

Moving from analytical to diagnostic quality

A study on acquired inhibitors



ECAT FOUNDATION

External quality Control of diagnostic Assays and Tests
with a focus on Thrombosis and Haemostasis

ECAT 14.11.2014

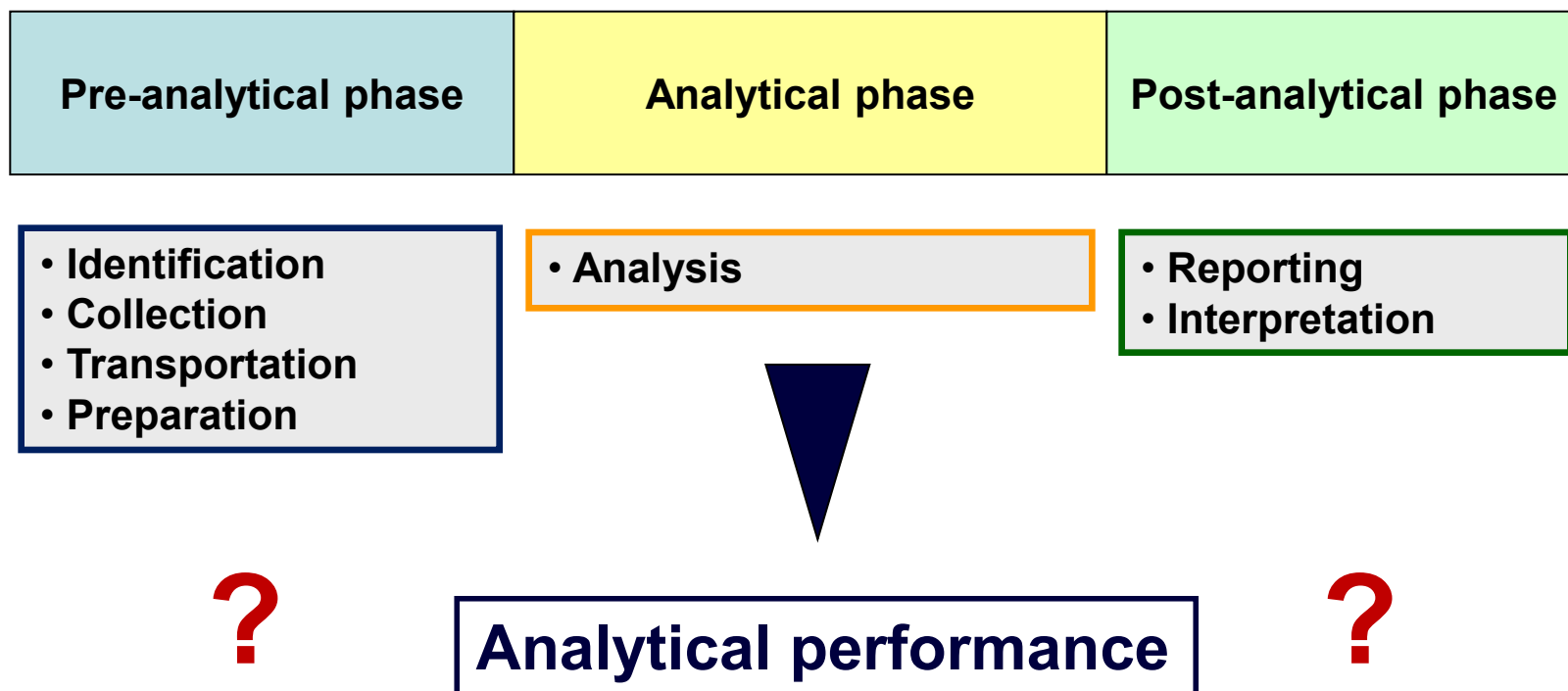
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Disclosures

- Unconditional grant from NOVO Nordisk



External Quality Assessment

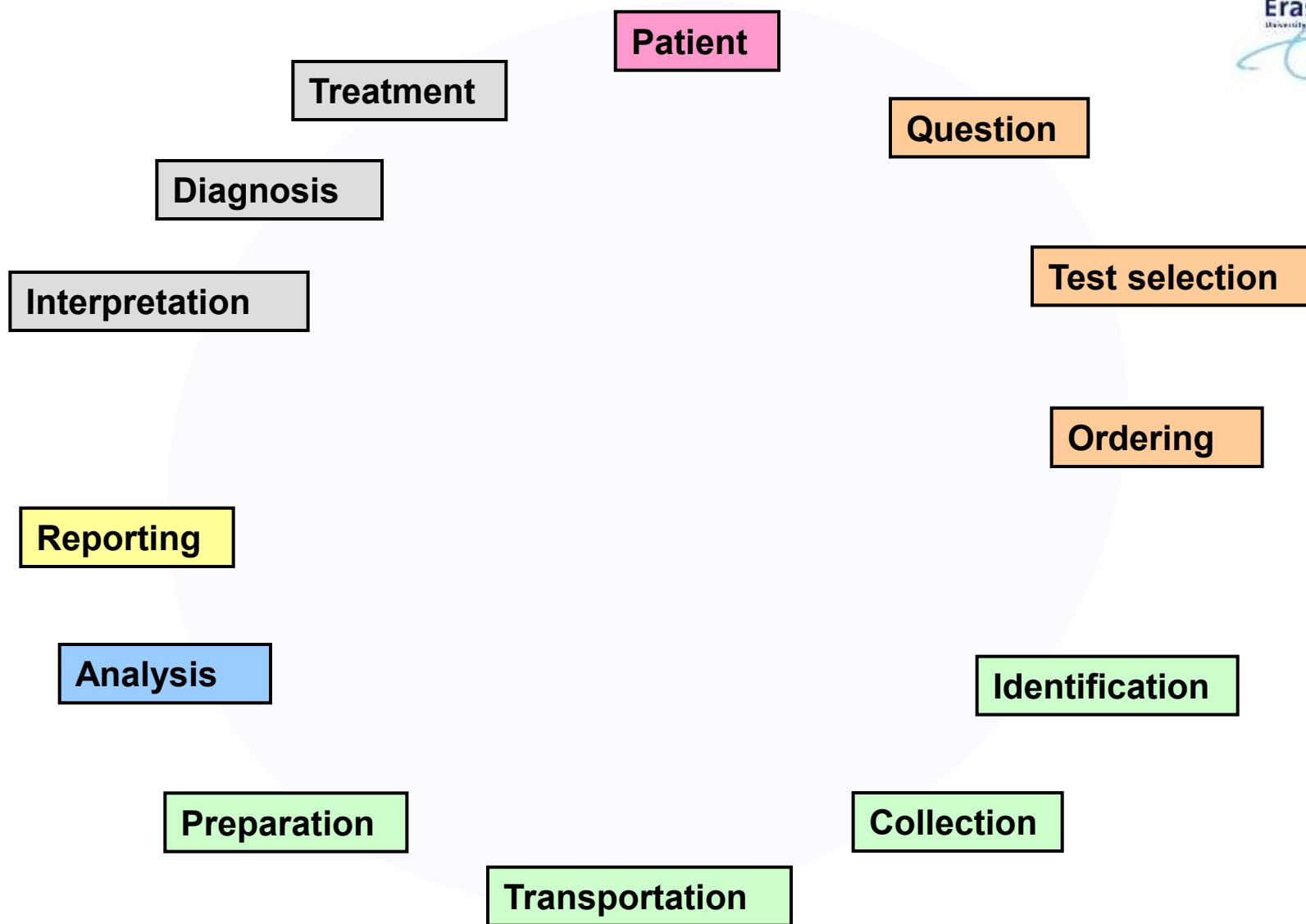


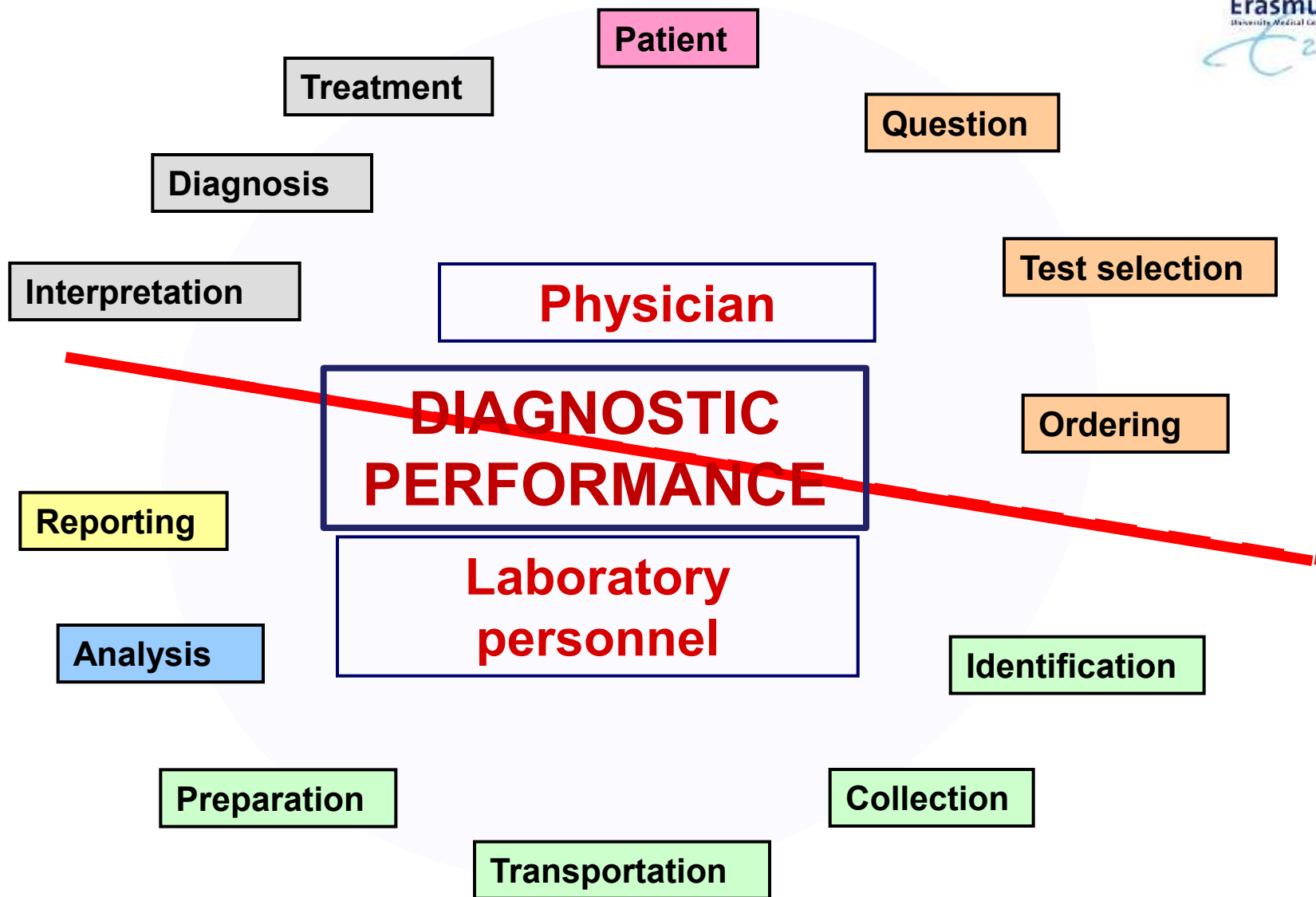
ISO STANDARD 15189

5.6.4 The laboratory shall participate in interlaboratory comparisons such as those organized by external quality assessment schemes. Laboratory management shall monitor the results of external quality assessment and participate in the implementation of corrective actions when control criteria are not fulfilled.

External quality assessment programmes should, as far as possible, provide clinically relevant challenges that mimic patient samples and have the effect of checking the **entire examination process, including pre- and post-examination procedures.**







CASE-BASED EQA

Scope of the project:

Correct diagnosis based on both clinical information and laboratory data

- Interpretation of clinical information
- Evaluation of test request
- Test performance
- Interpretation of laboratory data



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Nederland



Pilot: 10 centers
Dutch study: 34 centers

Reference center:
Erasmus MC Rotterdam

A center could only participate if both the clinicians and clinical chemist participated

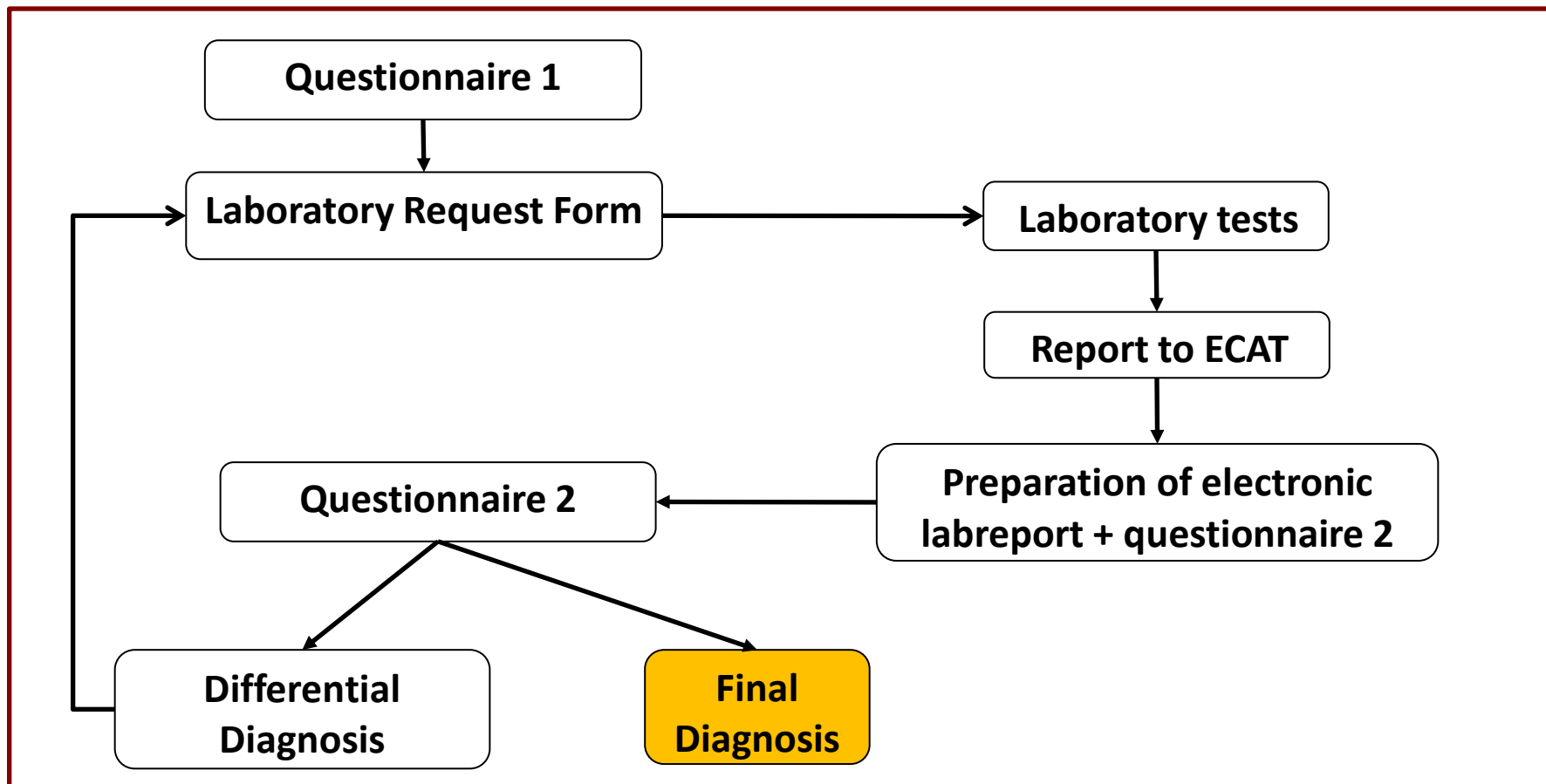


PHYSICIAN

Patient Case

LABORATORY

Plasma



Case Study

VRAAG

***2. Wat zou u nog meer willen weten ten aanzien van de historie van deze patiënt?**
[meerdere keuzes zijn mogelijk]

Familie-anamnese

Is er eerder wel eens een overloopte of langdurige

Heeft patiënt gemakkelijk bloedneuzen of tandvles

Zijn er andere aandoeningen waarvoor patiënt nu bi

Geen van deze

Case Study

CASUS (vervolg)

De familie-anamnese van deze patiënt is blanco en het antwoord op de overige vragen is ontkennend. De anamnese is een zeer belangrijk onderdeel bij het onderzoek naar een hemorrhagische diathase. Een kamout daarbij is of er eerder bloedingproblemen zijn geweest operatieve of tandheelkundige ingrepen, andere familieleden wijst op een aangeb dat dit zich nu pas zou openbaren.

Case Study

VRAAG

***3. Wat zou u nog meer willen weten ten aanzien van de klachten van deze patiënt?**
[meerdere keuzes zijn mogelijk]

geneesmiddelengebruik

buikpijn

misselijkheid

gewrichtsklachten

bloed bij de ontlasting

moeheid

gewichtswilke

koorts

Case Study

CASUS (vervolg)

Bij deze patiënt is het antwoord op al uw vragen ontkennend.

De meest voorkomende oorzaak van een verworven stoomis in de hemostase is gebruik van geneesmiddelen zoals NSAID's, aspirine, prednison, heparine of vitamine K-antagonisten. Vragen naar gebruik van geneesmiddelen is daarom een noodzaak.

U kunt naar moeheid of gewichtsverlies vragen om een eerste indicatie te krijgen of er mogelijk sprake kan zijn van een maligniteit met secundaire stollingsstoornissen.

Klachten in de bovenbuik of tractus digestivus kunnen wijzen op een leverfunctiestoornis met secundair tekort aan stollingsfactoren.

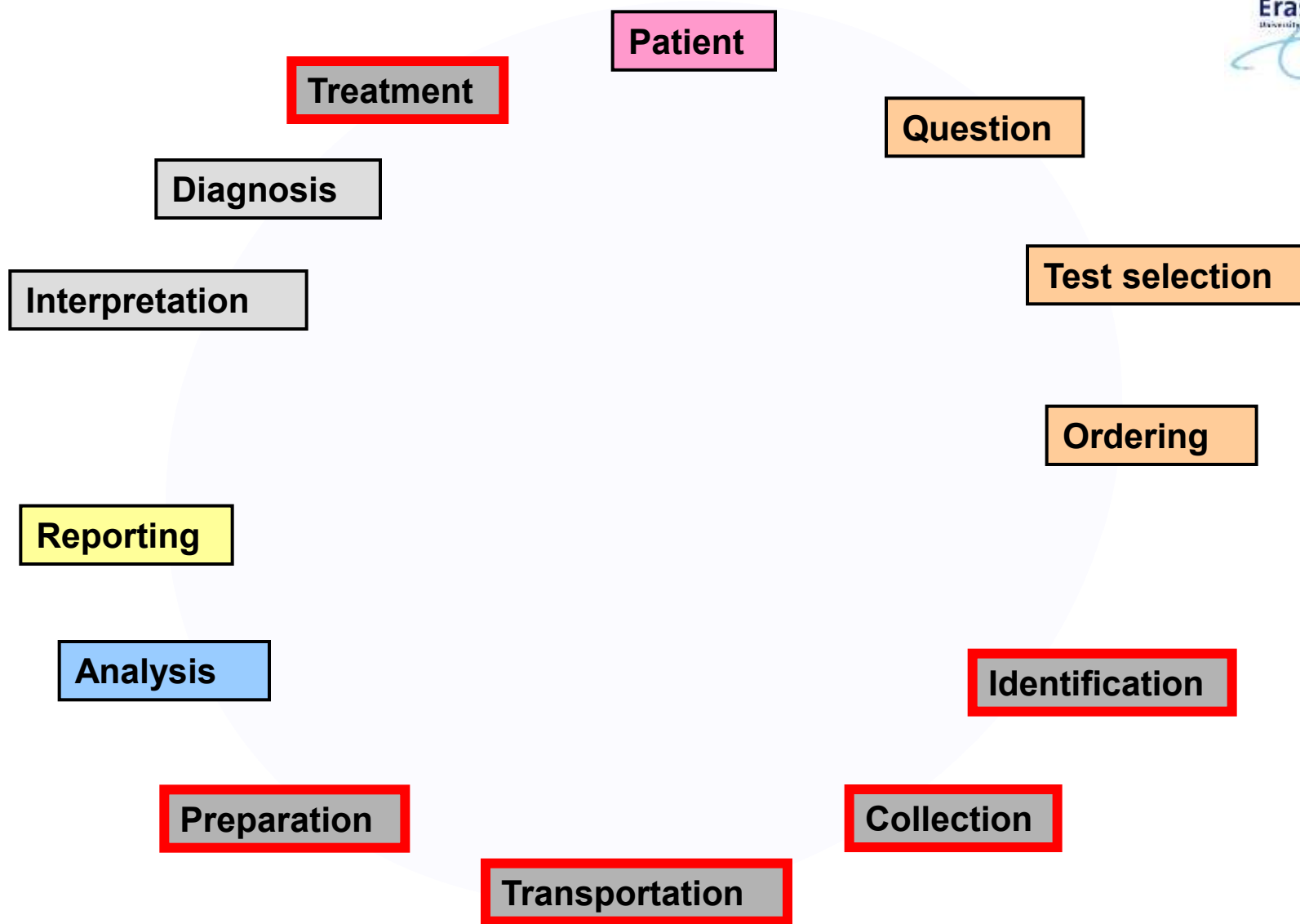
Niet-rheumatische gewrichtsklachten kunnen een aanwijzing zijn voor hemofilie A of B, hoewel deze doorgaans op veel jongere leeftijd wordt ontdekt.

De overige vragen helpen u niet om de kortste weg naar een juiste diagnose te vinden.

Questionnaire includes questions on:

- patient history
- clinical symptoms
- physical examination
- potential differential diagnosis





CASE DESCRIPTION

A general practitioner refers the following patient to you:

An apparently healthy Caucasian man of 67 years old

Increased bruising since a few days. No trauma.

Question: Any coagulation disorder?

Hematological parameters: normal

Prothrombin Time: normal

First examination:

At the left-hand side and on the back several purpura and ecchymoses.

These came spontaneously approx. 5 days ago. The bruising increases. The largest spot is now 15 cm.

These symptoms were not seen before.



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Differential diagnosis

Categories:

- Trauma
- Primary Hemostasis
- Secondary Hemostasis
- Other reasons

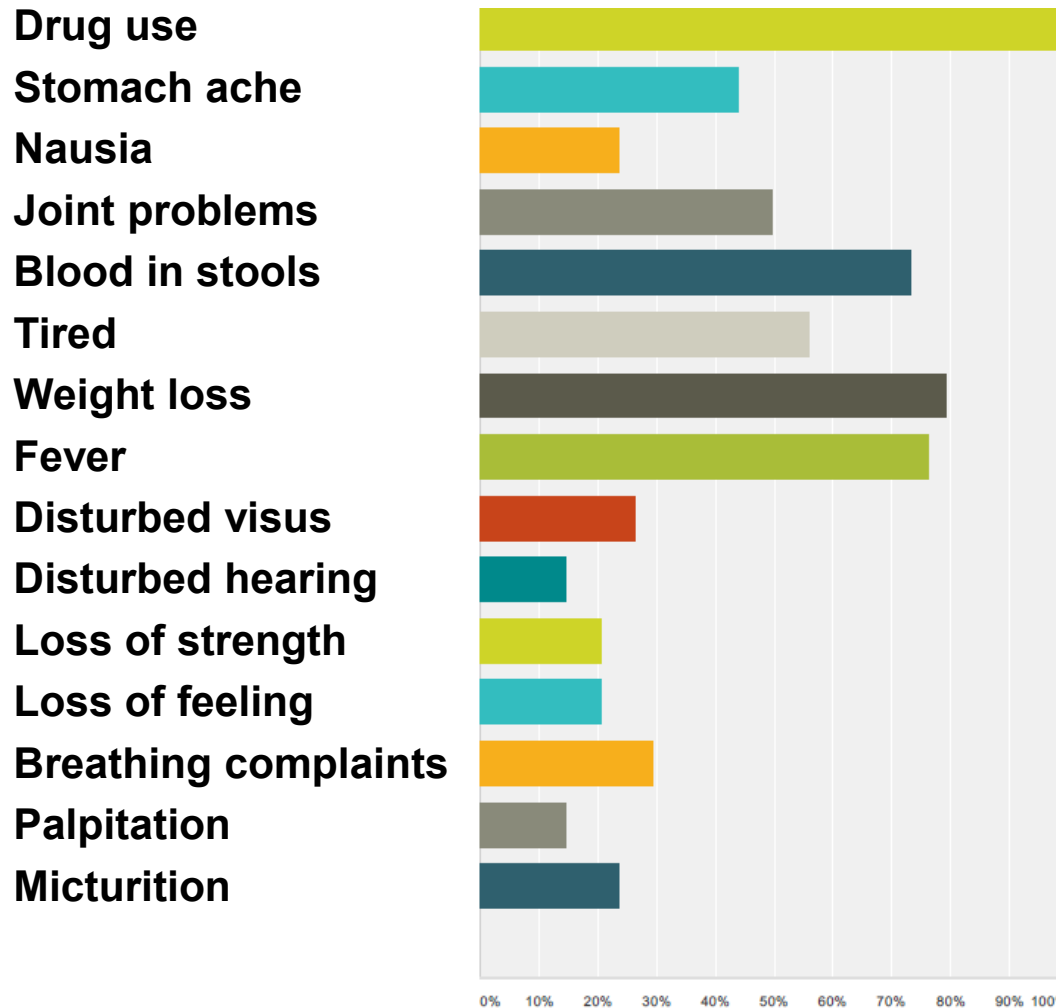


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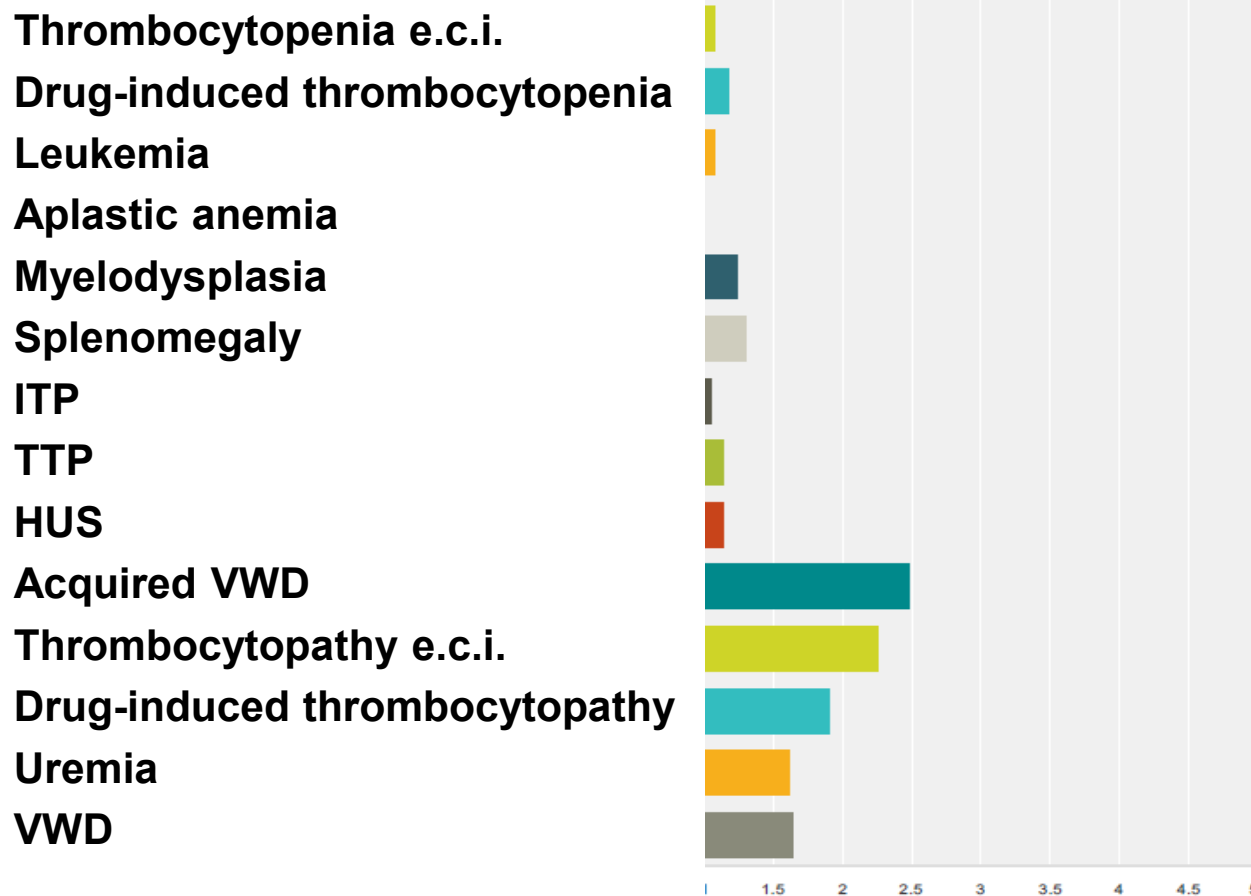
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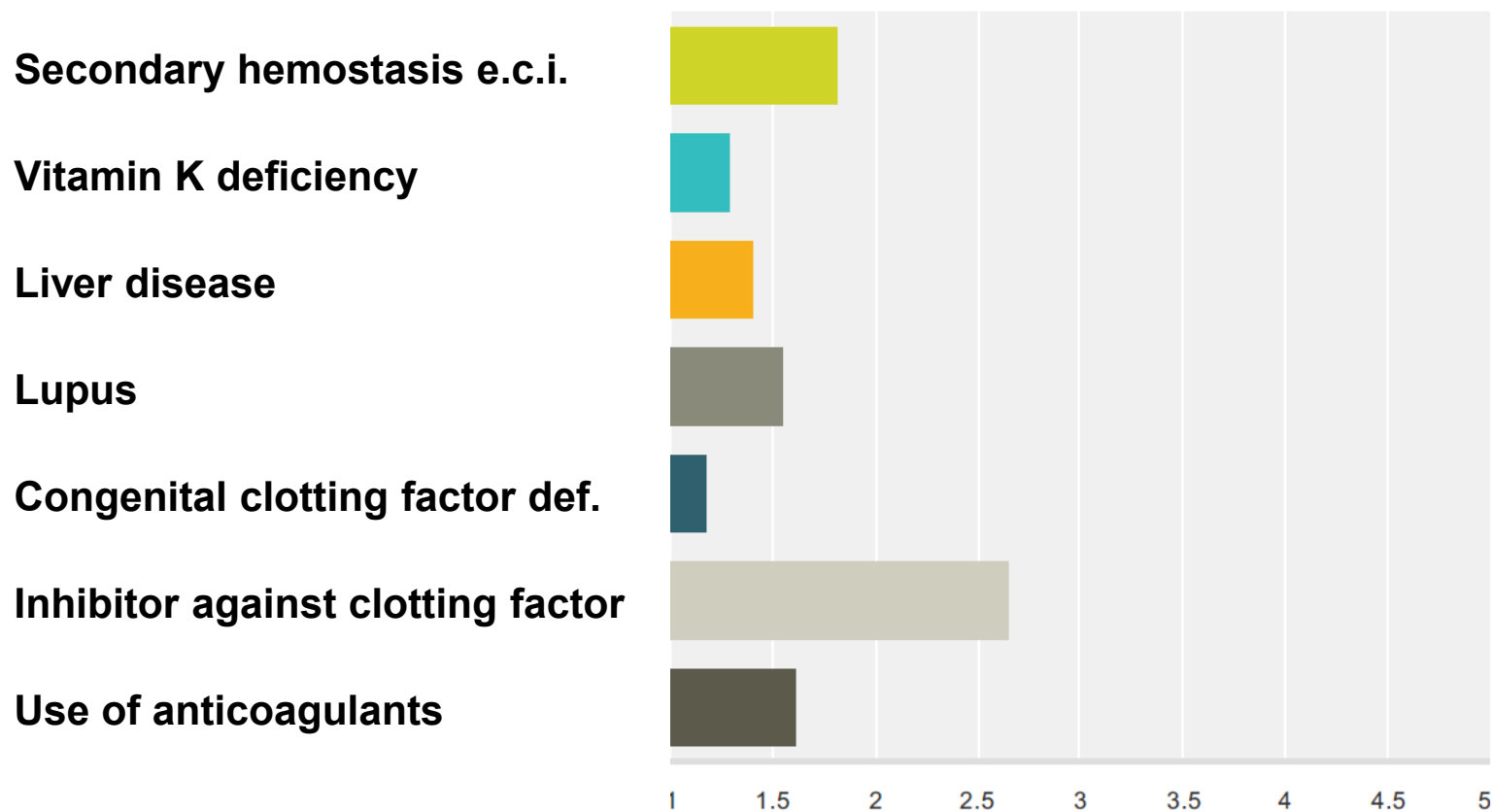
Additional patient information?



Primary hemostasis defects (round 1)

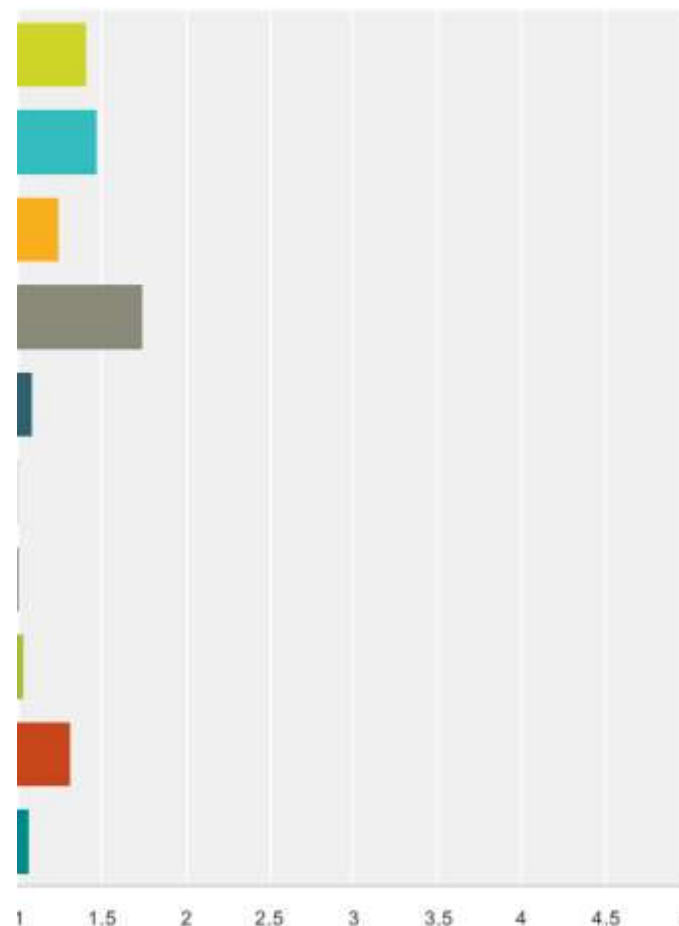


Secondary hemostasis defects (round 1)

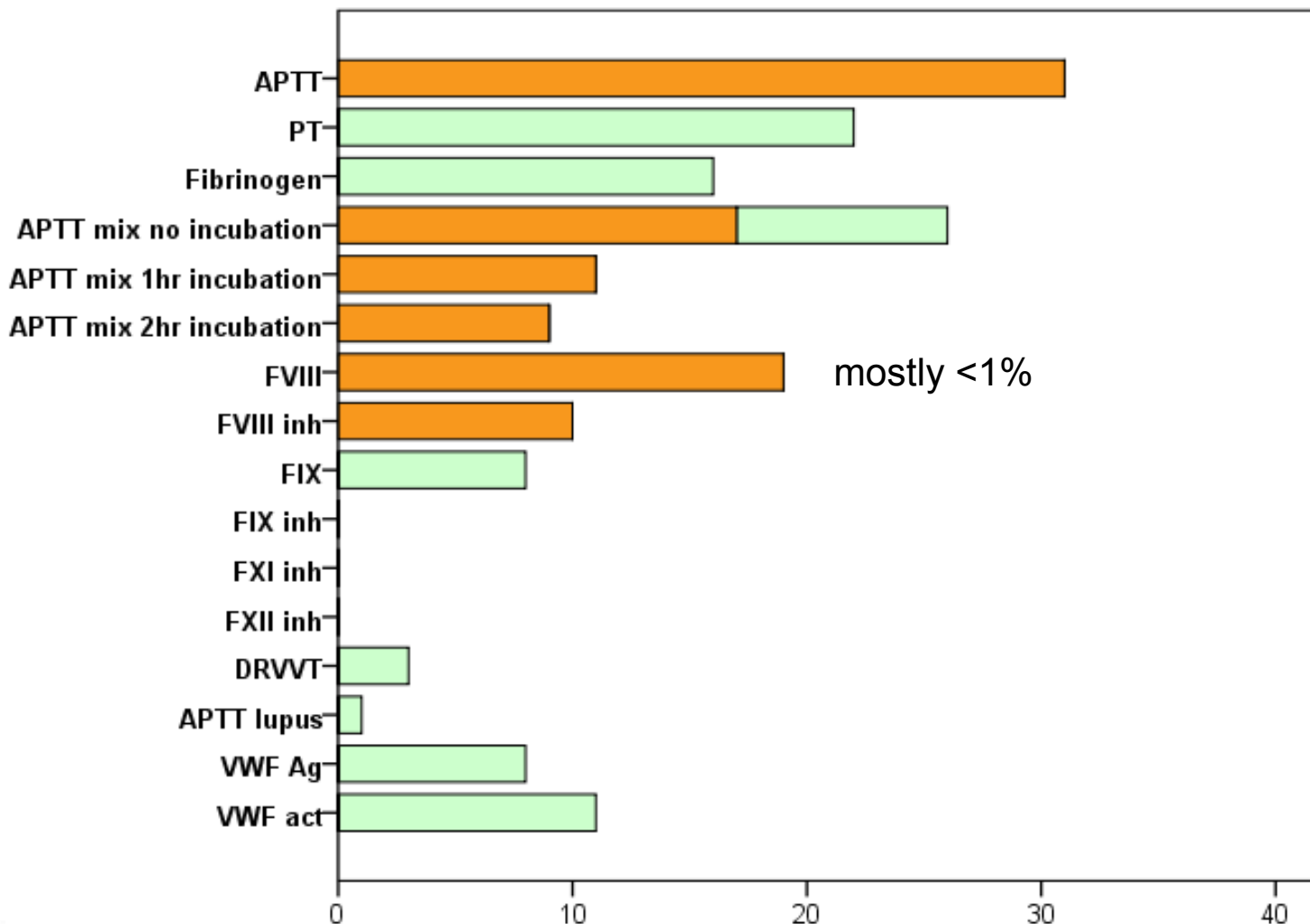


Other reasons (round 1)

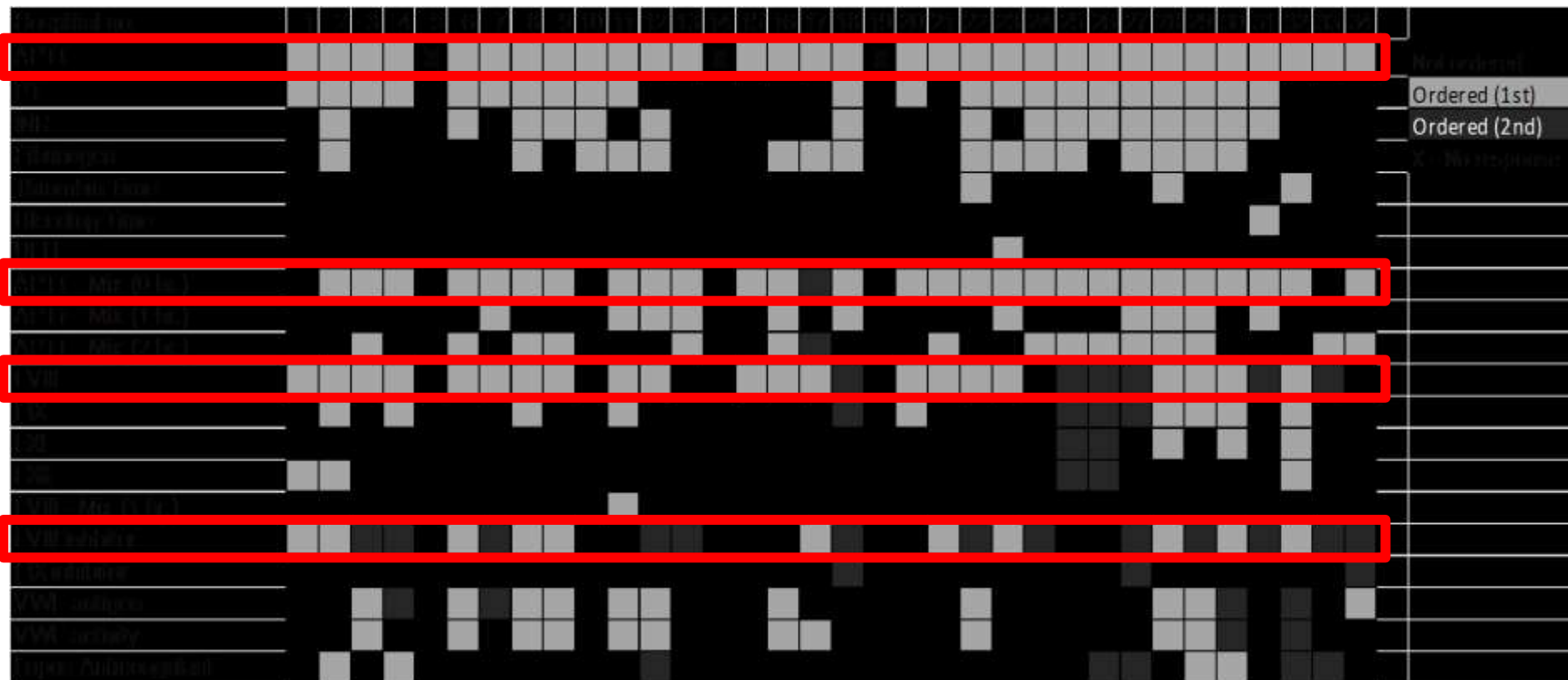
- Vascular e.c.i.
- Vitamin C deficiency
- Henoch-Schönlein purpura
- Amyloïdosis
- Ehlers-Danlos syndrome
- Osteogenesis imperfecta
- Marfan syndrome
- Hereditary hemorrhagic telangiectasia
- DIC
- sepsis



Laboratory results (round 1)



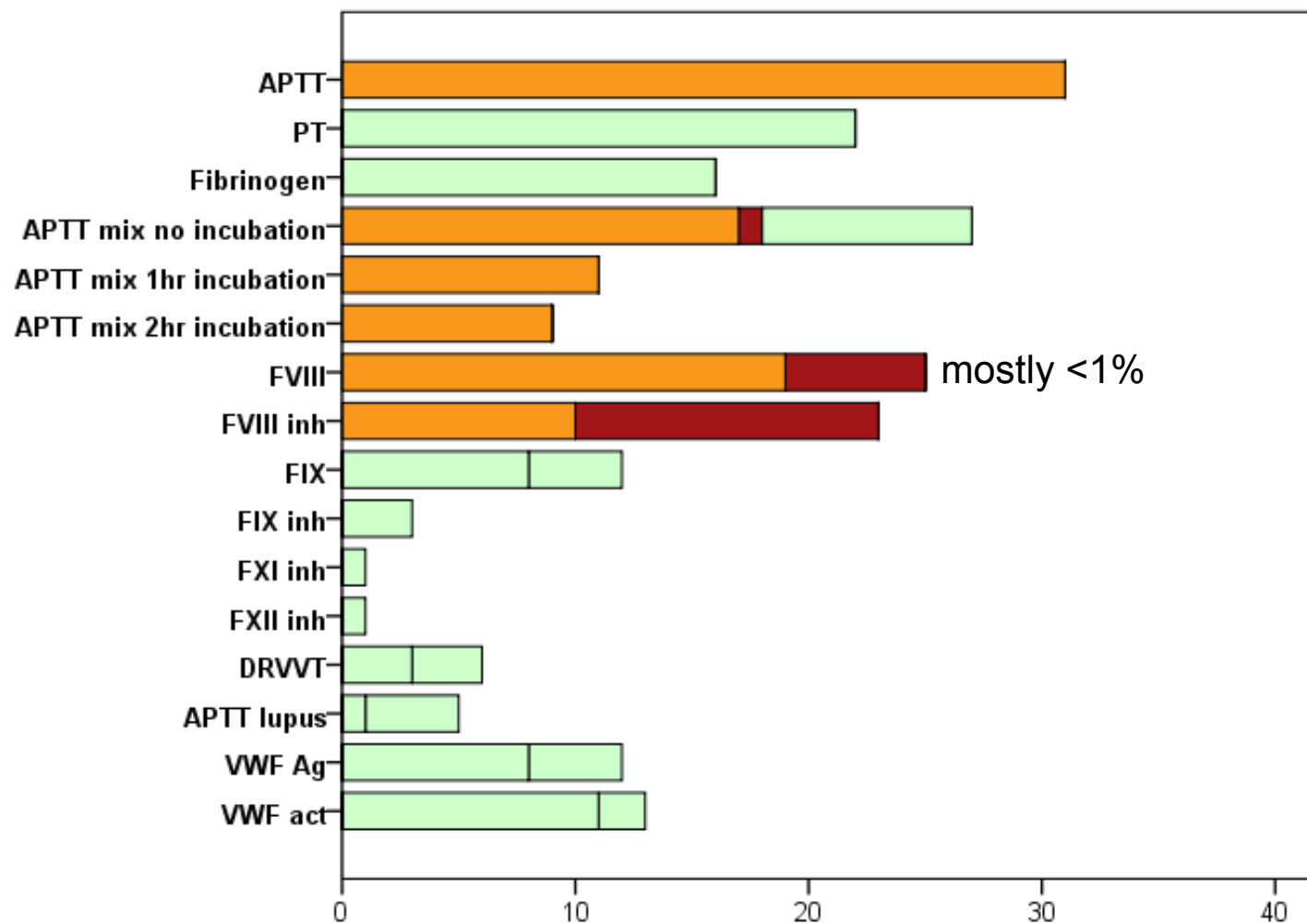
Ordered laboratory tests



Ordered (1st)
Ordered (2nd)



Laboratory results (round 2)



Main laboratory results

Parameter	Mean test result	Range
APTT ratio	2.52	2.09 – 3.25
APTT – mix (0 hr.)	1.15	0.83 – 1.35
APTT – mix (1 hr.)	1.35	1.02 – 1.53
APTT – mix (2 hr.)	1.63	1.09 – 2.68
Factor VIII	n.a.	< 1 – 4%
Factor IX	113%	94 – 132%
FVIII Inhibitor	4.4 BU/mL	0.6 – 8.5 BU/mL
Lupus Anticoagulant	Negative	
VWF antigen	150%	128 – 172%
VWF activity	120%	100 – 128%



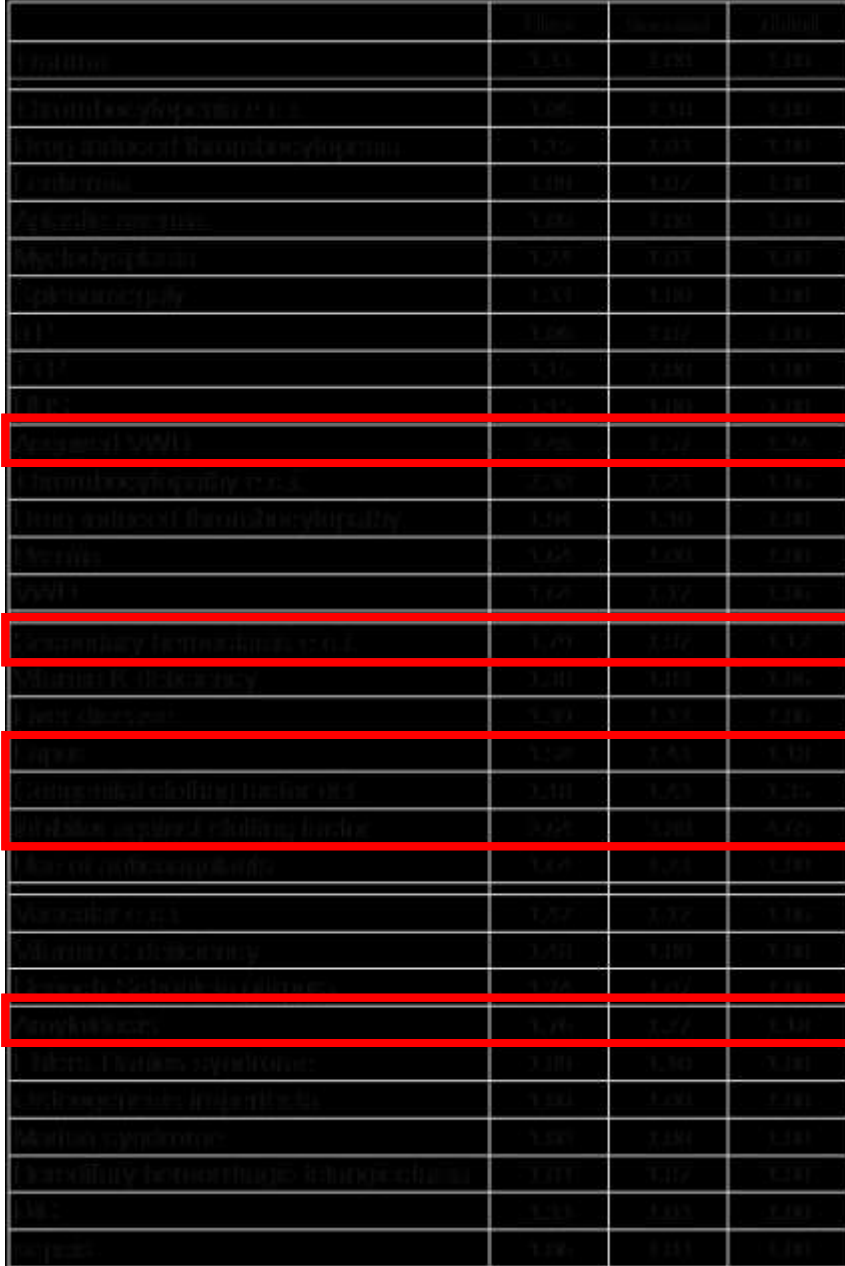
Central Laboratory characteristics

Parameter	Test result	Reference Range
APTT		
APTT ratio		
PT		
INR		
Fibrinogen		
Thrombin Time (10 IE)		
APTT – mix (0 hr.)		
APTT – mix (1 hr.)		
APTT – mix (2 hr.)		
Factor VIII		
Factor IX		
Factor XI		
FVIII – mix (0 hr.)		
FVIII – mix (0.5 hr.)		
FVIII – mix (1 hr.)		
FVIII Inhibitor		
Lupus Anticoagulant		
VWF antigen		
VWF activity		



Mean likelihood of the differential diagnosis per cycle.

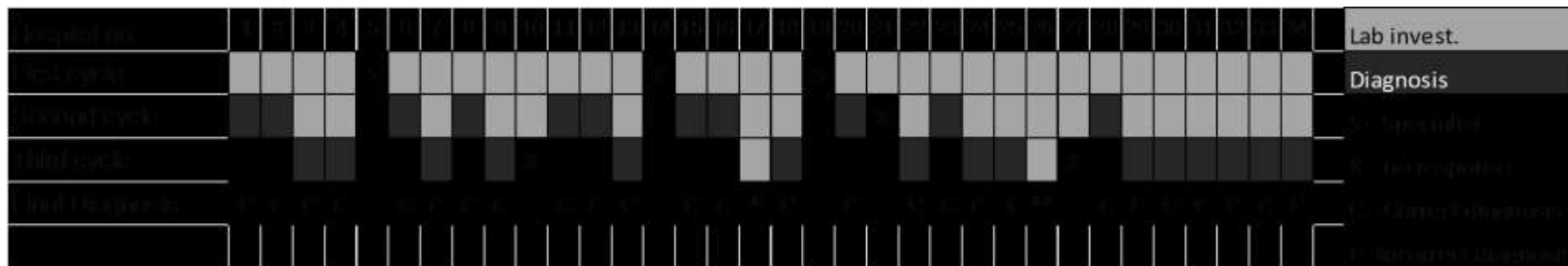
(cycle 1: n=33)
(cycle 2: n=32)
(cycle 3: n=17)



The image shows a large grid of data, likely a table, with several rows highlighted in red. A red arrow points to one of the highlighted rows. The grid is mostly black with white text, which is mostly illegible due to the low resolution and blurring. The highlighted rows appear to be in the middle and bottom sections of the grid.



Conclusion after each cycle



CASE-BASED EQA

Strengths:

- Focus on the entire diagnostic process.
- Both the physician and the laboratory is included.
- EQA challenge is based on a real clinical scenario

Weaknesses:

- Not all aspects of the total testing process can be included (e.g. sample collection and preparation).
- The physician is guided by an electronic questionnaire and not completely “self-supporting”.
- Potential selection of participating physician.



FUTURE DEVELOPMENTS

Based on the experiences so far we will further develop this type of EQA.

- **Further optimizing the flow of the survey, e.g. cross-talk between physician and laboratory.**
- **Other type of disorders.**
- **Developing electronic interactive tools**



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CONCLUSION

Diagnostic EQA, based on real case scenario's and focussing on the entire diagnostic process, may be an important addition to the current EQA approaches which mainly focus on analytical quality or separate parts of the pre- and post-analytical phase.



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Acknowledgement

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THANK YOU FOR YOUR ATTENTION

