Inherited thrombophilia testing in a large tertiary hospital in New Zealand: implementation of a Choosing Wisely protocol to reduce unnecessary testing and costs

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ABSTRACT

AIM: To evaluate the practice of inherited thrombophilia testing at Waikato Hospital Laboratory, benchmarked against the British Society of Haematology (BSH) guidelines with the plan to reduce unnecessary testing.

METHODS: We retrospectively reviewed data on all inherited thrombophilia tests performed in the Waikato Hospital Laboratory during August 2015. We then established a local Choosing Wisely guideline for testing. A clinical and laboratory programme was developed to facilitate the implementation of this guideline. Ordering practices were re-evaluated six months after the implementation of the Choosing Wisely programme.

RESULTS: Of the 94 requests received in August 2015, only one complied with BSH guidelines. Most abnormal results did not change the clinical management of patients. In the first six months following the implementation of our intervention, there was a significant reduction of tests performed with an estimated savings of $118,000.

CONCLUSIONS: The majority of inherited thrombophilia tests performed in our laboratory did not comply with BSH guidelines. A multimodal inherited thrombophilia Choosing Wisely programme was successful in reducing unnecessary testing. A laboratory protocol that required screening of every inherited thrombophilia request by a haematologist was necessary for the success of this programme.

Venous thromboembolism (VTE) represents a significant cause of morbidity and mortality in New Zealand.[1] Inherited thrombophilia is associated with an increased risk of VTE. The most common inherited thrombophilias include deficiencies in naturally occurring anticoagulants such as antithrombin (AT), protein C (PC) and protein S (PS) as well as gene polymorphisms for factor V Leiden (FVL) and prothrombin gene, G20210A (PGM).[2–4] These are all included in the inherited thrombophilia screening panel at Waikato Hospital Laboratory in Hamilton, New Zealand. However, testing for an inherited thrombophilia is controversial.

There is little evidence demonstrating the clinical utility of inherited thrombophilia testing in the majority of patients with a VTE.[5–7] Testing does not reduce the recurrence of venous thrombosis.[8–10] Also, if testing is performed in unselected patients at the incorrect time, you run the risk of attaining false-positive results.

Some inherited thrombophilia assays are affected by medications, acute thrombosis, pregnancy and liver failure. False-positive results can lead to overtreatment, complications from unnecessary treatment and the social, psychological and financial costs that arise from being labelled with an incorrect diagnosis. Testing patterns both internationally and nationally are renowned for being indiscriminate and reflect a lack of awareness of the futility of testing and the risk of harm arising from testing in unselected patients.[8,11–14]

Many guidelines have been published to reduce unselective testing. The British Society for Haematology (formerly British Committee for the Society of Haematology BCSH) has produced the most comprehensive restrictive guidelines that recommend testing in a few selected cases and only when the results will change clinical management.[7] Other guidelines include the American Society of Haematology (ASH) Choosing Wisely,[15] American College of Chest Physicians,[16] NICE guidelines[17] and National Laboratory guidelines in New Zealand.[18]

The National Laboratory guidelines for inherited thrombophilia testing was employed at Waikato Hospital prior to this study. An automatic laboratory reflex was implemented in 2005 that prevented repeat molecular testing for FVL and PGM. All other inherited thrombophilia screening tests, both initial and repeat requests were performed without a formal review of clinical indications for testing and compliance with the laboratory guideline.

Waikato Hospital Laboratory serves a large geographic catchment area with a population of approximately 765,500 people. The Hospital haemostasis laboratory draws requests from the hospital and community laboratories in Hamilton, Thames, Coromandel, Tauranga, Rotorua, Tokoroa, Te Kuiti, Taumarunui and Taupo. Approximately 1,200 inherited thrombophilia tests were being performed annually. In 2015–2016, a Choosing Wisely programme for laboratory testing was developed at Waikato Hospital. Inherited thrombophilia testing is on the 'Choosing Wisely' list endorsed by many speciality societies, including the American Society for Haematology.[15]

This study aimed to assess inherited thrombophilia testing practice at Waikato Hospital Laboratory and benchmark this against BSH guidelines. We aimed to reduce indiscriminate testing in our laboratory by implementing a multimodal inherited thrombophilia Choosing Wisely programme for hospital and community clinicians. Requesting and testing patterns were reassessed after implementation of the programme.

Methodology

Study design and data sources

We retrospectively reviewed all inherited thrombophilia tests performed at Waikato Hospital Laboratory during August 2015.

We assessed an electronic version of the original request form to identify clinical details provided, such as indications for testing and requestor details. We then extracted data such as patient age, gender, inherited thrombophilia tests requested and results of tests from the electronic medical records. If clinical details were lacking on the request form, clinical notes were reviewed, or the requestor was contacted to assess indication and eligibility for testing. When possible, a written note review was performed to gather further clinical data. Microsoft Excel 2008 was utilised to record and collate data.

Assessing the appropriateness of requests

The BSH inherited thrombophilia testing guideline was the standard against which this audit was undertaken (Table 1).[7]

The clinical utility of an abnormal result was defined as an abnormal result that changed clinical management, such as duration of anticoagulation or thromboprophylaxis. Costs associated with unnecessary inherited thrombophilia testing were calculated based on the cost of all tests performed that did not meet BSH criteria for testing in one month. The cost of a screening panel for inherited thrombophilia testing at Waikato hospital laboratory is $247.

A multimodal intervention was designed and implemented to reduce inappropriate testing. The intervention included establishing a local inherited thrombophilia Choosing Wisely guideline in collaboration

Table 1: BSH criteria for inherited thrombophilia testing.

Testing Indicated in the following clinical contexts: (level of evidence)	Testing MAY be indicated in the following clinical contexts: (level of evidence)
Neonates and children with purpura fulminans should be tested for protein C and protein S deficiency (1B).	Case finding of asymptomatic relatives with high-risk thrombophilia, such as antithrombin, protein C or protein S in thrombosis-prone families (1B).
Patients with skin necrosis in association with Vit K antagonists should be tested for protein S and protein C deficiency (2B)	Asymptomatic pregnant women with a strong first-degree family history of unprovoked VTE or VTE provoked by pregnancy or combined oral contraception exposure or a minor risk factor (2C). (indication for testing would increase if the first-degree relative had a known thrombophilia)
Patients with VTE and <40yrs old and must have a history of thrombosis-prone family members (>2) (C).	

with the Waikato Hospital Laboratory and Waikato Hospital Departments of Haematology, General Medicine, Obstetrics and Neurology. The BSH, National Laboratory Test Referral and RCOG Green-top guidelines[7,18,19] along with the guiding principles of 'Choosing Wisely' and outcomes from meetings with the above stakeholders influenced the final guideline design (Tables 2 and 3). Testing for patients with obstetric indications continued as there were large randomised control trials underway.

Communication with key stakeholders in the hospital was vital for organisational and clinician buy-in for the new testing protocol. The findings from the first phase of our study were presented at the Waikato Hospital medical presentations and grand round. The new guidelines were then disseminated to all general practitioners in our region, informing them of the need for testing in selective patients and the implementation for the new testing protocol in July 2016 (See supplementary article).

Table 2: Waikato Hematology Laboratory criteria for inherited thrombophilia testing, 2016.

• Idiopathic venous thromboembolism in young patients (<45 years).
• Warfarin-induced skin necrosis (patients should be tested for protein C deficiency and protein S deficiency one month after stopping vitamin K antagonist therapy if this can safely be discontinued).
• Children presenting with purpura fulminans (test for protein C and protein S deficiency).
• Siblings of patients with homozygous FVL, homozygous PT20210A or compound heterozygotes for these mutations.
• Thrombosis in unusual sites (eg, cerebral, mesenteric, portal). Cryptogenic stroke in the young (<50yrs) will be performed after exclusion of other causes.
• Recurrent miscarriage, IUGR, IUD.
In all other situations, testing should only be undertaken after consultation with a haematologist or as part of a clinical trial.

Table 3: Waikato Haematology Laboratory Guidelines for inherited thrombophilia testing, 2016.

• Request forms MUST provide clinical details of which criteria for testing the patient meets, or the sample will not be tested. The sample will be held for 14 days and will be tested if the requesting clinician subsequently provides appropriate clinical details.
• In the absence of meeting one of the testing criteria and testing is still thought to be appropriate, the requestor must discuss with a clinical haematologist and requestor name clearly identified on the request form along with clinical details.
• Where low levels of antithrombin III, protein C or S are found, a repeat sample will be requested to confirm the abnormal finding.
• Patients will only be tested for FVL and prothrombin gene mutation once in their lifetime. **Context and timing of tests :**
Wherever possible, thrombophilia testing should be avoided in the following settings as one or more of the laboratory tests may give false-positive results: • In people taking hormone replacement therapy (oestrogen) • Acute thrombosis • During warfarin therapy or other vitamin K antagonists, DOAC or heparin therapy • During pregnancy and for eight weeks post-partum

A laboratory programme using the existing laboratory information service (LIS) was set up specifically for inherited thrombophilia testing. The capacity to add on tests for an acquired thrombophilia or to complete a thrombophilia screen was embedded into this program. From 4 July 2016, all thrombophilia requests were reviewed by a haematologist working in the laboratory. Any request that did not fulfil criteria for testing and requests lacking necessary clinical details were declined. The capacity to ask the requestor for more clinical information and communicate the reasons for declining a test was embedded in the LIS program. The requestor of a test that was declined was sent an electronic link to the new Waikato Hospital Laboratory inherited thrombophilia Choosing Wisely guidelines along with contact details for the laboratory haematologist if a further discussion was required. Declined samples were held for 14 days.

A re-audit of inherited thrombophilia testing patterns was performed six months after implementation of the Choosing Wisely programme from July 2016–December 2016.

Results

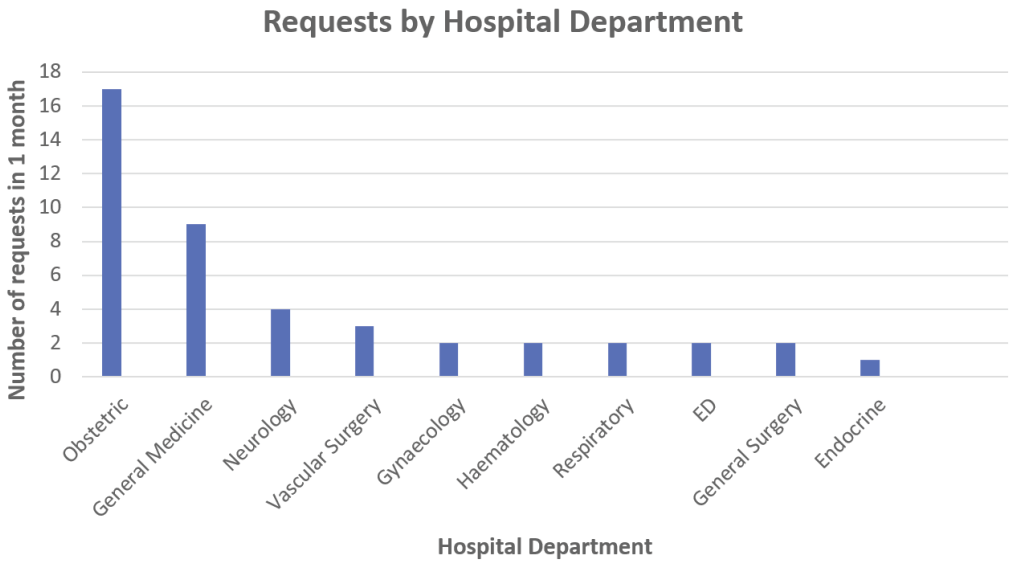
A total of 94 inherited thrombophilia requests were performed in August 2015. Most requests were for female patients (75%, n=70). The median age was 38 years for females and 52 years for males. A significant number of request forms lacked clinical information or indication for testing (21%, n=20).

There was only one inherited thrombophilia request that complied with BSH guidelines. This patient was young (<45 years) had a VTE and a sibling with a history of VTE during pregnancy and known to be compound heterozygote FVL/Prothrombin gene mutation.

There was an equal distribution of requests for inherited thrombophilia tests generated from hospital and community clinicians 46% and 48% respectively.

Within the hospital, the obstetric and general medical departments generated the majority of requests (Figure 1). Personal and Family history of VTE and obstetric complications comprised the majority of indications for testing (Figure 2). There were a few requests for patients with bleeding issues.

Figure 1: Inherited thrombophilia requests by hospital department.



Clinical utility of abnormal results

A total of 21 patients had abnormal results. Of these, 76% (n=16) results would not have changed clinical management (Table 4).

The clinical utility of test results was uncertain in 3 of 21 patients with abnormal results. These included two patients with low protein S levels tested at the time of pregnancy loss with no repeat level performed eight weeks post event. The third patient was tested for a presumed pulmonary embolus (PE). No PE was identified on CTPA, there was no personal or family history of thrombophilia, but the patient had a low AT III level.

Figure 2: Indications for testing identified on 74/94 laboratory request forms, 16/94 had no indication for testing on the request form but were identified following clinical note review or discussion with the requestor. "Bleeding and others" include easy bruising, epistaxis and menorrhagia.

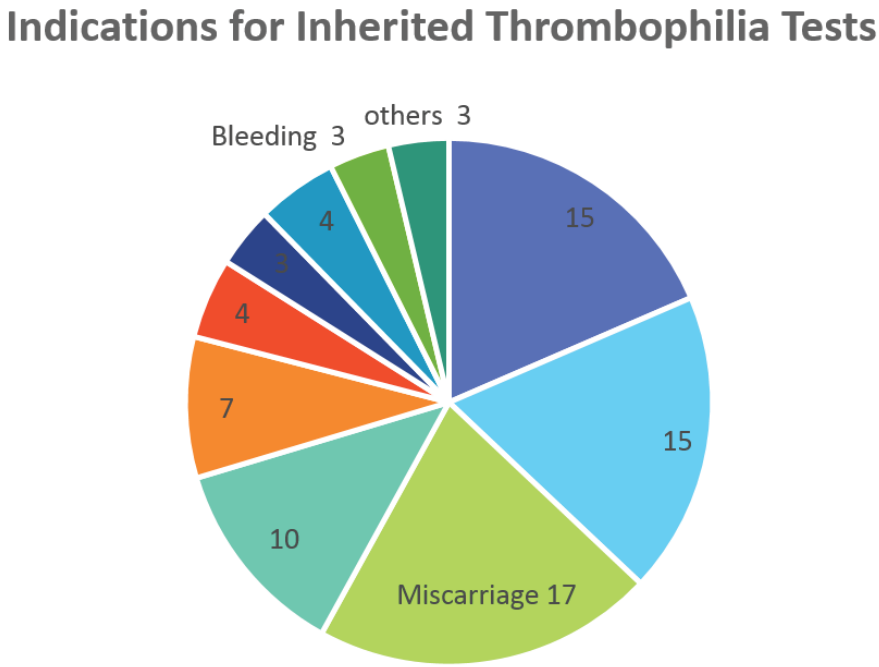


Table 4: Abnormal results would not change clinical management.

Inappropriate testing
Five patients tested at the time of pregnancy loss resulting in a decreased PS level. (A)
All five were normal on repeat testing eight weeks later.
One patient tested for DVT during pregnancy resulting in low PS and AT levels. (A)
Repeat testing eight weeks post-partum showed normal PS and AT levels.
One low protein S and protein C while on warfarin therapy. (A)
Three heterozygous for FVL tested before commencing the combined oral contraceptive pill (COCP). All would require alternative contraception regardless of results due to a strong family history of VTE. (B)
Four patients >60 yrs. Tested for unprovoked VTE, found to be heterozygous for FVL. No personal or family history of thrombophilia. (B)
Two patients with an established diagnosis of prot S deficiency were retested. (C)

Inappropriate timing of tests (A), inappropriate indication for testing (B), repeated test despite having an established diagnosis (C).

Two patients had abnormal results that would have changed clinical management. One patient with compound heterozygosity FVL/prothrombin gene mutation and a family history of thrombophilia. The other patient was tested for a recurrent miscarriage and found to be heterozygous for FVL mutation with a true protein S deficiency. Both complied with criteria for testing where clinical management would or may be influenced by the result.

The cost for unnecessary inherited thrombophilia tests for the month of August 2015 was $23,282. A total of 1,233 tests were performed in the 12-month period from Sept 2014–Aug 2015. The estimated cost of unnecessary tests in that 12-month period is around $300,000.

Six months after the implementation of the new guidelines, the overall number of requests for testing had decreased, and the number of requested tests that were performed reduced significantly (Figure 3). Overall, 376 requests were received, of which 138 fulfilled criteria for testing. Only 312 of the 376 requests had adequate clinical information provided on the initial request. Sixty-four requestors were asked for additional clinical information.

The majority of requests performed were for obstetric complications, 66% (n=91). DVT and VTE in those <45 yrs old comprised 20% of requests (n=28). Cryptogenic stroke in the young patient made up 8% of requests (n=11). Test results are detailed in Table 5.

Figure 3: AT III testing volumes at Waikato Hospital—used as a marker for inherited thrombophilia screening volumes.

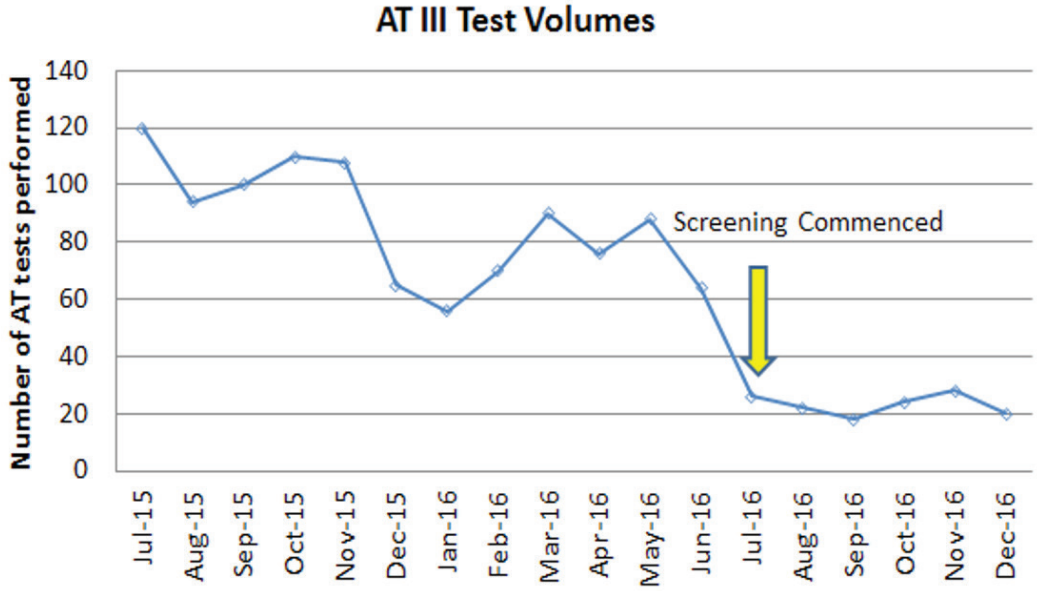


Table 5: Test results by indication.

Obstetric complications	**n (%)**
Normal	91 (53)
Low protein S (tested at the time of pregnancy loss)	33 (36)
Heterozygous FVL	5 (6)
DVT/PE, <45 yrs old with a family history of VTE	
Normal	18 (64)
Heterozygous FVL	5 (19)
Low AT	2 (7)
Low PC	2 (7)
Heterozygous prothrombin gene mutation	1 (3)
Neurology- cryptogenic stroke	
Normal	10 (91)
Low PC	1 (9)
Others	
Normal	8 (100)

The total cost of inherited thrombophilia testing in selected patients for the first six months since programme implementation was $34,914, with an estimated savings of $120,000.

Discussion

The BSH provides comprehensive guidelines for selective inherited thrombophilia testing. Our laboratory fell well below the recommended guidelines for testing with only 1 of 94 requests complying with the BSH criteria for testing. This pattern of inappropriate ordering practice is seen elsewhere in New Zealand[8] and internationally.[2,10,20] A retrospective study in a large tertiary haemostasis referral laboratory, Westmead NSW, Australia found that less than 20% of requests for inherited thrombophilia were appropriate for testing.[20]

In our study, the majority of test requests were for female patients (75%, n=70) with a median age of 38 years, reflecting the perceived value of testing in the context of obstetric complications and testing to inform suitability for the COCP. To date, guidelines recommend against inherited thrombophilia testing to guide decisions around commencing the COCP. A family history of thrombophilia in the context of oestrogen exposure is a reliable criterion for avoiding the COCP. However, a recent large study of women taking the COCP demonstrated a similar prevalence of an inherited thrombophilia among those with and those without a family history of VTE.[21] This may result in a change in testing practice in future, but further validation studies are required. The role of testing prenatally in asymptomatic women with a family history for inherited thrombophilia is on the BSH criteria for testing where results may change clinical management.[7] The Royal Australian and New Zealand College of Obstetricians follow the RCOG UK green top guidelines which recommend testing in this context.[19] The RCOG guidelines for recurrent miscarriage also recommend testing in women with second-trimester miscarriage. After consultation with the obstetric department at Waikato Hospital, the decision was made to test in asymptomatic women with a family history for thrombophilia and obstetric complications such as recurrent miscarriage, second-trimester fetal loss, IUGR and IUD. For obstetric complications, a strong recommendation was made to test at least 6–8 weeks post-event to remove the ambiguity of interpreting abnormal protein S levels. A local database of all obstetric requests performed since the implementation of the programme has been created with the plan to evaluate the clinical utility of testing for those patients.

An important and reassuring finding from this study was that no clinically significant abnormal results were missed when applying the BSH criteria to the cohort. Overall there were 21 patients with abnormal results. Two of 21 patients had clinically significant abnormal results, one patient who fulfilled criteria for testing and another who fulfilled BSH criteria where testing may be indicated. The majority of abnormal results (76%, n=16) would not have changed clinical management. A significant number of false-positive results were due to the inappropriate timing of tests. Interpretation of tests performed during pregnancy loss, the acute phase of a VTE or while on warfarin therapy is problematic, even more so if the clinician reviewing the patient's results does not have expertise in haemostasis and thrombosis. These findings highlighted the need to emphasise the appropriate timing of testing when designing our local protocol.[11]

The Waikato Hospital Laboratory inherited thrombophilia Choosing Wisely guidelines were developed in collaboration with various departments in the hospital. There is a paucity of large randomised controlled trials to guide testing decisions in many circumstances. The collaboration provided an opportunity to discuss clinical areas where the utility of testing is uncertain and arrive at a consensus for testing. The BSH, National Laboratory Test Referral and RCOG Green-top guidelines, along with the guiding principles of 'Choosing Wisely' influenced the final guideline design. We developed a guideline that was selective, restrictive and reduced harm but allowed for testing in situations where there is no clear evidence for or against testing.

Implementation of the guidelines required a multimodal approach covering the organisational, clinical and laboratory arms of testing. When implementing the laboratory arm for this inherited thrombophilia programme, we had underestimated the ongoing need for fine tuning the LIS programme so that it was fit for purpose. Optimising the capacity to individualise test approval and feedback to requestors took six months.

The results from our initial audit showed that education and wide dissemination of guidelines alone do not ensure a change in requesting behaviour. The decision to have all requests screened by a haematologist was a necessary measure to support a change in behaviour. This process of screening is time-consuming and requires ongoing dedication and commitment from the haematologists working in the laboratory. There was a significant reduction in testing overall within the first six months of protocol implementation with 376 requests overall. This suggests clinicians were more mindful of appropriate test ordering practices. However, the majority of requests received did not meet the criteria for testing (63% n=238) and reflected the need for ongoing clinical education around appropriate ordering practices.

In future, electronic laboratory requesting would circumvent the issue of insufficient clinical details provided on request forms and the labour-intensive screening of all requests by a laboratory haematologist. Algorithms and embedded decision-making tools, indicating criteria for testing and appropriate timing of testing would help clinician decision making at the time of ordering the test.

Thrombophilia testing is expensive. Studies repeatedly demonstrate the unnecessary financial costs associated with indiscriminate testing.[22] The estimated annual cost for unnecessary testing at Waikato Hospital Laboratory was $306,208.65. This estimate does not account for the costs associated with retesting abnormal results, carrying an incorrect diagnosis such as long-term anticoagulation and cost of complications arising from bleeding and overtreatment.

Limitations of this study

There are some limitations to this study. The small sample size and duration period of assessing inherited thrombophilia testing in the first and second phase of the study are significant limitations. In recognition of this, the study data was supplemented by looking at trends of AT testing over 12 months to ensure the testing behaviour in August 2015 was typical for the 12 months prior.

A retrospective design means that collection of data relying solely on adequate documentation introduces information bias. Compliance of inherited thrombophilia requests with BSH may have been underrepresented due to this bias rather than a

true finding. There is also a potential for investigator error and bias when collecting the data from electronic records and written clinical notes.

The strengths of this study included the assessment of consecutive thrombophilia requests and clinical note review to gain detailed clinical information and outcomes. In addition, the collaborative design of the new guideline and multimodal implementation programme facilitated clinician buy-in and early adoption of the Choosing Wisely programme. The benefits of implementing this laboratory programme have been far-reaching beyond our laboratory. Subsequent to presenting the findings of this study at the 2017 New Zealand branch meeting of the HSANZ (Haematology Society of Australia and New Zealand) another reference haematology laboratory in New Zealand has decided to implement an inherited thrombophilia programme based on our laboratory model of selective testing.

Conclusion

Our retrospective study demonstrated indiscriminate patterns of inherited thrombophilia testing in the Waikato region. There was a reduction in requests and costs following the implementation of multimodal Choosing Wisely programme. The critical success factor for the implementation of this programme was having all requests reviewed by a laboratory haematologist and restricting access to testing. Although time-consuming, this was a necessary measure to support appropriate testing in our laboratory. We expect in future; inherited thrombophilia testing will be more selective and performed only on patients who are likely to derive benefit from testing.

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Appendix

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Inherited Thrombophilia Testing

SUMMARY OF CHANGES

From 4th July 2016, inherited thrombophilia testing performed at Waikato Hospital, for the Waikato & BOP region, will only be performed in the following clinical situations:

- Idiopathic venous thrombo-embolism in young patients (<45 years)
- Warfarin-induced skin necrosis (Patients should be tested for protein C deficiency and protein S deficiency one month after stopping vitamin K antagonist therapy if this can safely be discontinued.)
- Children presenting with purpura fulminans (Test for protein C and protein S deficiency).
- Siblings of patients with homozygous FVL, homozygous PT20210A or compound heterozygotes for these mutations
- Thrombosis in unusual sites (e.g. cerebral, mesenteric, portal).

In all other situations testing should only be undertaken after consultation with a Haematologist or as part of a clinical trial.

Samples MUST provide clinical details of which criteria for testing the patient meets or the sample will not be tested.

In the absence of meeting one of the testing criteria and testing is still thought to be appropriate, it must be discussed first with a clinical haematologist and their name clearly identified on the request form along with clinical details.

Wherever possible, thrombophilia testing should be avoided in the following settings as one or more of the laboratory tests may give misleading results:

- In people taking hormone replacement therapy (oestrogen)
- Acute thrombosis
- During warfarin or other vitamin K antagonist or DOAC or any heparin therapy
- During pregnancy and for 8 weeks post-partum

Situations where testing is NOT indicated:

- Recurrent VTE
- Recurrent VTE despite adequate therapeutic anticoagulation
- VTE in the context of a family history of unprovoked VTE in a first degree relative
- VTE in association with a history of thrombophlebitis
- Arterial thrombosis (Lupus testing is indicated in this setting)
- Women with a history of miscarriage, pre-eclampsia, abruption or intrauterine growth restriction (Lupus testing is indicated in this setting).
- Prior to use of combined oral contraceptives in patients with a family history of VTE (Current British guidelines recommend avoidance of the combined oral contraceptive pill in women with a history of VTE in a first degree relative regardless of the thrombophilia results)
- In unselected women considering the use of the combined oral contraceptive pill.

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See overleaf for more information and background:

CLINICAL UPDATE

Background

The currently recognised conditions resulting in heritable thrombophilia are:-

1. Antithrombin III deficiency
2. Protein C deficiency
3. Protein S deficiency
4. Factor V Leiden (FVL)
5. Prothrombin G20210A mutation (PT20210A)
6. Dysfibrinogenaemia
7. Inherited antiphospholipid syndrome

Patients with deficiencies of the naturally occurring anticoagulants (antithrombin, protein C and protein S) in thrombosis-prone families have a severe thrombophilic tendency with a relative risk for venous thromboembolism (VTE) of approximately 10-20 fold compared to unaffected people. This compares to a relative risk of approximately 3-5 fold for people who are heterozygotes for FVL or PT20210A.

People who are homozygous for FVL or PT20210A or double heterozygotes for these conditions are rarely seen but appear to have a particularly high risk of VTE, with a relative risk rate estimated at approximately 50-80 fold.

The dysfibrinogenaemias and inherited antiphospholipid syndrome are extremely rare and should be discussed with a haematologist prior to ordering any further tests.

Testing for Inherited Thrombophilia

Waikato hospital laboratory recently performed an audit on inherited thrombophilia testing requests performed in a month and bench marked them against international and national standards for performing these tests. (1-3). Results showed that testing for inherited thrombophilia was not being performed wisely or in accordance with these guidelines with only 1/97 tests being performed appropriately.

As a result of this, **from Monday 4th July** testing for inherited thrombophilia will only be permitted in the following situations based on the national NZ laboratory testing guidelines and Waikato DHB laboratory testing guidelines. (3-5)

Testing Indications for inherited thrombophilia:

- Idiopathic venous thrombo-embolism in young patients (<45 years)
- Warfarin-induced skin necrosis (Patients should be tested for protein C deficiency and protein S deficiency one month after stopping vitamin K antagonist therapy if this can safely be discontinued.)
- Children presenting with purpura fulminans (they should be tested for protein C and protein S deficiency).
- Siblings of patients with homozygous FVL, homozygous PT20210A or compound heterozygotes for these mutations (they will be offered testing for FVL and PT20210A as they have at least a 1 in 4 chance of being similarly affected by these severe thrombotic disorders).
- Thrombosis in unusual sites (e.g. cerebral, mesenteric, portal).

In all other situations testing should only be undertaken after consultation with a Haematologist or as part of a clinical trial.

Situations where testing is NOT indicated:

- Recurrent VTE
- Recurrent VTE despite adequate therapeutic anticoagulation
- VTE in the context of a family history of unprovoked VTE in a first degree relative
- VTE in association with a history of thrombophlebitis
- Arterial thrombosis (Lupus testing is indicated in this setting)
- Women with a history of miscarriage, pre-eclampsia, abruption or intrauterine growth restriction (Lupus testing is indicated in this setting).
- Prior to use of combined oral contraceptives in patients with a family history of VTE (Current British guidelines recommend avoidance of the combined oral contraceptive pill in women with a history of VTE in a first degree relative regardless of the thrombophilia results)
- In unselected women considering the use of the combined oral contraceptive pill

Patient counselling
Testing for heritable thrombophilia may reveal the presence of a genetically determined disorder and patients should be counselled appropriately before testing is performed.
Patients should also be advised that testing for heritable thrombophilia may affect their insurance risk and that their access to insurance policies may be changed, regardless of the result of the test result.

Genetic Testing
Index case sequencing (if initial testing has been negative) should only occur at the request of a haematologist.

Requesting an inherited thrombophilia panel from Monday 4th July

The tests comprising an inherited thrombophilia screen are:

- Antithrombin III
- Protein S and C
- Factor V Leiden (FVL); this is a molecular test
- PT20210A (prothrombin gene): this is a molecular test

Testing for antiphospholipid antibodies such as Lupus anticoagulant, IgG anticardiolipin antibodies and beta glycoprotein antibodies is more likely to be informative in cases of arterial thrombosis or in women with pregnancy loss, intrauterine growth restriction, pre-eclampsia and abruption.

Wherever possible, thrombophilia testing should be avoided in the following settings as one or more of the laboratory tests may give misleading results:

- In people taking hormone replacement therapy (oestrogen)
- Acute thrombosis
- During warfarin or other vitamin K antagonist therapy
- During treatment with any form of heparin
- During pregnancy and for 8 weeks post-partum

Testing will only be performed on samples accompanied by appropriate clinical details stating which of the above indications for testing the patient meets.

In the absence of meeting one of the recognised indications, the sample will not be tested unless it has been discussed with a clinical haematologist and this has been clearly documented on the request form.

Samples arriving in the laboratory without appropriate clinical details will not be tested but the sample will be held for 14 days and will be tested if the requesting clinician subsequently provides appropriate clinical details.

Where low levels of antithrombin III, protein C or S are found, a repeat sample will be requested to confirm the abnormal finding.

Patients will only be tested for FVL and prothrombin gene mutation once in their lifetime.

Conclusion

It is hoped by these measures that testing inappropriately for inherited thrombophilia where the result of testing does not alter subsequent management of many patients will be significantly reduced and will bring the Waikato region in line with other areas of New Zealand that have already adopted these practices.

Please contact the haematology laboratory at Waikato Hospital on 07 8398606 for more information if required.

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CLINICAL UPDATE

Competing interests:
Nil.

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URL:
www.nzma.org.nz/journal-articles/inherited-thrombophilia-testing-practice-in-a-large-tertiary-hospital-in-new-zealand-implementation-of-a-choosing-wisely-protocol-to-reduce-unnecessary-testing-and-costs

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