

Validation of a *de novo* Paediatric Warfarin Nomogram



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BACKGROUND

Warfarin therapy in children is impacted by many variables, including diet and concurrent illness⁽¹⁻⁴⁾. The development of specialist paediatric anticoagulation clinics has led to an increased focus on enabling families to take on a more active role in their child's warfarin therapy through patient self-testing and patient self-management (PSM)^(1,2). PSM involves families undertaking an INR test with a point of care device and altering the child's warfarin dose to maintain their INR within their target therapeutic range. To support the implementation of a PSM program within a paediatric anticoagulation service, a paediatric-specific warfarin nomogram was needed. A literature review revealed no published paediatric nomograms therefore a nomogram was developed drawing upon the hospital's Warfarin Information for Clinicians evidence-based guideline. This study aimed to validate a *de novo* pediatric warfarin nomogram (Figure 1).

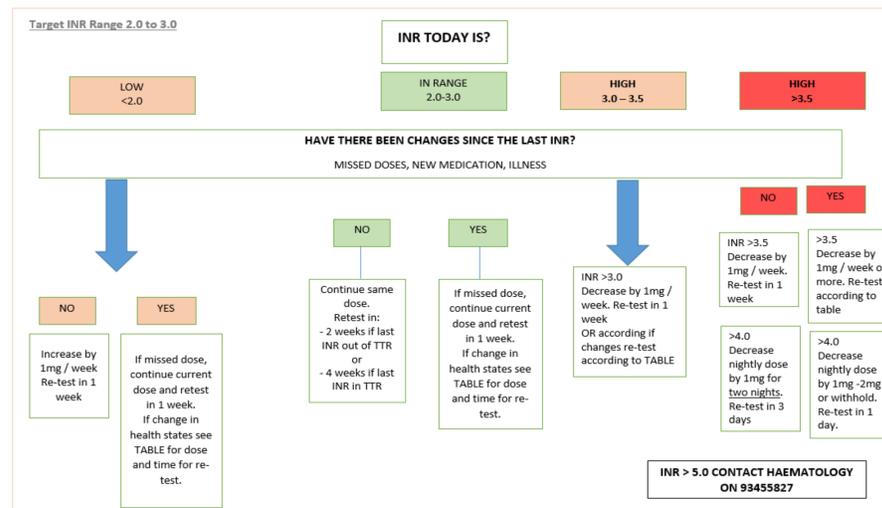


Figure 1: Example of warfarin nomogram for Target INR range 2.0-3.0

METHOD

A retrospective audit of electronic medical records compared the dosing and INR retest decisions made by haematology clinicians to the dosing and INR retesting recommended by a *de novo* warfarin nomogram at a tertiary pediatric hospital. Children (aged six months-18 years) on warfarin therapy for longer than six months were included. Data was collected between September 2019 and February 2020. A level of agreement of greater than 75% was expected between the clinician decisions and the recommendation of the nomogram (warfarin dose and INR retest date) to deem the nomogram reliable. Descriptive data analysis was performed and percentage of INRs within participants' target INR range was presented using cluster analysis. The study was approved by the hospital human research ethics committee (QA/60343/RCHM-2020).

RESULTS

Warfarin dosing and INR retest decisions made by haematology clinicians for 39 children were included. Missing data resulted in 517 warfarin dosing decisions and 441 INR retest dates that could be compared to the nomogram. Table 1 summarises participants' demographics and target INR achievement. The nomogram matched 81.4% (n=421) of dosing decisions (Figure 2) and 30% (n=132) of INR retest decisions. Clinicians suggested an earlier time to retest the INR compared to the nomogram (Figure 3). The nomogram recommendation matched to more clinician's warfarin dosing and INR retest recommendations when participants had a greater percentage of their INR results within their target therapeutic range.

Table 1: Demographic characteristics of participants

Variable	Participants (n= 39)
Median age (range)	10.6 (2.1-18.4)
Time on warfarin, median (range), years	5.5 (0.5 -14.9)
Indication, number (%)	
Fontan procedure	20 (51.3)
Prosthetic valve	8 (20.5)
Central venous catheter	5 (12.8)
Kawasaki disease	3 (7.7)
Other	3 (7.7)
Target therapeutic range, number (%)	
1.5-2.0	2 (5.1)
2.0-2.5	1 (2.6)
2.0-3.0	26 (66.7)
2.5-3.5	7 (17.9)
3.5-4.0	3 (7.7)
Number of INR tests per patient, median (range)	12 (2 - 50)
Percentage of all INRs in Therapeutic range	N=521 319 (61.2%)
Time in Therapeutic Range per patient, median % (range)*	N=38 65.9% (30-100%)

* Cluster analysis per patient

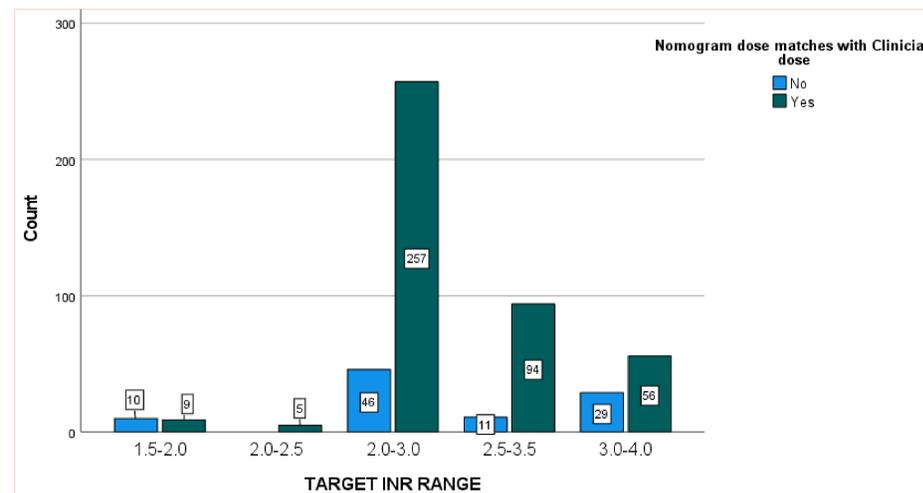


Figure 2: Agreement between clinician warfarin dose and nomogram recommended warfarin dose.

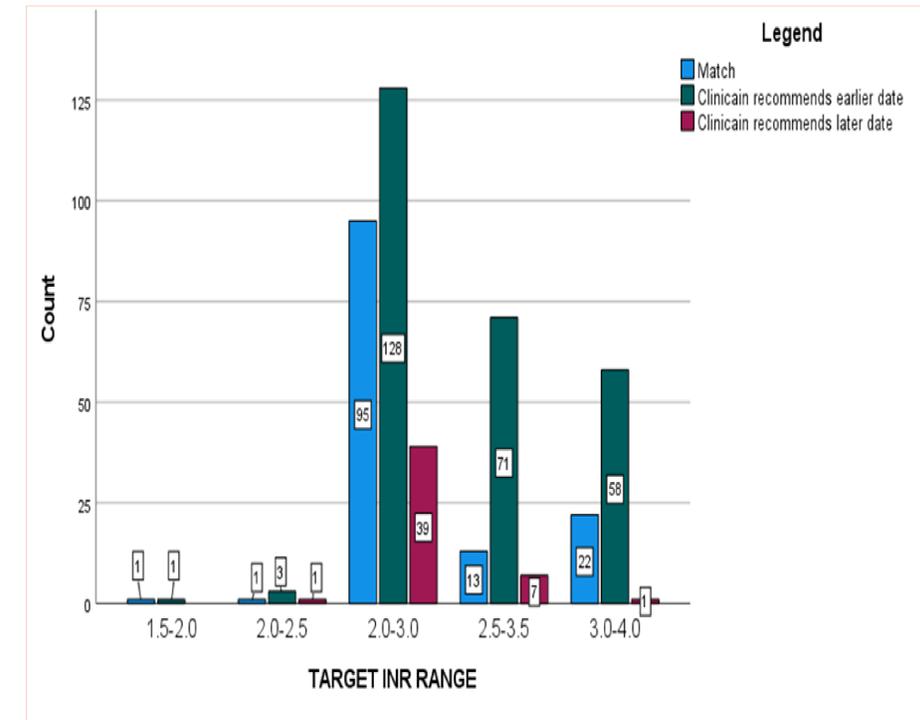


Figure 3: Agreement between clinician warfarin date of INR retest and nomogram recommended date of INR retest.

CONCLUSIONS

- The important findings of this study demonstrate that this *de novo* paediatric warfarin nomogram is valid as indicated by agreement with specialised clinician warfarin dosing.
- Dosing decisions and INR retesting recommendations from the nomogram most accurately matched clinician decisions when the INR was in target range.
- Ongoing validation of the nomogram should be carried out to further refine the recommendations for INR retesting based on the many factors influencing warfarin stability in children.
- The availability of a warfarin nomogram is crucial to support children and families to self-manage their warfarin but may also be an important resource for clinicians practicing outside of specialised anticoagulation clinics or those with less experience in warfarin dosing in complex paediatric patients.

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