

Are Clinical Laboratories Following ISTH Recommendations for Lupus Anticoagulant Testing? *Results of a 2nd NASCOLA Questionnaire*

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on behalf of

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Lupus Anticoagulant Testing



- Laboratory testing for the Lupus Anticoagulant (LA) is important in the diagnoses of
 - Thrombophilia
 - Suspected Antiphospholipid Syndrome (APS)
- 1st questionnaire was distributed to NASCOLA and ECAT members in 2005
 - Although valuable information was collected, questions were raised about compliance to specific ISTH recommendations
- NASCOLA membership were supportive of participating in a 2nd questionnaire to address these questions

Goal of Second Questionnaire



- First questionnaire did not include specific questions about compliance to each of the ISTH recommendations for LA testing
 - Algorithms (provided on test procedures) had been used to indirectly assess compliance to each of the ISTH recommendations
- The goal of the Second Questionnaire was to ask direct and specific questions about compliance to each of the ISTH recommendations for LA testing

ISTH SSC Recommendations



- Nine recommendations were offered in the 1995 SSC report on LA
 - Four of these became diagnostic criteria
 - One recommendation concerned nomenclature (retention of term “lupus anticoagulant”)
- Remaining four recommendations dealt with:
 - Platelet count of platelet poor plasma ($< 10 \times 10^9/L$)
 - Confirmatory assays
 - Use same assay principle as screening test that was initially found to be abnormal
 - Performance of routine clotting tests, such as PT and APTT
 - Use to evaluate possibility of other coagulation disorders that may interfere with LA methodology
 - If chosen method for screening or confirmation is known to be sensitive to heparin, a Thrombin Time may be helpful in detecting its presence
 - Solid phase assays for phospholipid antibodies should not be considered as a confirmatory procedure for LA activity

ISTH SSC Criteria for Diagnosis of LA



1. Prolongation of at least one phospholipid-dependent clotting test
2. Evidence of inhibitory activity shown by the effect of patient plasma on pooled normal plasma
3. Evidence that the inhibitory activity is dependent on phospholipid

This may be achieved by addition or alteration of phospholipid, hexagonal phase phospholipid, platelets, or platelet vesicles in the test system

4. LAs must be carefully distinguished from other coagulopathies that may give similar laboratory results or may occur concurrently with LAs

Specific factor assays and the clinical history may be helpful in differentiating LAs from these other possibilities

Methods



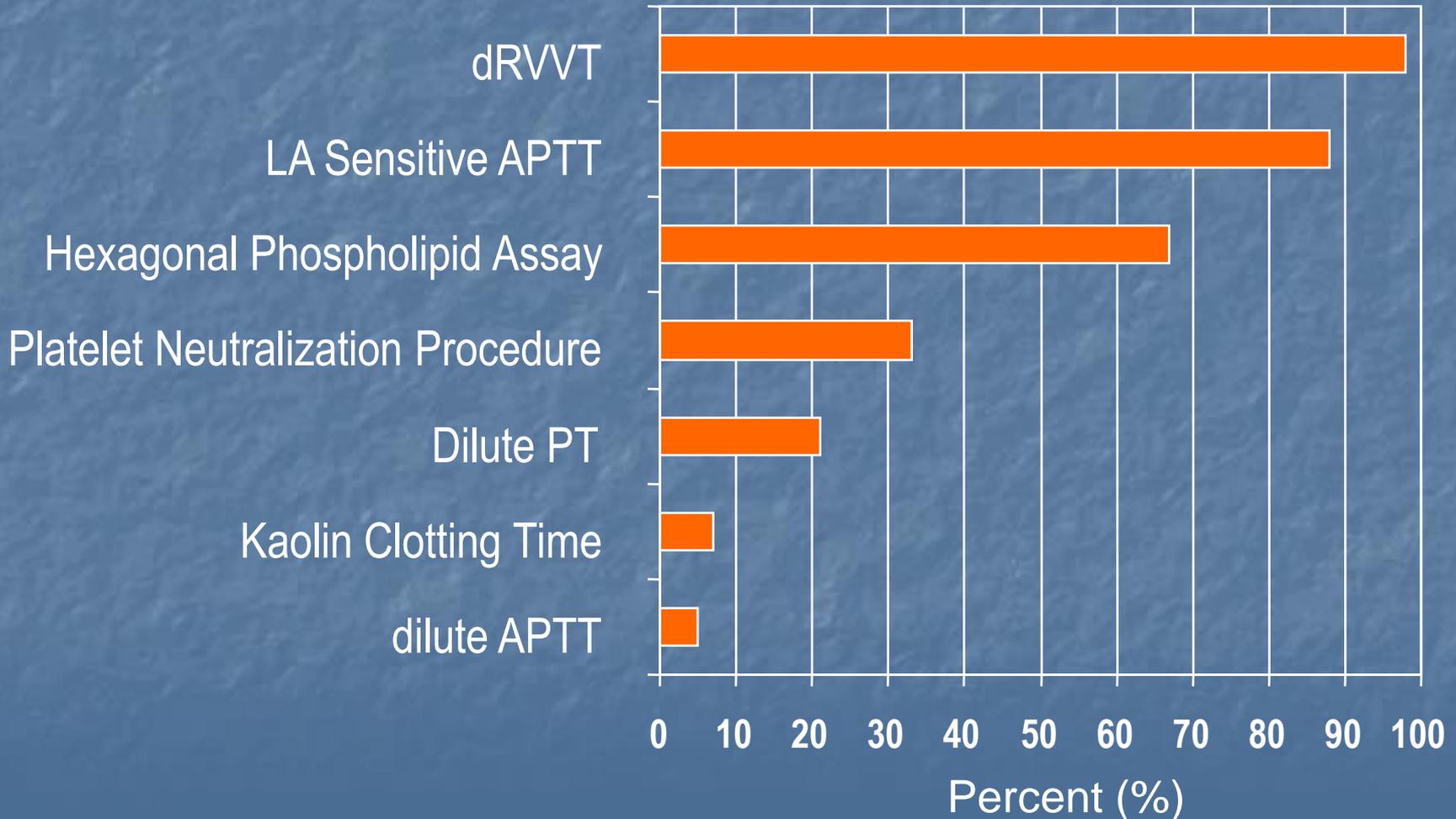
- A patterns-of-practice questionnaire, containing 26 questions, was built on SurveyMonkey.com®
- Distributed in January 2007 to NASCOLA and ECAT members
 - NASCOLA : electronic data collection complete
 - High level of participation - 79% (49 of 62 labs)
 - ECAT : collection stage

NASCOLA Results



- Life and moving targets:
 - 19% changed practices since participating in the first survey
 - 26% changed reporting practices since participating in the first survey
 - 21% planned to change LA testing practices after participating in 2nd study
- How many follow all ISTH recommendation?
 - 87% reported that they did.....

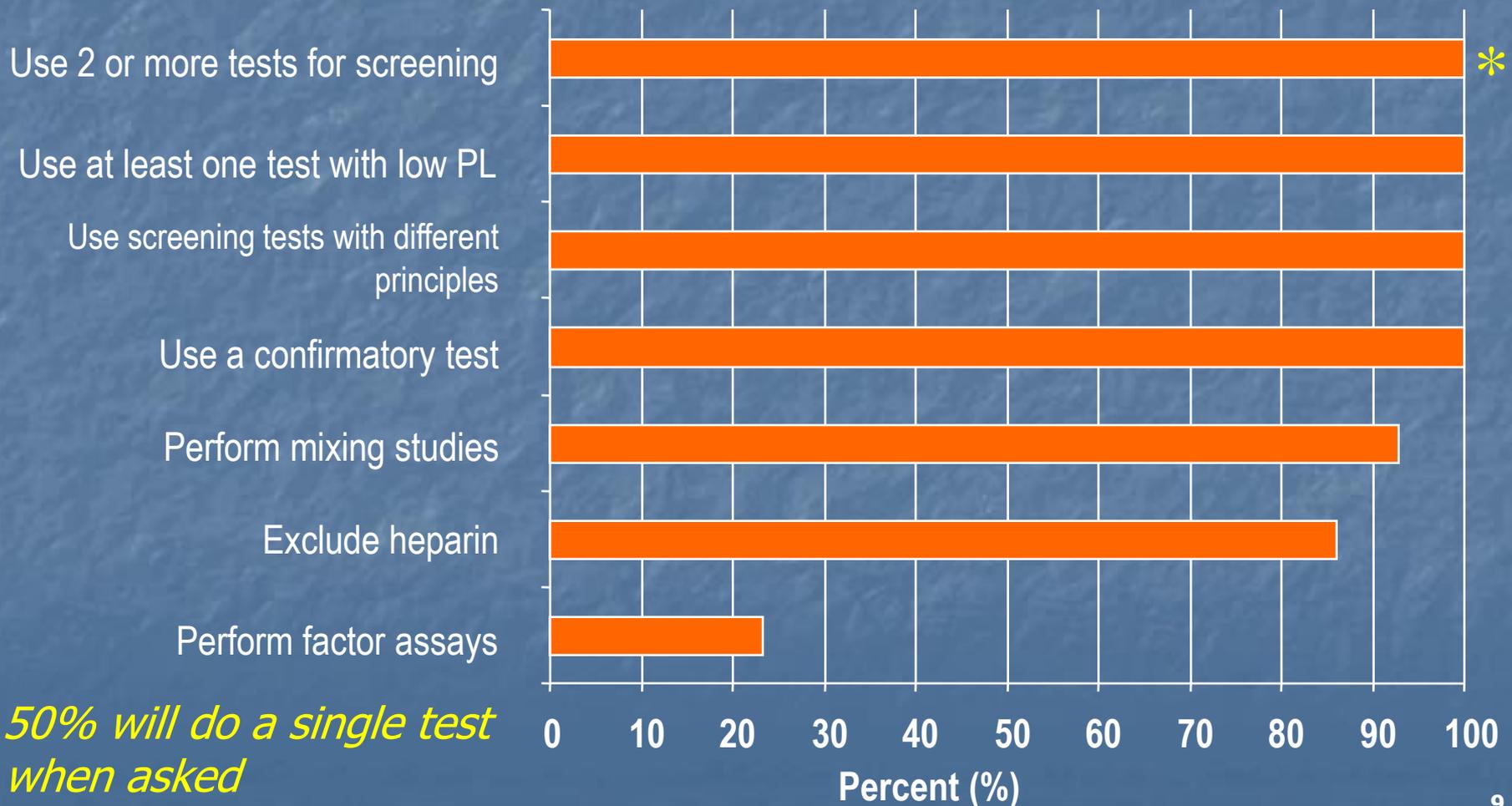
LA Tests Commonly Used by NASCOLA Members



Analysis of NASCOLA Data



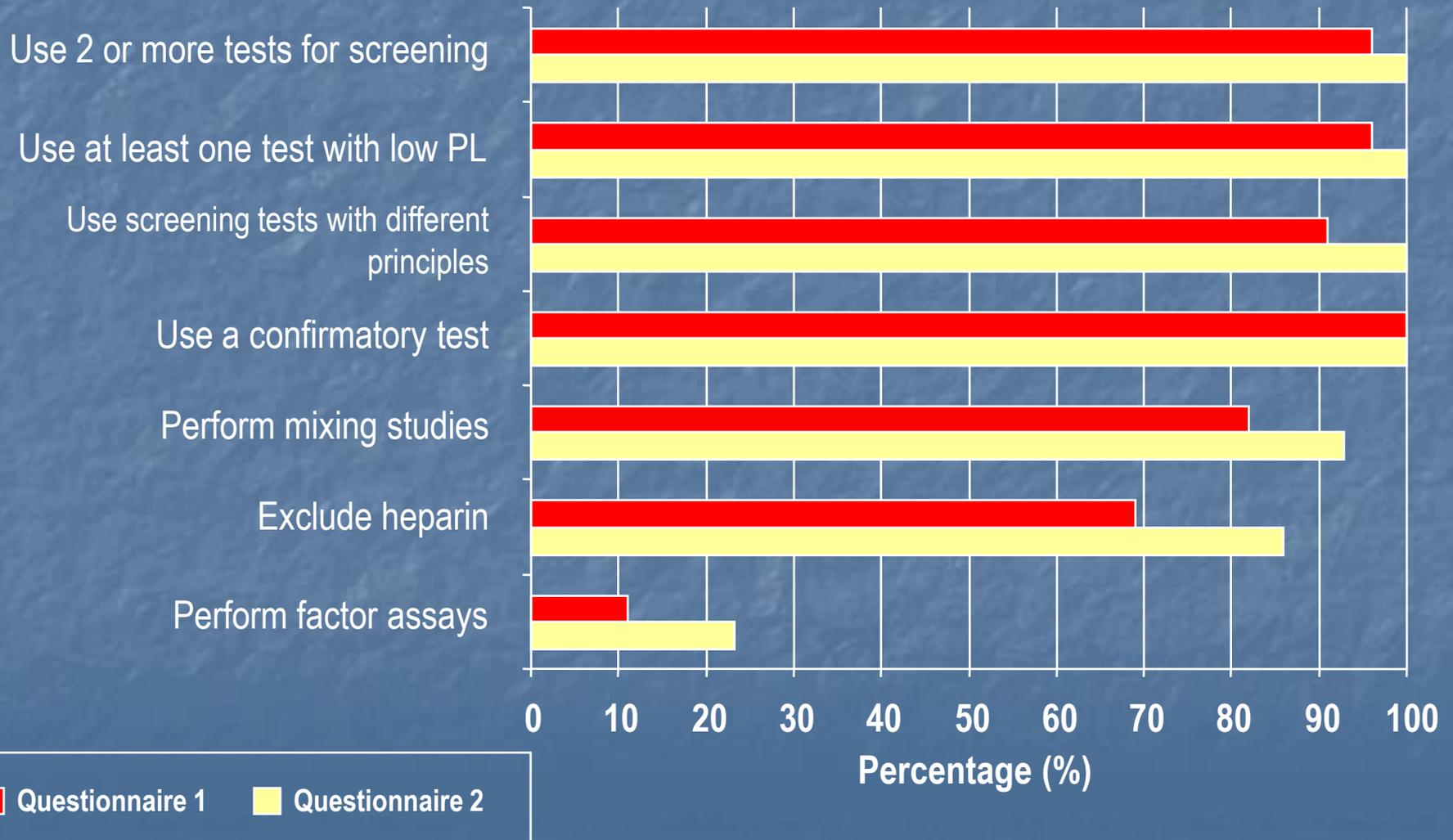
2nd Questionnaire Results from 49/62 (79%) NASCOLA Laboratories as to their Conformity to ISTH Recommendations & Criteria



** 50% will do a single test when asked*

Conformity to ISTH Recommendations?

Comparison of 2 NASCOLA LA Survey Responses



Mixing Studies



- 7% (3 of 42 labs) reported that they did not perform mixing studies to document an inhibitor effect on pooled normal plasma
- Of the laboratories that performed mixing studies:
 - Lupus sensitive APTT : 87%
 - dRVVT : 86%
 - KCT : 75% (only 4 laboratories)

Heparin Exclusion



- For the exclusion of heparin as the cause of the coagulopathy:
 - 14% of respondents (6 of 43 labs) did not exclude heparin as the cause of an abnormal LA result
- Of the laboratories that did exclude heparin:
 - 57% of respondents did not repeat the abnormal LA test with a neutralized sample

Factor Assays on LA samples?



- When questioned if factor assays are performed to exclude a coagulopathy
 - 30% of respondents reported that their LA test panel does not include testing for a factor deficiency or specific factor inhibitor
- Of the 30 laboratories that reported performing factor assays
 - 67% (n=20) only perform them when the additional testing is approved by a client

Revision of ISTH Recommendations?



- Do the ISTH recommendations need to be updated?
 - 32% of NASCOLA laboratories indicated in the affirmative
 - 17% identified that the following requirement needed to be changed: “factor assays should be performed whenever there is suspicion of a specific factor deficiency or inhibitor.”

Conclusions



- The 2nd NASCOLA questionnaire on LA testing practices showed that the majority of NASCOLA laboratories follow most of the 1995 ISTH LA testing recommendations
- A significant number of laboratories do not investigate for other coagulopathies as the cause of an abnormal LA test result (e.g. test for heparin, factor deficiency or a specific inhibitor)
 - A majority of laboratories (58%) dealt with this issue by including an interpretative comment, suggesting that testing be done to evaluate other causes of abnormal result, if clinically indicated

Closing Comments

Future Initiatives



- Our data also indicate that NASCOLA questionnaires have had an impact on the quality of laboratory testing for LA, assessed by compliance to ISTH testing recommendations
 - Questionnaires may help improve the quality of other coagulation tests, complementary to other initiatives, such as proficiency testing exercises
- It would be interesting to compare performance of the different LA test algorithms used in practice by proficiency testing exercises with different types of abnormal samples