Calculation of APTT and PT Reference Intervals from Patient Data and Evaluation of Test Utilisation in Surgical Patients

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Introduction

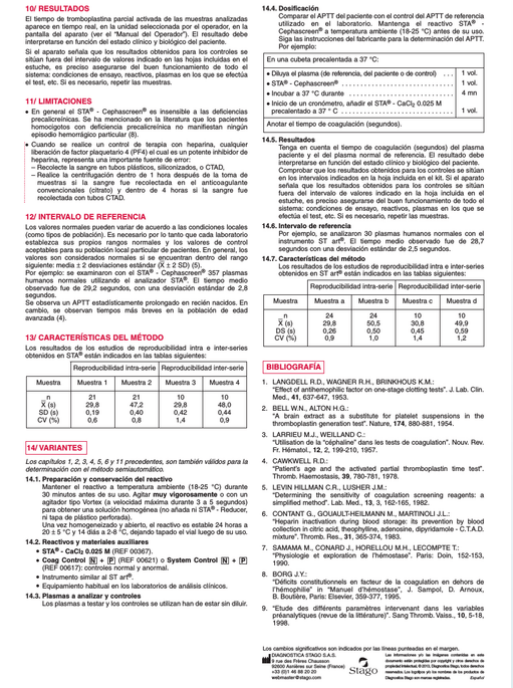
- Reference intervals (RI) are useful for providing information to clinicians for
- ✓ **screening**
- ✓ **decision- making**
- ✓ **follow up disease**
- Results supported by RI ➡ aid interpretetion
- Clinicians compare the test results and RI to estimate patient's health status
- The concept of RI is well defined and is based on

fixed percentage of reference population within interval described by upper and lower reference limits (RLs)

Generating the RIs is **responsibility** for all laboratories

use RI derived elsewhere (kit insert)*

determine their own interval for use with their population and analytical methods



- Recommended approach is having **own RI** for every laboratories.
- Population, ethnic, diet, laboratory, technique and selection of reference groups could be different.
- * Published RIs may not be compatible with existing analytical methods and tested populations

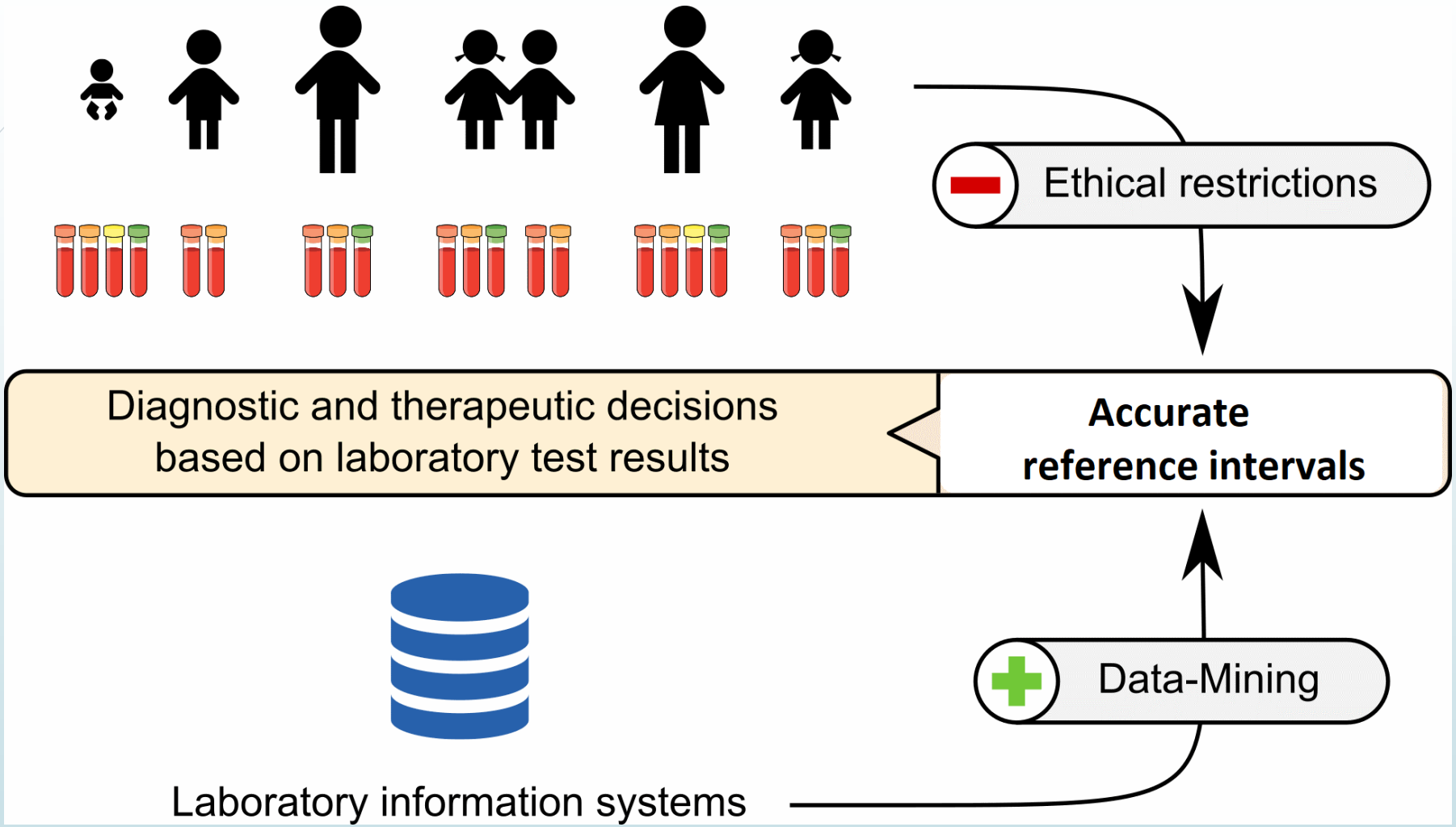
Defining the RI

Direct approach

- Recommended way
- Reference population selected and sample then analyzed for this purpose
- Randomly selected patients
- Outlier exclusions must be well defined
- Difficulty with the definition of health and the prevelance of subclinical case (selection bias)
- Time-consuming
- Expensive
- Patient convenience factors
- Small number of cases may not reflect biologocial diversity
- Clinical and Laboratory Standart Institute EP28-A3C

Indirect approach

- Alternative way
- Results from specimen from routine purposes
- All results in database can be used and don't have to belong the reference population
- Patients come for screening, diagnosting or monitoring
- Faster
- Cheaper
- No patient inconvenience, discomfort
- No risk of ass. with generating new patient health info
- Large number of samples
- Same preanalytical and analytical process
- **Possible effects on disased subpopulation (contamination)xx**
- **Influenced by extreme results**


Ethical restrictions
Diagnostic and therapeutic decisions
based on laboratory test results
Accurate
reference intervals
Data-Mining
Laboratory information systems

Systematic preoperative testing

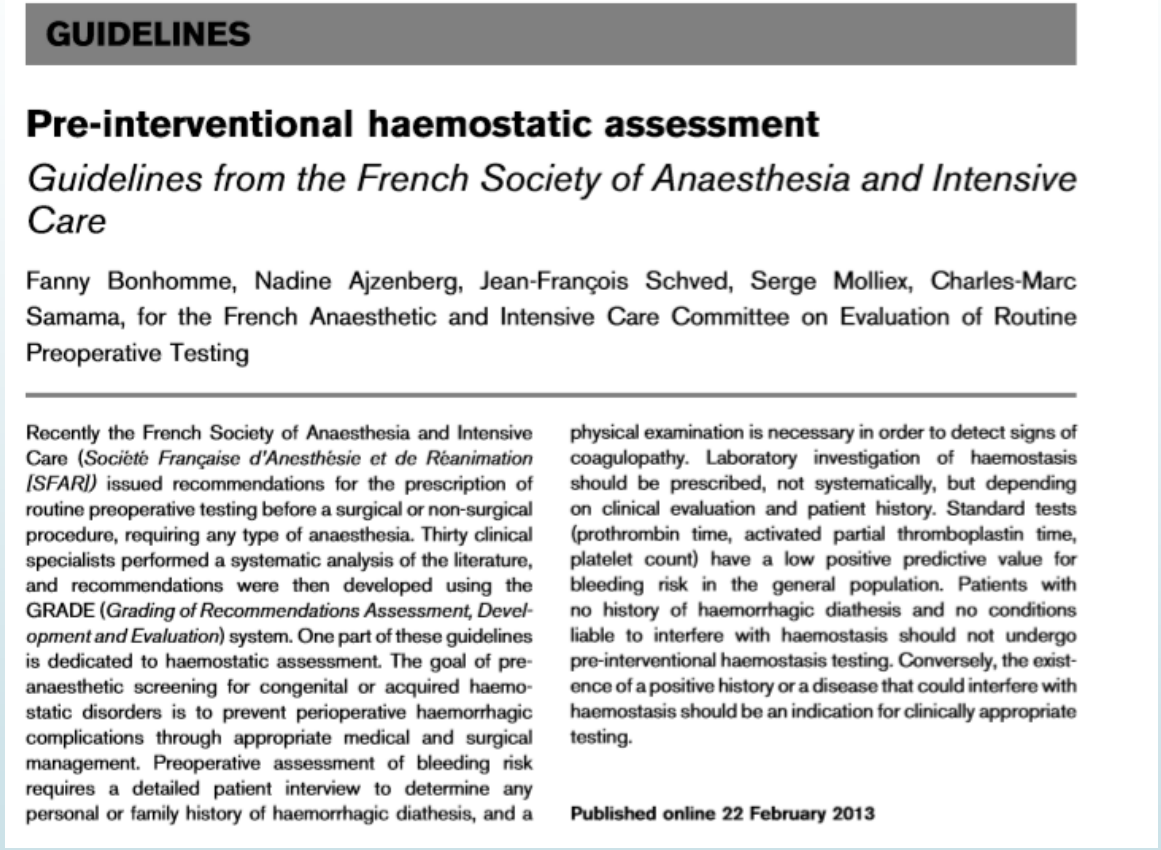
- Routine testing is part of preoperative assessment designed to

1) reduce the risks associated with the procedure and/or anaesthesia;

2) detect unsuspected conditions

3) provide a reference for postoperative assessment;

4) evaluate the risk of postoperative complications with an independent predictive value



GUIDELINES

Pre-interventional haemostatic assessment

Guidelines from the French Society of Anaesthesia and Intensive Care

Fanny Bonhomme, Nadine Ajzenberg, Jean-François Schved, Serge Molliex, Charles-Marc Samama, for the French Anaesthetic and Intensive Care Committee on Evaluation of Routine Preoperative Testing

Recently the French Society of Anaesthesia and Intensive Care (*Société Française d'Anesthésie et de Réanimation [SFAR]*) issued recommendations for the prescription of routine preoperative testing before a surgical or non-surgical procedure, requiring any type of anaesthesia. Thirty clinical specialists performed a systematic analysis of the literature, and recommendations were then developed using the GRADE (*Grading of Recommendations Assessment, Development and Evaluation*) system. One part of these guidelines is dedicated to haemostatic assessment. The goal of pre-anaesthetic screening for congenital or acquired haemostatic disorders is to prevent perioperative haemorrhagic complications through appropriate medical and surgical management. Preoperative assessment of bleeding risk requires a detailed patient interview to determine any personal or family history of haemorrhagic diathesis, and a physical examination is necessary in order to detect signs of coagulopathy. Laboratory investigation of haemostasis should be prescribed, not systematically, but depending on clinical evaluation and patient history. Standard tests (prothrombin time, activated partial thromboplastin time, platelet count) have a low positive predictive value for bleeding risk in the general population. Patients with no history of haemorrhagic diathesis and no conditions liable to interfere with haemostasis should not undergo pre-interventional haemostasis testing. Conversely, the existence of a positive history or a disease that could interfere with haemostasis should be an indication for clinically appropriate testing.

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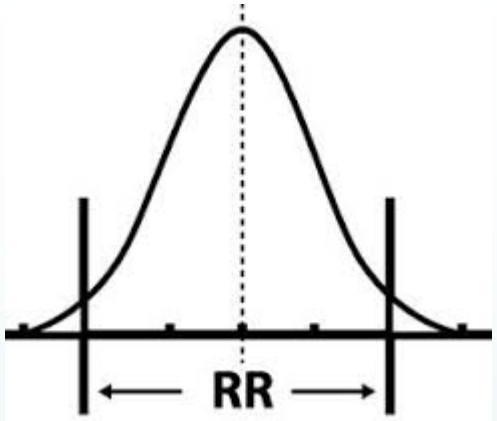
Preoperative testing is frequently <u>overused</u> against the recommendations of international guidelines

Aims

- verify the reference intervals of our own laboratory by indirect procedure for activated partial thromboplastin time (APTT) and prothrombin time (PT)
- investigate whether preoperative coagulation test requests are necessary.

Materials and Methods



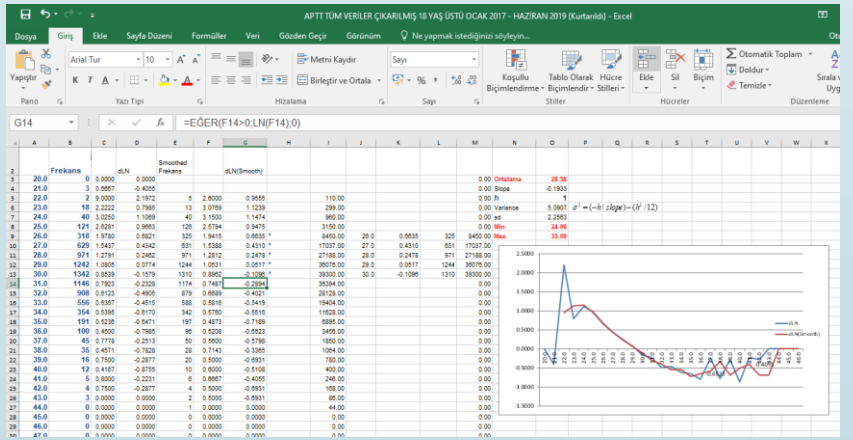
Subject data collection for RIs

- Subject data were selected retrospectively by screening coagulation results from hospital LIS between January 2017- June 2019
- We eliminated the test requests made by clinics of Emergency Department (Child and Adult), Anesthesia and Reanimation, Obstretrics and Gynecology, Nephrology, Infectious Disase, Pediatric and Adult Hemotology outpatients, inpatients and intensive care units.
- Repeated test requests were eliminated.

- Subject data collection for preoperative coagulation testing
- Preoperative APTT and PT requests were used between July 2018 - June 2019 (for 1 year)
- Cardiology, Cardiovascular surgery and Oncosurgery patients and repeated test requests were eliminated.
- Laboratory analysis
- An evacuated tube system of 4 mL plastic tube containing %3.2 buffered trisodium citrate (Becton Dickenson Diagnostics, Franklin Lakes) was used
- All samples were centrifuged at 2500 g for 10 min
- APTT and PT levels were assayed on automated Stago Sta R Max coagulation analyzer.
- Kit insert RIs are APTT 29.2 ± 2.8 (23.6-34.8) sec
- PT 13.5 ± 1.8 (11.7-15.3) sec

} for all ages and sex

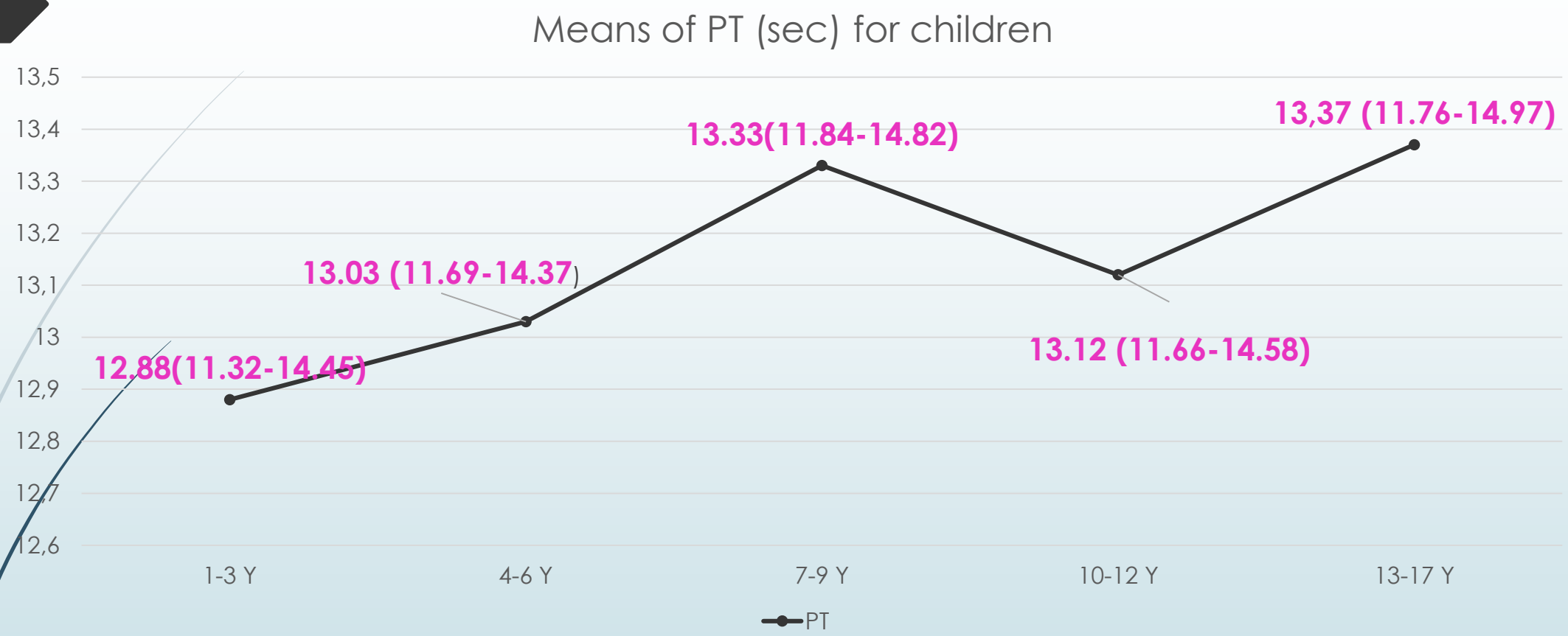
- Statistical methods
- We performed Excel macro with Bhattacharya procedure used for determination of RIs
- After RIs were calculated, preoperative patients' results and calculated RIs were compared.



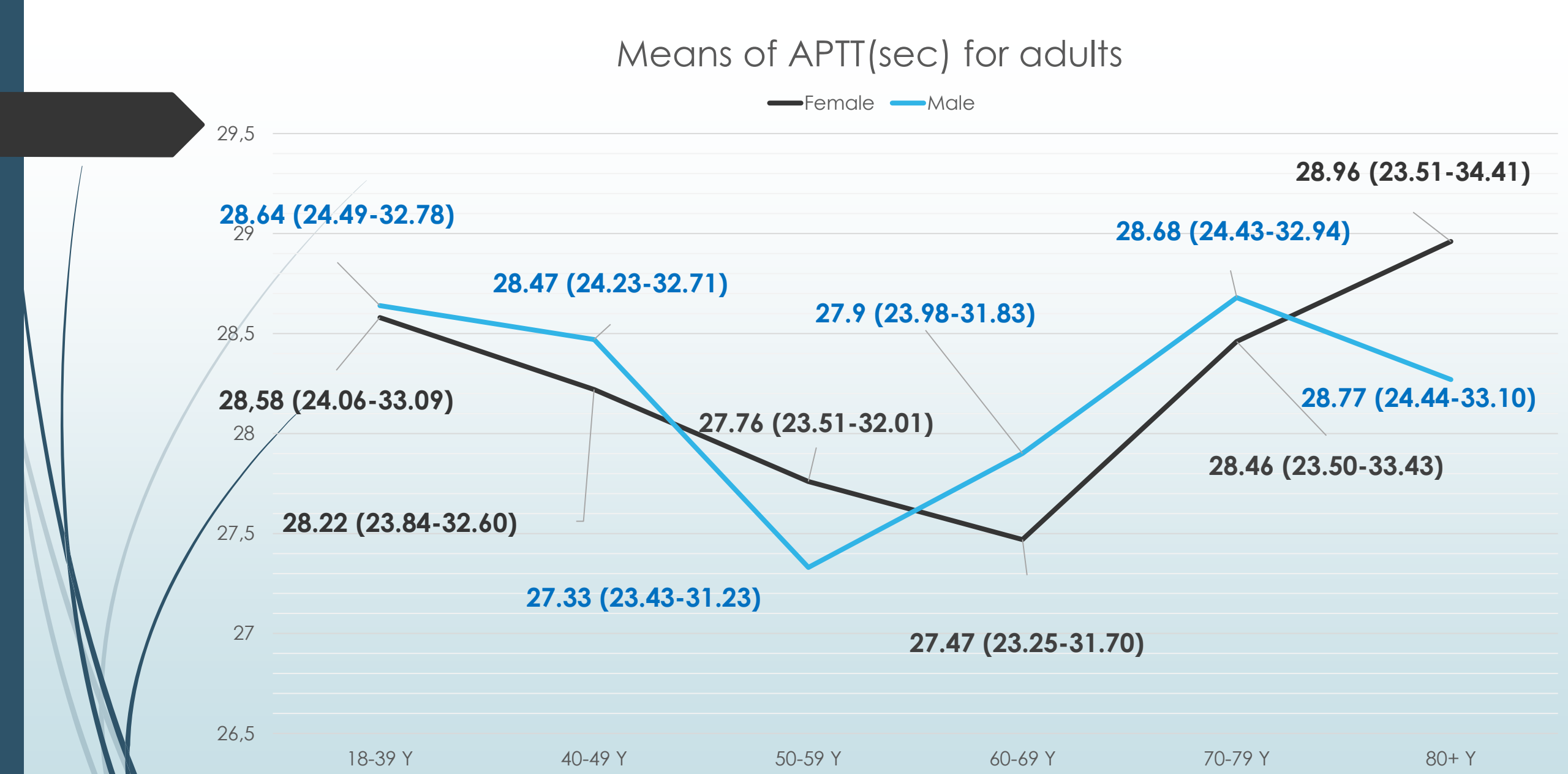
Results

Test parameters	APTT (sec) n=13611 (h=1)		PT (sec) n=13062 (h=0.5)	
Age groups (years)	Mean	Lower - Upper limit	Mean	Lower - Upper limit
1-3	29.97	24.88-35.05	12.88	11.32-14.45
4-6	30.39	25.70-35.07	13.03	11.69-14.37
7-9	29.71	25.94-33.48	13.33	11.84-14.82
10-12	30.49	25.91-35.07	13.12	11.66-14.58
13-17	30.47	26.14-34.79	13.37	11.76-14.97

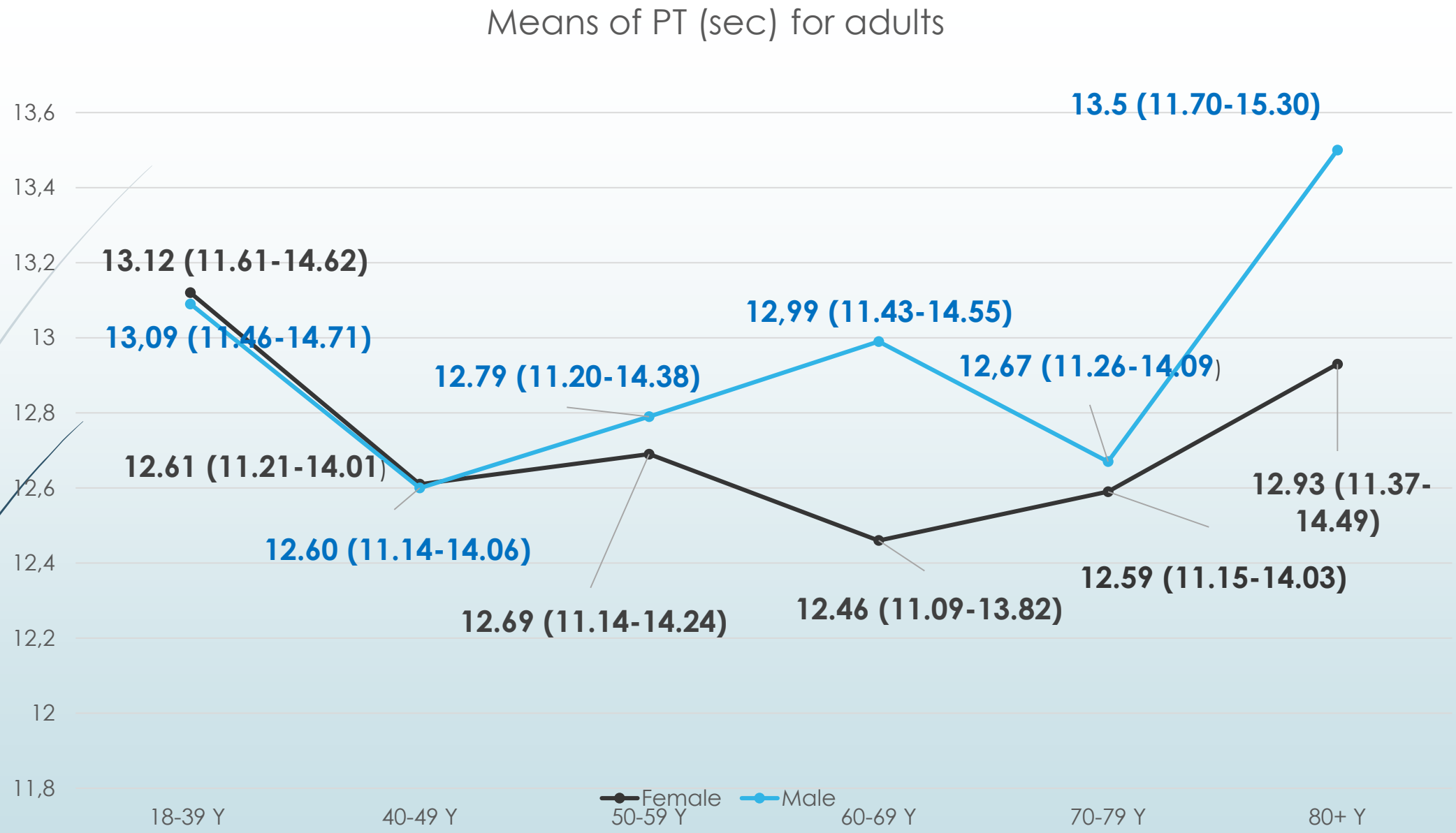
Table 1: Padiatric APTT and PT (sec) mean levels and reference limits in subgroups according to age.



Graph 1: Means and reference limits of PT for children according to age



Graph 2: Means and reference limits of APTT for adults according to age and sex



Graph 3: Means and reference limits of PT for adults according to age and sex

Ages (years)	Total n of operated patients	Test parameter (sec)	Below lower limit	Above upper limit	N of patients within the RI	% of patients within the RI	% of patients within the Present RI
1-3	**114**	APTT	**6**	**7**	**101**	**87**	**89**
		PT	0	34	80	70	85
4-6	**114**	APTT	**8**	**7**	**99**	**87**	**94**
		PT	0	34	80	70	90
7-9	**121**	APTT	**3**	**16**	**102**	**84**	**91**
		PT	0	33	89	73	84
10-12	**82**	APTT	**5**	**6**	**71**	**87**	**91**
		PT	0	33	49	60	78
13-17	**156**	APTT	**4**	**11**	**141**	**90**	**94**
		PT	1	56	99	64	72

Table 2 : Status of preoperative coagulation tests for children

Ages (years)	Sex	Total n of operated patients	Below lower limit	Above upper limit	N of patients within the RI	% of patients within the RI	% of patients within the Present RI
18-39	F	984	29	142	818	**83**	**93**
	M	887	34	146	707	80	91
40-49	F	298	4	49	245	**82**	**93**
	M	386	8	59	319	83	92
50-59	F	325	6	54	265	**82**	**91**
	M	343	2	87	254	74	**92**
60-69	F	343	2	87	254	**74**	**92**
	M	353	10	94	249	71	**86**
70-79	F	243	7	40	196	**81**	**85**
	M	217	3	58	156	72	**85**
80+	F	183	13	27	143	**78**	**80**
	M	131	4	25	102	78	**78**

Table 3: Status of preoperative APTT (sec) for adults

Ages (years)	Sex	Total n of operated patients	Below lower limit	Above upper limit	N of patients within the RI	% of patients within the RI	% of patients within the Present RI
18-39	F	984	8	187	789	**80**	**88**
	M	887	1	279	607	**68**	**79**
40-49	F	298	0	78	220	**73**	**92**
	M	386	0	127	259	**67**	**87**
50-59	F	325	0	56	269	**83**	**90**
	M	343	0	89	254	**74**	**83**
60-69	F	343	0	89	254	**74**	**91**
	M	353	0	91	262	**74**	**84**
70-79	F	243	0	105	138	**57**	**83**
	M	217	0	115	102	**47**	**79**
80+	F	183	0	87	96	**52**	**74**
	M	131	0	40	91	**70**	**70**

Table 4: Status of preoperative PT (sec) for adults

Discussion

- Laboratory specific RIs are important for accurate interpretition of patient results. Indirect methods could be a good solution for this purpose.
- Minimal elevation of PT may be the only clue for coagulapathy.
- APTT levels under the minimum reference limit is related to risk prediction for myocardial infarction and thromboembolic events.
- In accordance with the literature, perioperative events were not different in patients with or without preoperative testing.
- The French Society of Anaesthesiology and Intensive Care (SFAR) recommend that bleeding and family history should be asked before requesting the coagulation tests
- Recent studies continue to report over-requesting of preoperative tests reflecting the lack of clear guidelines or consensus.

Thank you..