOL Patient self-management supported by an experienced comprehensive anticoagulation program [45] is strongly recommended in appropriate patients.

## Role of authors

M.E. Bauman was responsible for the concept and design, analysis and interpretation of data, critical writing, revising intellectual content and final approval of the manuscript. M.P. Massicotte was responsible for concept and design, critical writing, revising intellectual content and final approval of the manuscript. S. Kuhle was responsible for analysis and interpretation of data, critical writing, revising intellectual content and final approval of the manuscript. S. Siddons was responsible for final approval of the manuscript. A. Bruce was responsible for critical writing, revising intellectual content and final approval of the manuscript.

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