Can you tell me the reason of my patient' bleeding from this sample? Study in 270 European laboratories

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On behalf of the Working Group on Postanalytical Phase of the European Federation of Clinical Chemistry and Laboratory Medicine and European Organisation for External Quality Assurance Providers in Laboratory Medicine

EQALM
European Organisation For External Quality Assurance Providers in Laboratory Medicine

EFLM
EUROPEAN FEDERATION OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE

Working group on postanalytical phase








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EQALM
European Organisation For External Quality Assurance Providers in Laboratory Medicine

Aims of WG-POST

- To promote importance of activities that improve clinical utilisation of lab tests
- To support laboratories in taking an active, prominent role in these activities
- We focus on the followings
  - assistance to clinicians in finding the appropriate laboratory tests to meet their clinical needs
  - translation laboratory results to diagnostic information.

Activities of WG-POST

- Organising surveys: Investigate existing practices in steps of PA and post-PA phase and test requesting
- Main methodological approach: electronic questionnaires
  - clinical situation is presented (case histories are given) + laboratory tests results playing crucial role in the investigated clinical decision making
  - questions on the investigated PA activities of the participants are provided.
  - Evaluation of the practice-variants: characterisation of shortcomings with the potential consequence of delayed or misdiagnosis or treatment
- Feedback reports
  - summary of the main findings
  - summary of the recent literature and guideline recommendations

Survey+ feedback (report/paper) with practice recommendations ➔implementation: conferences, trainings

KEY TEST IN MEDICAL DECISION MAKING: APTT

Unexpected APTT prolongation (uAPTT)

- APTT is on the repertoire of most laboratories
- Fatal medical errors exist due to non-interpreted unexpected APTT prolongations*
- Even mild uAPTTs without prior history of bleeding are expected to be investigated promptly by laboratories detecting uAPTT results first, because of the potentiality of acquired haemophilias**
- The urgent laboratory information needed for therapeutic decision-making in a patient with uAPTT:
  - after excluding spurious reasons decide whether the uAPTT is due to inhibitor effect or factor deficiency.
    - Correct PA actions + Correct test interpretation

*Zeitler H et al. Haemophilia 2010;16:95–101.
**Huth-Kühne A et al. Haematologica 2009; 94:566-75.

TTP steps where laboratories can support medical decision-making in a patient with uAPTT prolongation?

Analysis *

* **Interpretation of the results of the requested tests**

Added tests if needed *
- to exclude spurious reasons (UH), unknown medications (DTI)
- to provide therapeutically important classification (inhibitor or not)

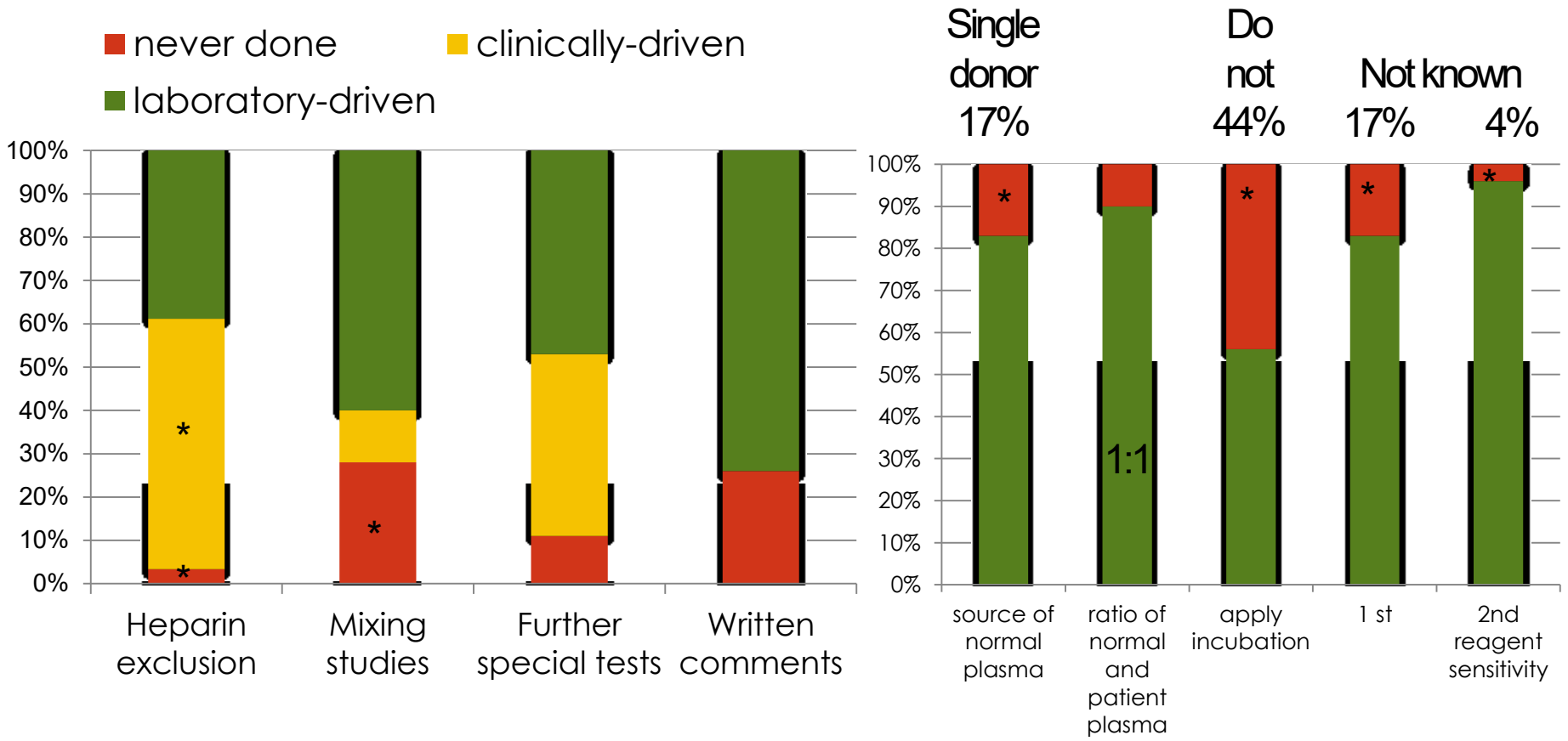
* *

* **Interpretation of the results of the added tests**

Report to the clinician *

- **Results with aiding tools to recognise "not normal values"** *
- **Interpretive comments** *

Large heterogeneity in uAPTT investigation in 990 European laboratories

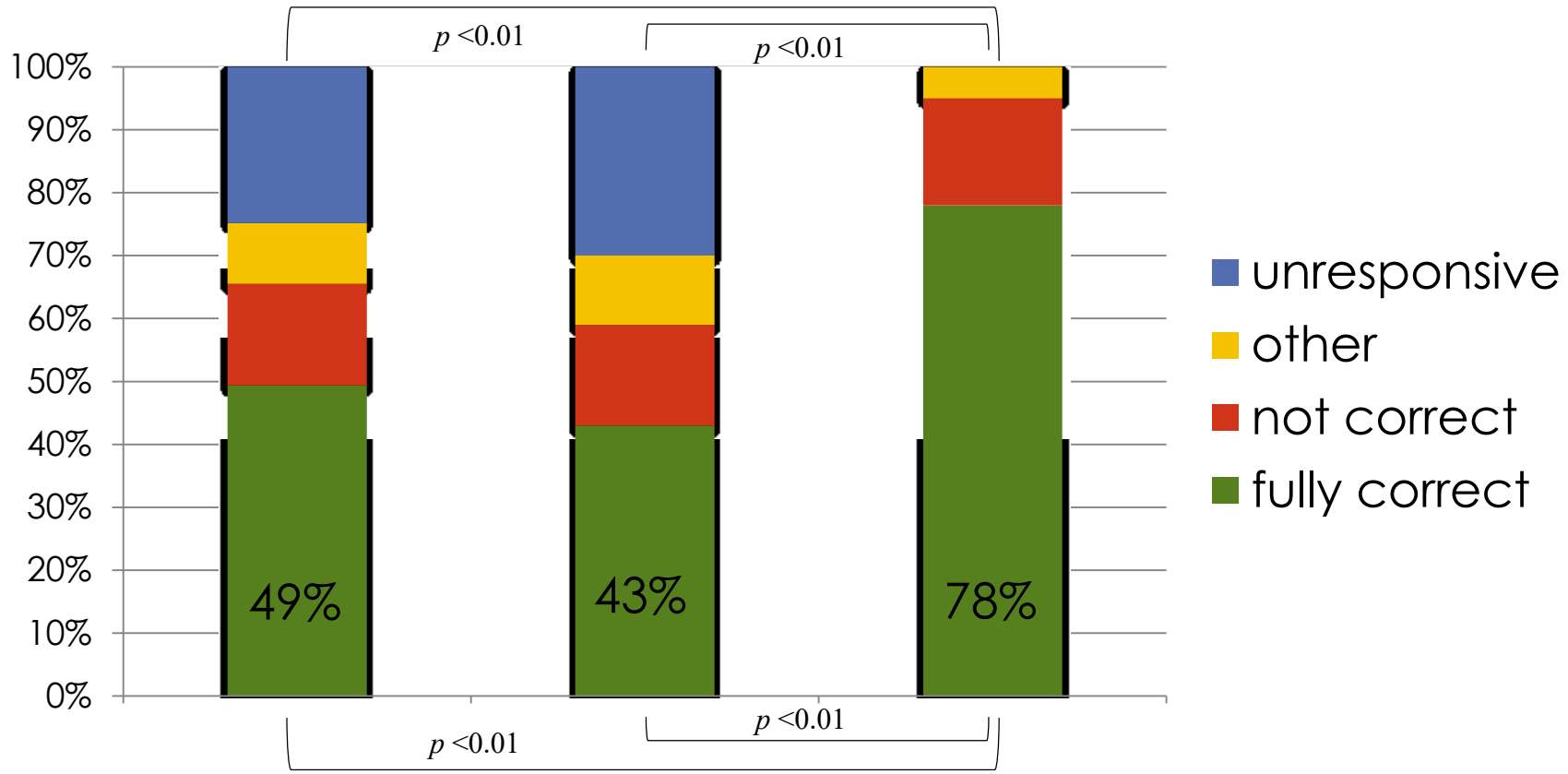


*Practice variants with potential delays in interpretation and misinterpretations (exist in 88% of laboratories !)

*

Clin Chem Lab Med. 2015 Sep 1;53(10):1593-603.

Interpretations of mixing study scenarios in a patient with uAPTT prolongation

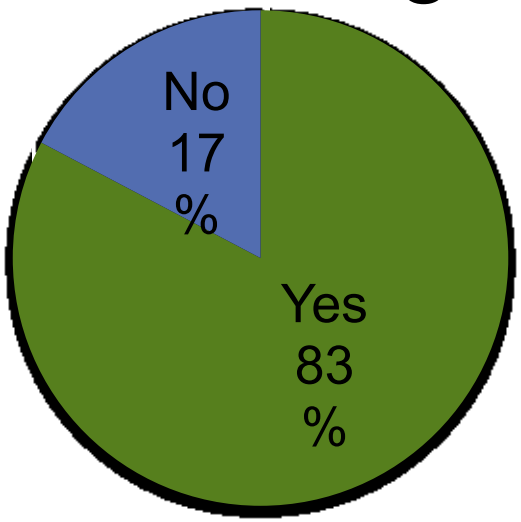


No. of labs: **713 (70% of all participating labs)**

*

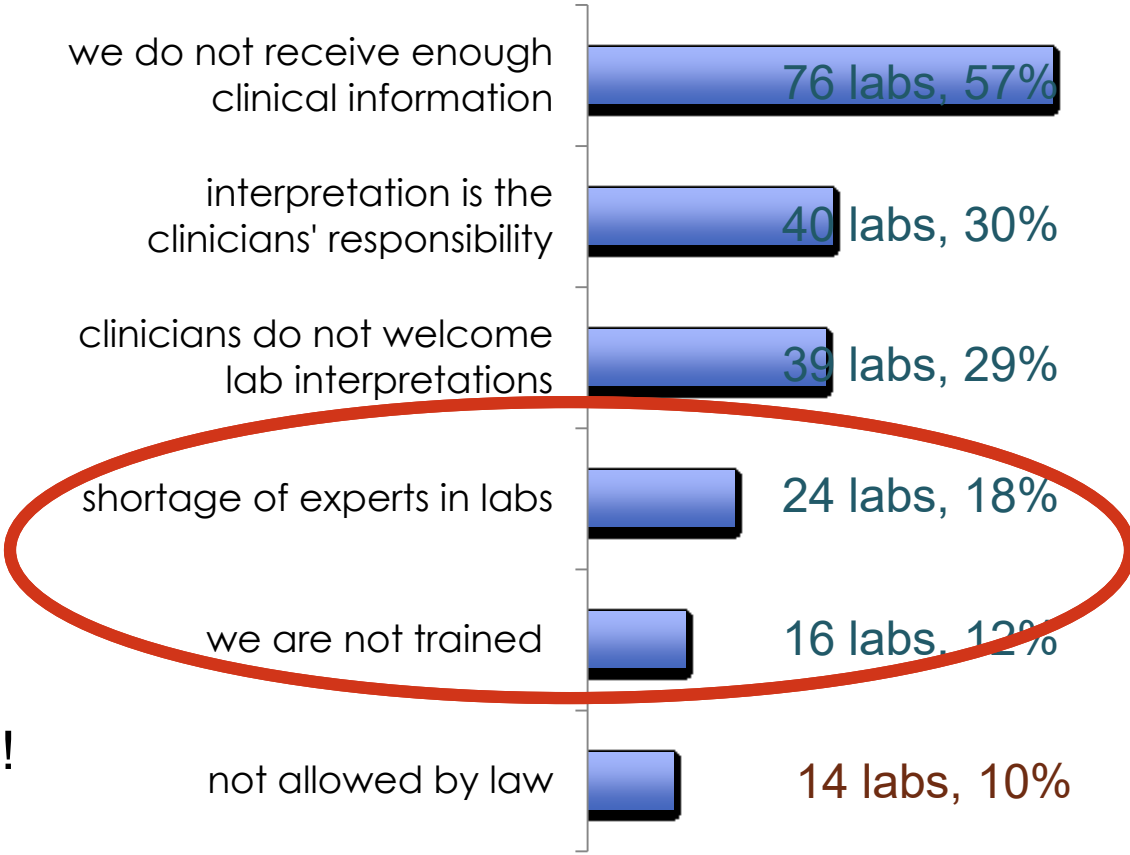
Clin Chem Lab Med. 2015 Sep 1;53(10):1593-603.

Do you apply interpretive commenting?*



IC in haemostasis:
57% of labs
4th most frequent
after clin chem, haemat, micro!

If your laboratory does not provide interpretive commenting, what is the reason for that?



*Interpretation of laboratory results in the context of clinical situation of the patient

EFLM-EQALM survey on how laboratories assist clinicians in utilisation of laboratory tests? An international survey in 833 European laboratories. 2017.

Each step of TTP supporting medical decision-making of a patient with uAPTT prolongation is included in the survey

Analysis *

* **Interpretation of the results of the requested tests**

Added tests if needed *
- to exclude spurious reasons (UH), unknown medications (DTI)
- to provide therapeutically important urgent diagnostic information (inhibitor or not)

* **Interpretation of the results of the added tests**

Report to the clinician *

*
- **Results with aiding tools to recognise "not normal values"**
- **Interpretive comments with classification (lab diagnosis)**

Study design

1. Two case histories + relevant laboratory data + liophylised samples

1. Measure and interpret APTT!
   - Prolonged
   - Equivocal
   - Normal

2. If you would mix in this case in real life, do mixing studies (MS)!

1. Interpret MS:
   - Prolonged
   - Equivocal
   - Normal

2. Classify the two samples!
   - *normal sample*
   - *coagulation factor deficiency*
   - *inhibitor (coagulation factor specific or non-specific like lupus anticoagulant)*
   - *presence of anticoagulant (due to unknown therapy or contamination of the sample)*

3. Comment into your native language if you would do IC in real life!

Case 1.

72-year-old female with suspicion of septicaemia hosp in ICU since 24 hours, antibiotics, central venous line

yesterday:

PT,APTT,TT,fib ✓

today:

haematuria, PT, Fib ✓

now:

APTT is requested

A 72-year-old woman was admitted to the intensive care unit (ICU) due to high fever and a suspicion of septicemia. Upon admission, a central venous line was inserted and broad-spectrum antibiotics given. Biochemical and coagulation testing upon admission were normal; only a mild increase in glucose concentration and leukocytosis were detected.

No medication known to interfere with coagulation tests was noted in the medical history. After 24h of hospitalisation, hematuria was detected and new routine coagulation tests were requested. Prothrombin time/INR and fibrinogen were normal, and your laboratory is now requested to measure APTT.

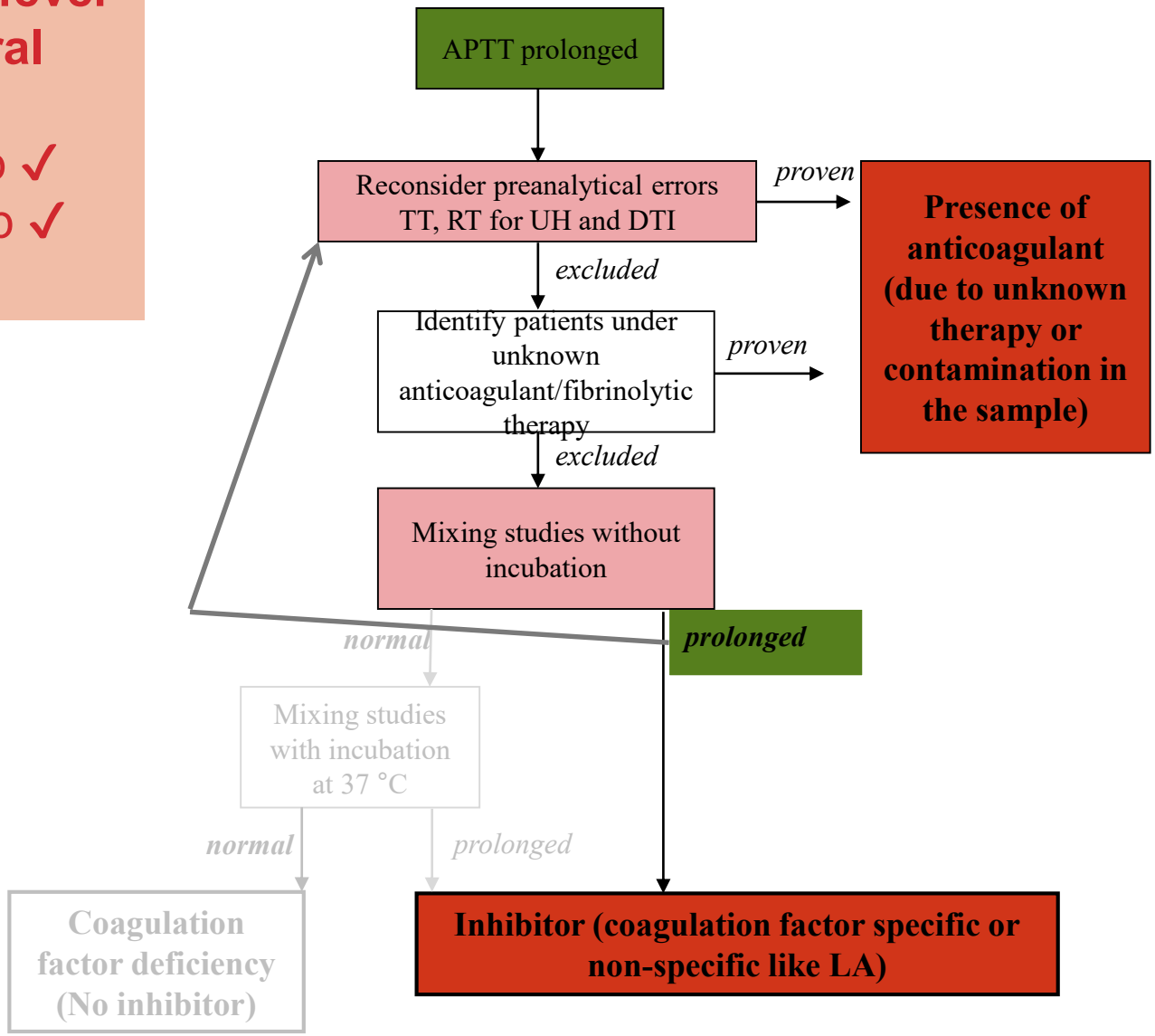
Case 1.

72-year-old female with fever in ICU, antibiotics, central venous line

yesterday: PT,APTT,TT,fib ✓

today: haematuria, PT, Fib ✓

now: APTT is requested



Result interpretations

Added tests

Laboratory diagnoses

Case 2.

41-year-old man with excessive bleeding after dental extraction

PT, fib ✓

APTT is requested

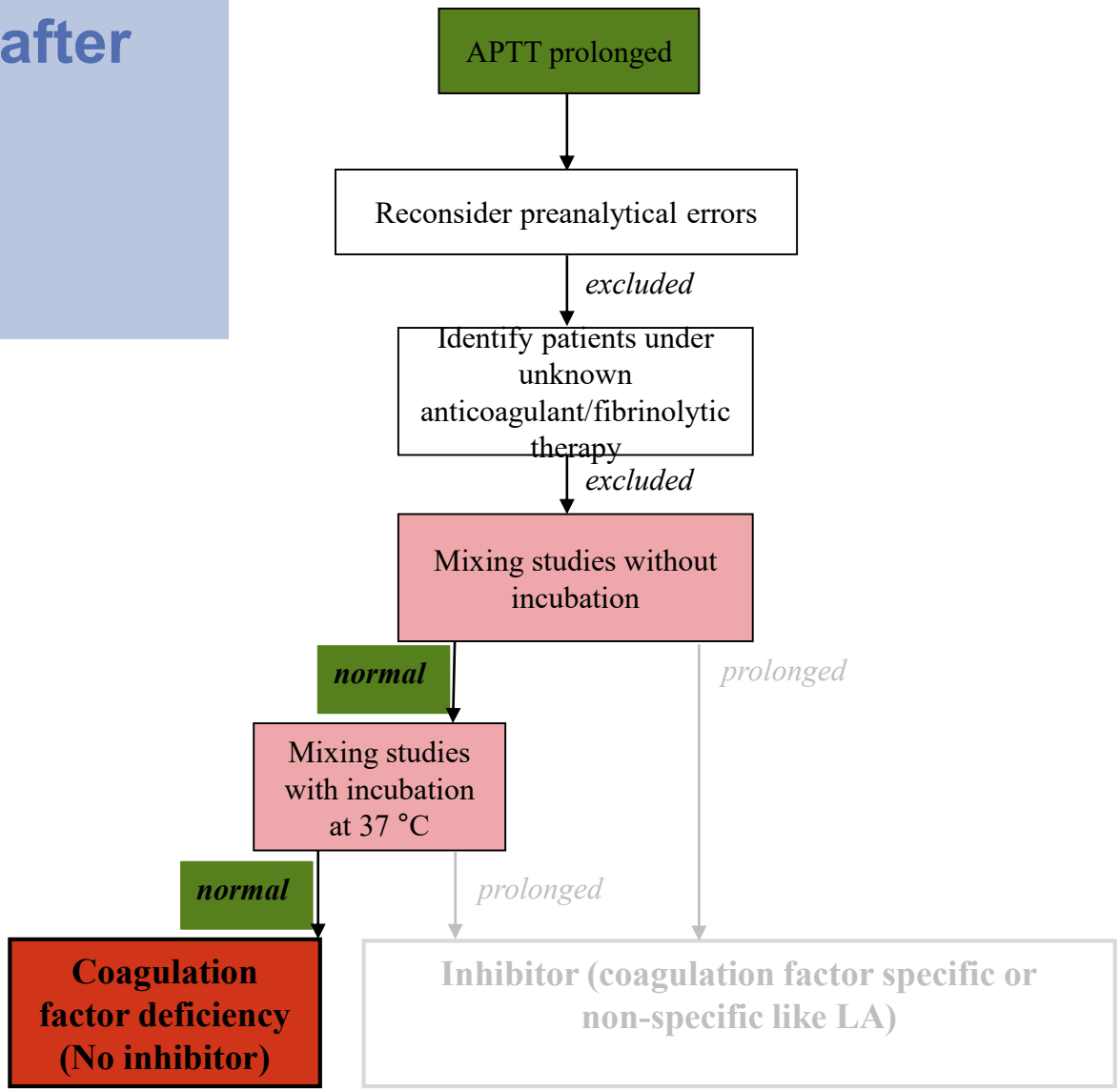
A 41-year-old man working in the metallurgical industry had a recent dental extraction, upon which excessive bleeding was detected, so routine coagulation testing was requested. He is under chronic enalapril treatment (20mg/day) due to his hypertensive status, and ibuprofen for pain relief for the last few days.

Prothrombin time/INR and fibrinogen were normal, and your laboratory is requested to measure APTT. There is no further medical history known from this person.

Case 2.

41-year-old man with excessive bleeding after dental extraction

- PT, fib ✓
- APTT is requested

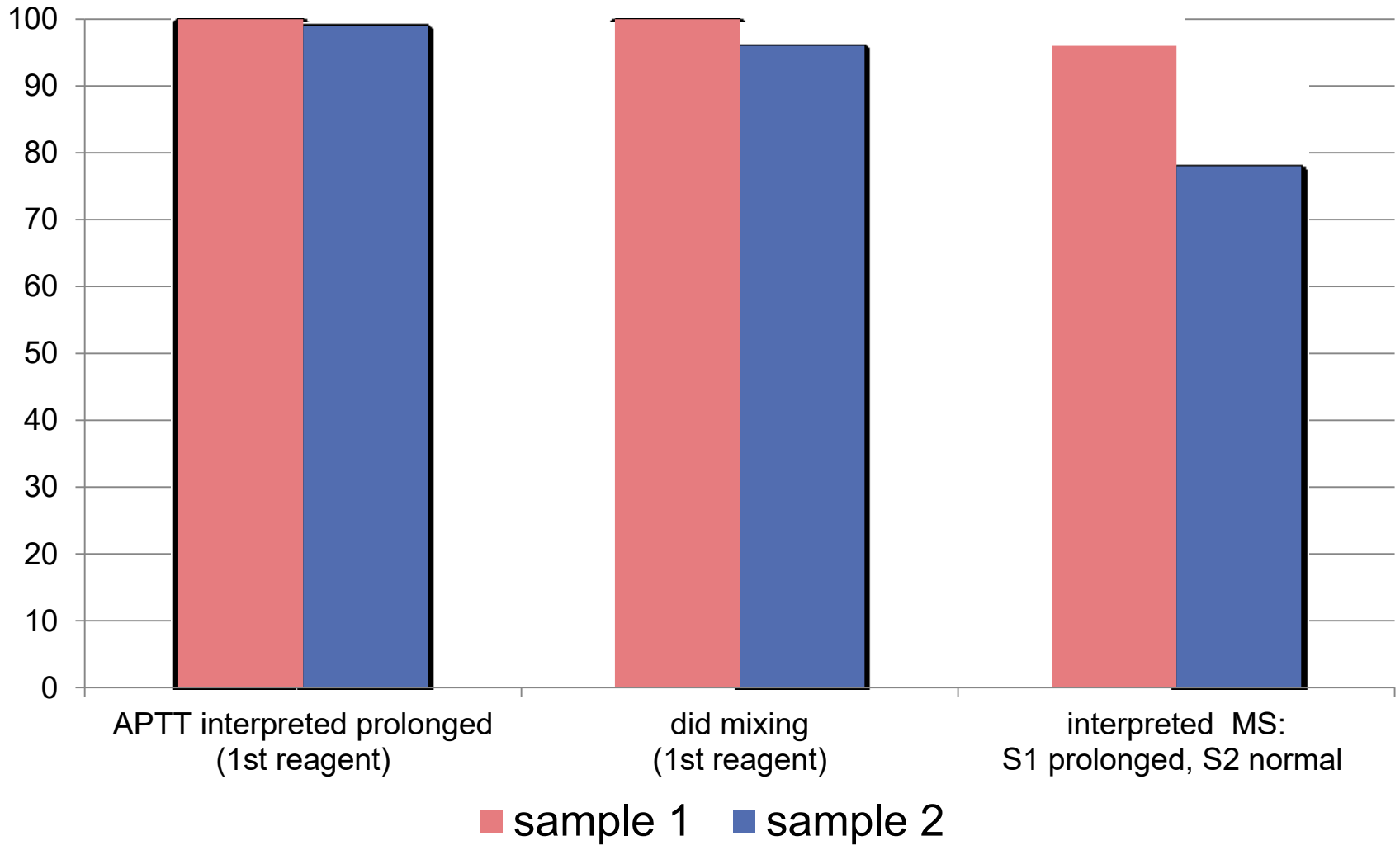


Result interpretations

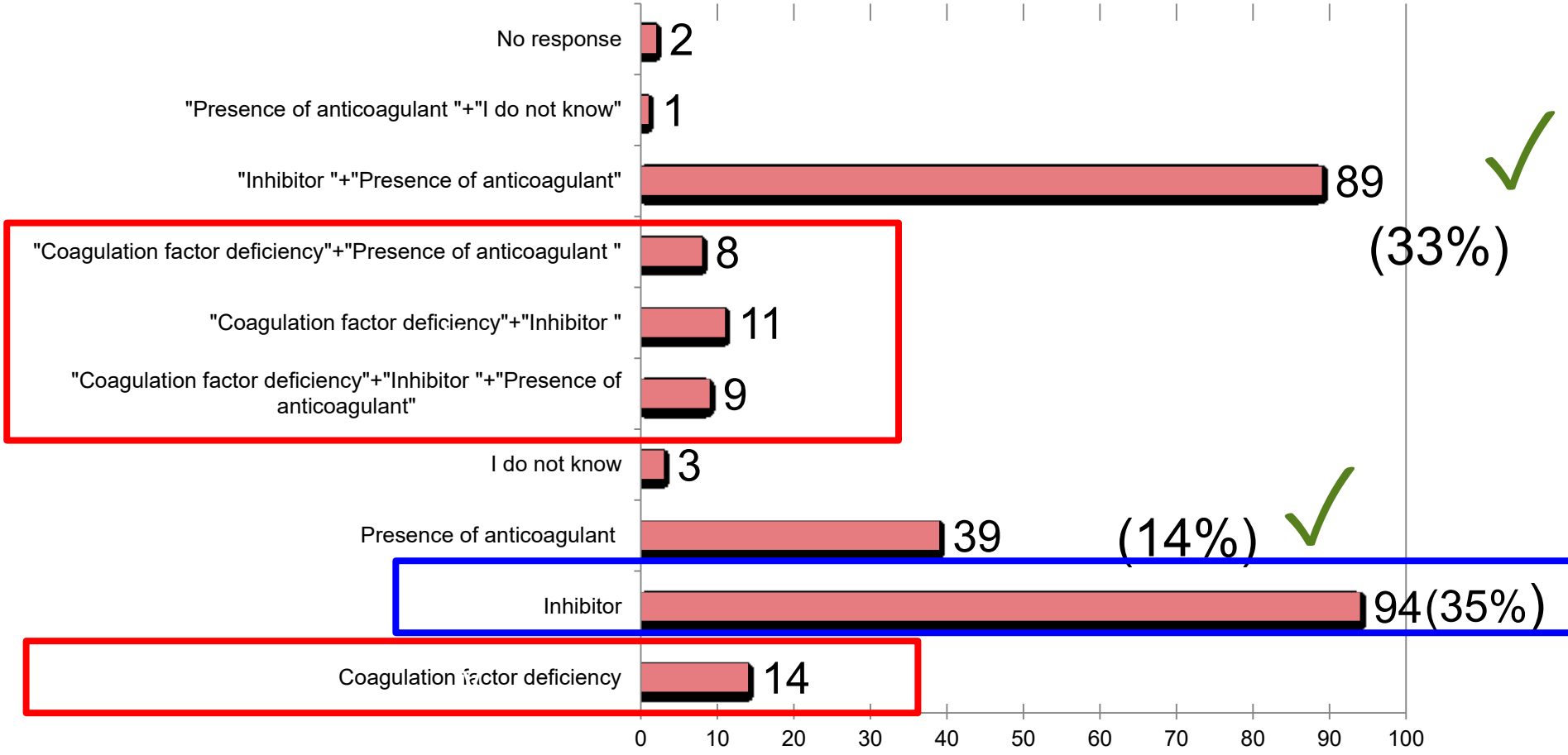
Added tests

Laboratory diagnoses

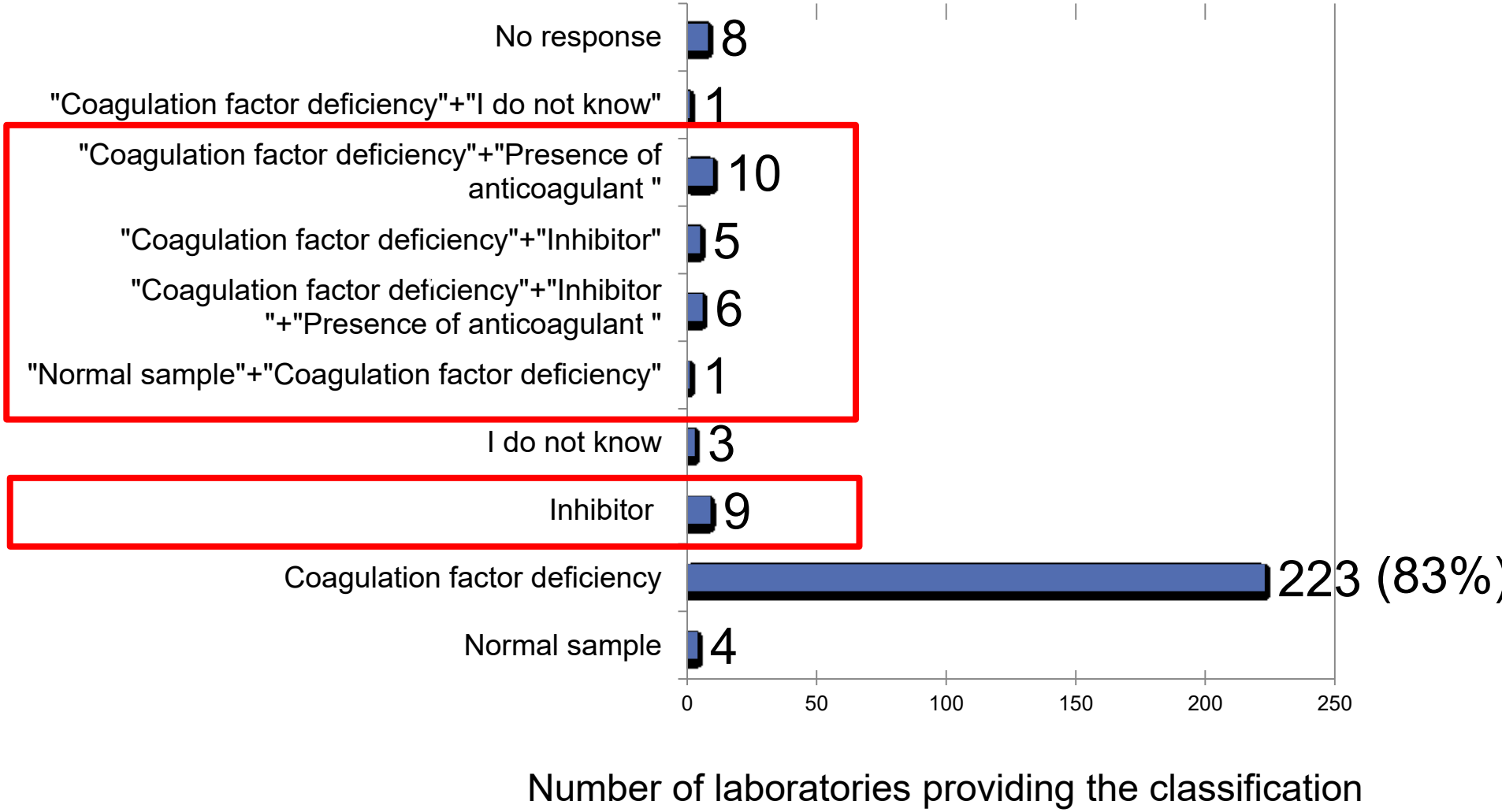
Analysis, interpretation



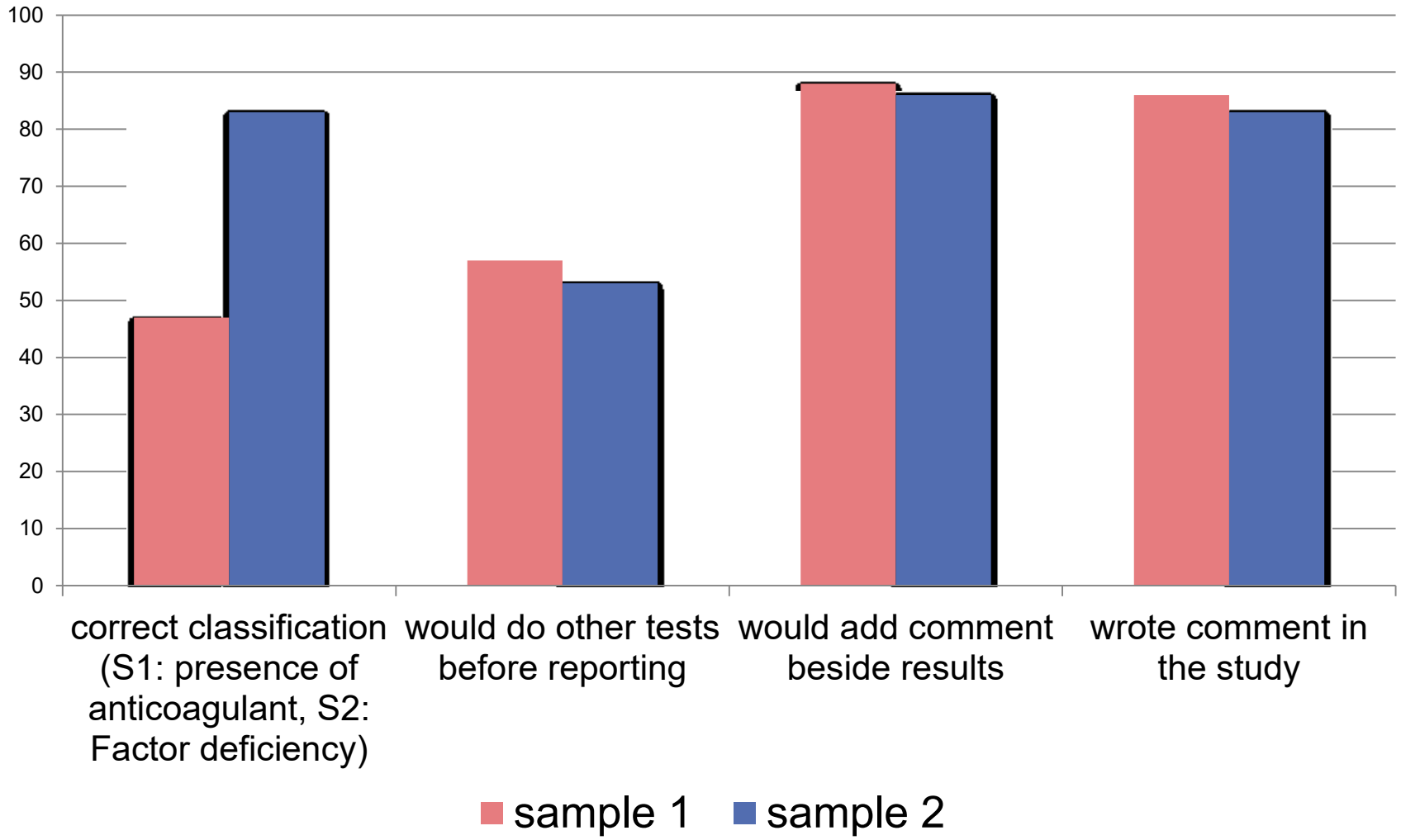
Classifications of case 1



Classifications of case 2



Classification and commenting



High quality interpretive comment: content and phrasing

Best practice recommendations on IC

Who?	**Only professionals with clear expertise in the particular laboratory field** should be charged with interpreting laboratory results. • The definition of standards of qualification and training for performing this activity are not harmonized due to global differences in institutions • Evidencing personal proficiency: assessment through an interpretive EQA exercise needs to be integral part.
When ?	**Comments should only be added when they will add clinical value** • a decision on management or treatment is indicated by the results in combination with the clinical details provided • a result is unexpected • a specific question has been posed but it is not obvious whether the results provide the answer • a clinician has requested a test with which they are not likely to be familiar.
What?	• Highlighting **analytical data;** • **pattern of the data applying medical knowledge** (The interpretation of laboratory information in the specific medical context of the patient distinguishes “patient-focused” reports from“ canned” comments.) **LAB DIAGNOSIS** • **Further actions to achieve diagnosis: ADVICE**
How?	• **Clarity:** clear wording, suggested wording for interpretive confidence • **Length** • Tracebility of the commentator • Comments should be linked to results (avoid its loss downstream) • Uncertainity should be indicated

Vasikaran et al. IFCC position paper. Clin Chem Lab Med 2016;

Method of IC evaluation

- Grading system according to content and phrasing

1. Relevant analytical findings
2. Laboratory diagnosis
3. Advice to the clinician

correct/partially correct/ wrong/missing

4. Length
5. Clarity

adequate/not

- Translations by native experts
- Evaluation in expert panel: consensus of 6 experts

ID of responding lab	1.Analytical data (C/P/W/M)			2. Lab dg (C/P/W/M)			3. advice to the clinician (C/P/W/M)			4. Length (A/N)			5. Clarity (A/N)		
	Expert 1	Expert 2	consensus	Expert 1	Expert 2	consensus	Expert 1	Expert 2	consensus	Expert 1	Expert 2	consensus	Expert 1	Expert 2	Sum
H-001	C	P	P	P	W	No cons	M	M	M	A	N	N	N	N	N

Case 1: Evaluation quality of IC

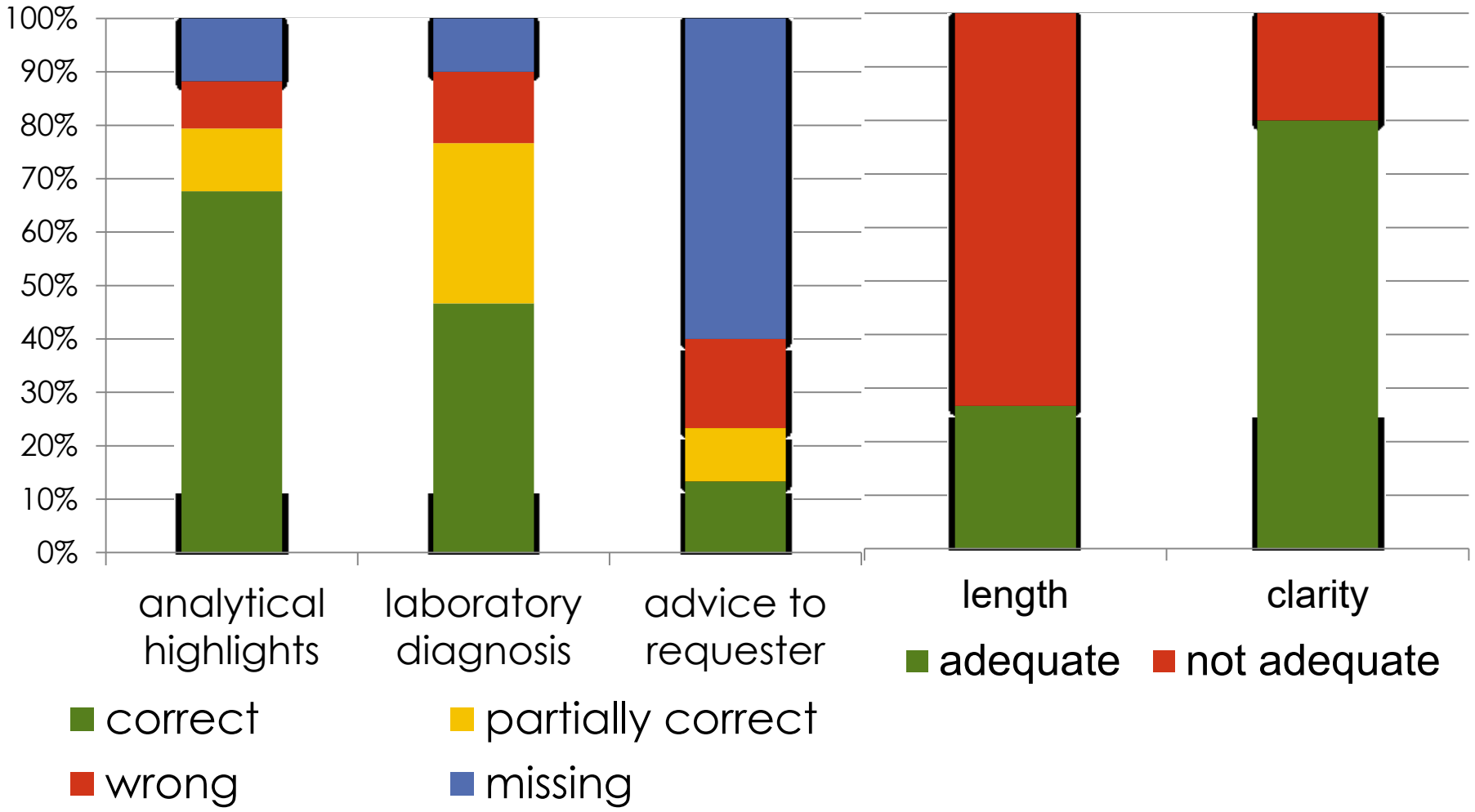
	Analytical result	Interpretation	Advice to clinician
Correct	APTT ↑ and no correction in mixing and tests indicating UH presence or Both APTT, TT↑ and TT with polybren normal	UH contamination or suspicion of UH contamination (or LA or unknown DTI)	request new sample without heparin contamination
Partially correct	APTT ↑ correction in mixing or UH tests not mentioned	only LA or unknown DTI	request new sample
Wrong	APTT normal or APTT ↑ and correction in mixing studies	factor deficiency	anything else
Missing	not mentioned in the IC	no diagnosis given in IC	no advice given in IC

Case 2: Evaluation quality of IC

	Analytical result	Interpretation	Advice to clinician
Correct	APTT prolonged and correction in mixing studies	Factor deficiency	measure factors and or refer to the haematologist
Partially correct	APTT prolonged MS not mentioned	X	Refer to the haematologist
Wrong	-APTT normal -APTT prolonged and no correction in mixing studies	inhibitor	inhibitor investigations
Missing	not mentioned in the IC	no diagnosis given in IC	no advice given in IC

CASE 1: SAMPLE WITH HEPARIN (UH) CONTAMINATION

n=30 laboratories, from one country one expert



Conclusion

- This survey covered TTP in a routine haemostasis investigation

- Differences in lab protocols: exclusion preanalytical error type UH contamination is often not part of it
- Analytical: 100-96% labs found APTT prolonged
- Postanalytical:

Added testing

  - No tests for UH detection in many labs
  - vast majority of labs do MS (100, 96%) and interpret correctly on analytical level (96, 78%)

Classification and IC

  - Classifications were correct in 47, 83%
  - IC provided in >80% of labs
  - Content and phrasing of comments showed heterogeneity

Can you tell me the reason of my patient' bleeding from this sample (based on the provided clinical context) ?

Case 1

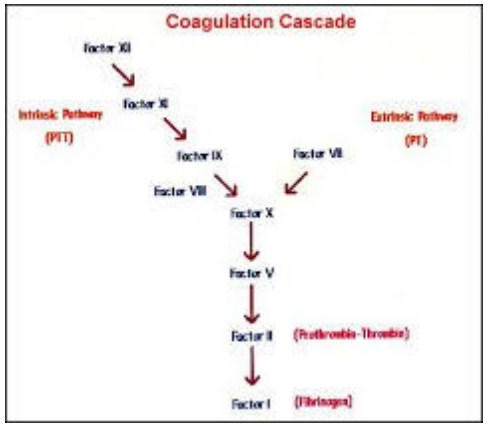
I cannot answer if your patient' haemostasis is altered until we exclude UH and DTI effect!

Correct Classification: 47%

Correct IC?

Case 2

Yes, your patient can have a bleeding disorder. We should investigate his haemostasis further!



Correct classification 83%

Correct IC?

Harmonisation of IC in haemostasis is needed