

ECAT survey results for HIT

Period 2011 – 2013

Fred J.L.M. Haas



ECAT FOUNDATION

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

ECAT survey results for HIT

The HIT EQA programme

- Start in 2008
- Methods:
 - Functional testing
 - Immunological
 - Qualitative
 - Quantitative

The HIT EQA programme

- Actual:
 - Only qualitative tests and quantitative assays ($\pm 60\%$ IgG-specific)
 - Approximately 300 participants (some 2 methods)
 - Response rate around 80%

Methods

HEPERIN-INDUCED THROMBOCYTOPENIA

IMMUNOLOGICAL TEST

<u>Code</u>	<u>Description</u>
106	Aesku Diagnostics Aeskulisa HIT II
109	Akers PIFA Heparin/PF4
101	Biorad PAGIA
150	Gen-Probe Lifecodes PF4 IgG
114	GTI PF4 Enhanced IgG/IgA/IgM
111	GTI PF4 IgG
108	Haemochrom HIT II IgG
103	Hyphen BioMed Zymutest HIA IgG
107	Hyphen BioMed Zymutest HIA IgGAM
104	Hyphen BioMed Zymutest HIA IgM
115	I.L. HemosIL HIT-Ab
117	I.L. Acustar HIT-Ab
118	I.L. Acustar HIT-IgG
135	IQ Products HIT Alert
120	Milenia Quickline HIT
105	Stago Asserachrom HPIA
113	Stago Asserachrom HPIA-IgG
130	Stago Stic Expert HIT
125	Technoclone Technozym HIT IgG
190	Homemade
199	Other, please specify

qualitative

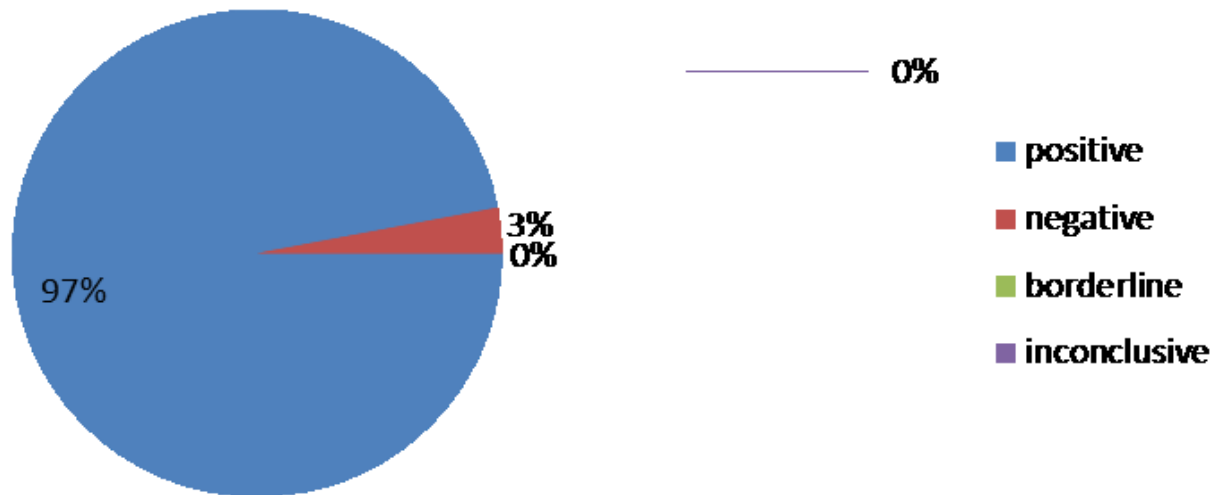


Participants

	2011	2012	2013
Qualitative testing	74	82	86
Quantitative testing	155	171	195

Results 2011

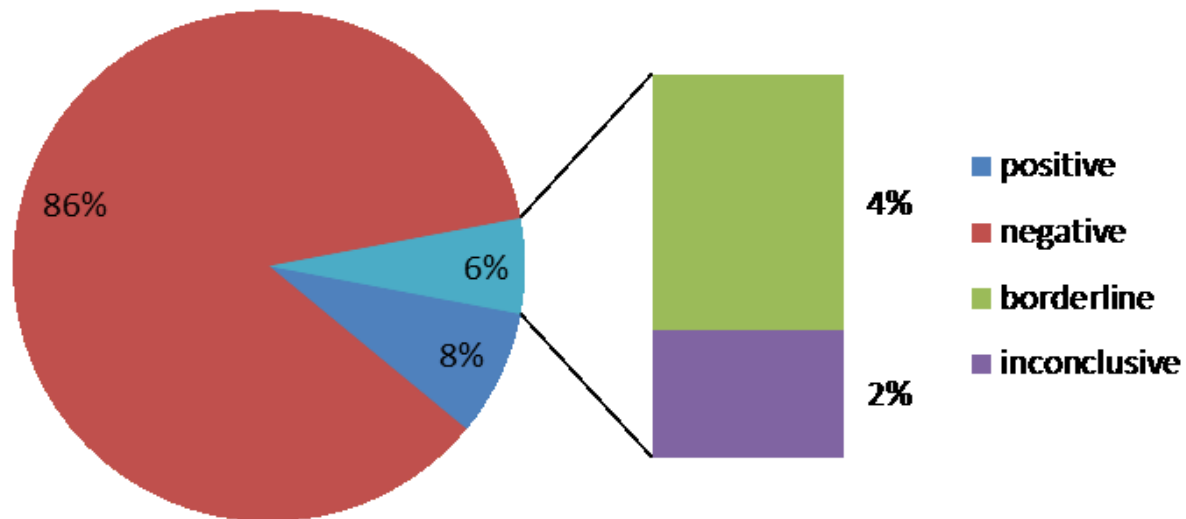
11.119 positive



HIT positive human plasma

Results 2011

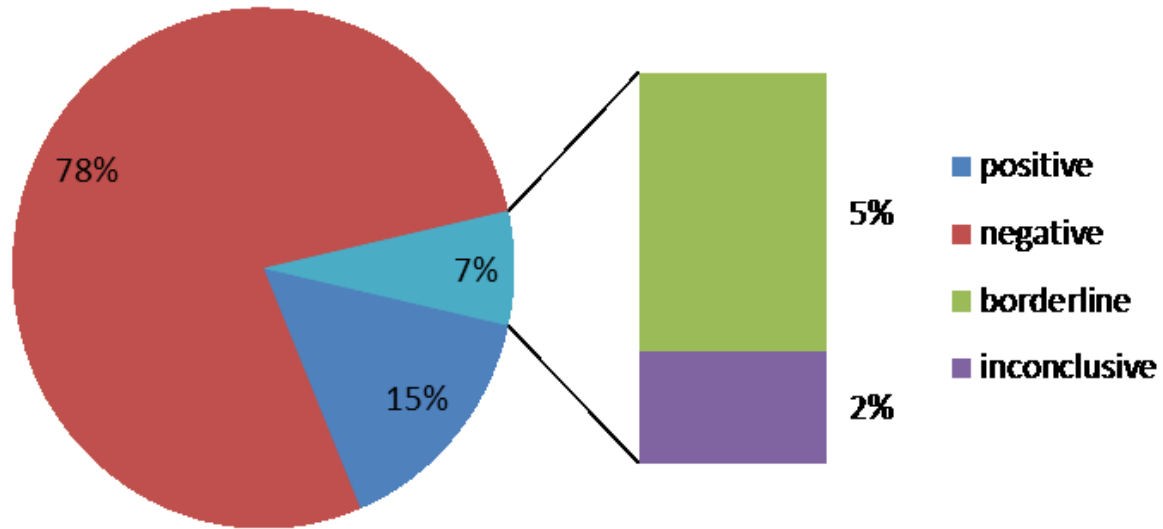
11.120 negative



Commercial plasma control sample

Results 2012

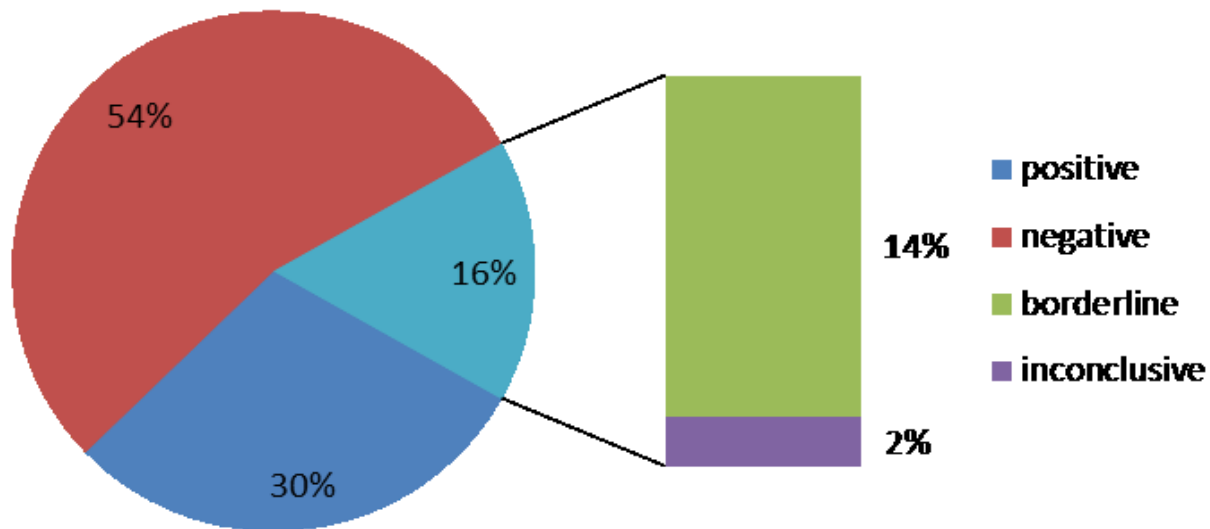
12.94 negative



Normal citrated pooled plasma

Results 2012

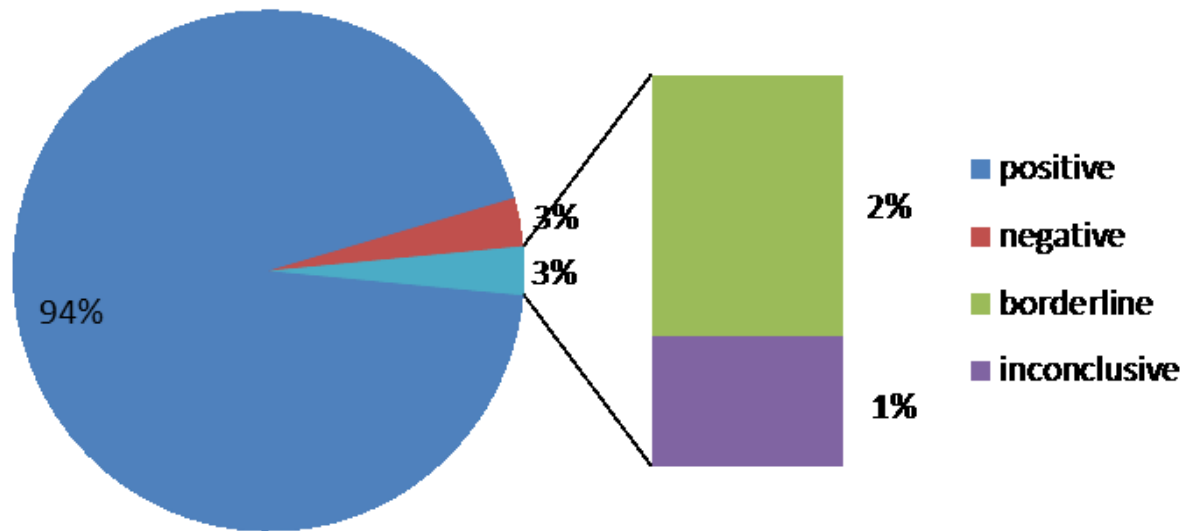
12.95 borderline



Diluted HIT positive human plasma

Results 2013

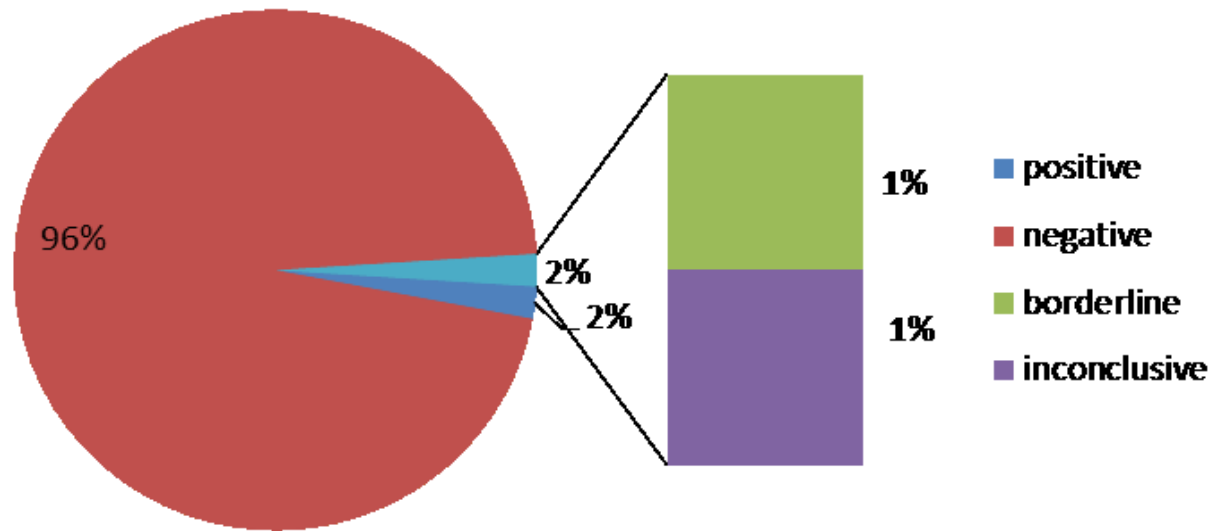
13.98 positive



HIT positive human plasma

Results 2013

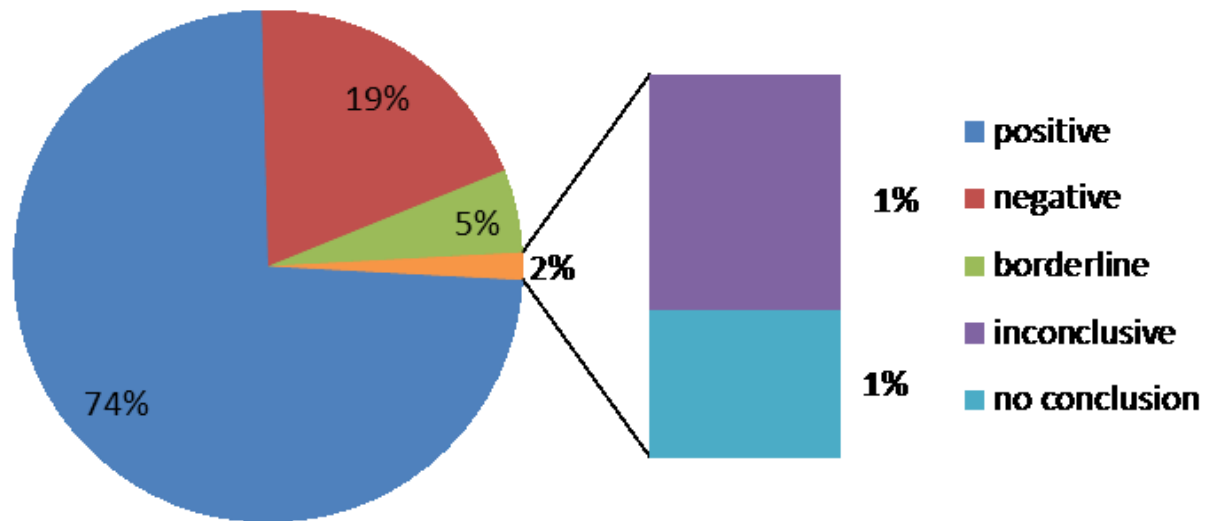
13.99 negative



Normal citrated pooled plasma

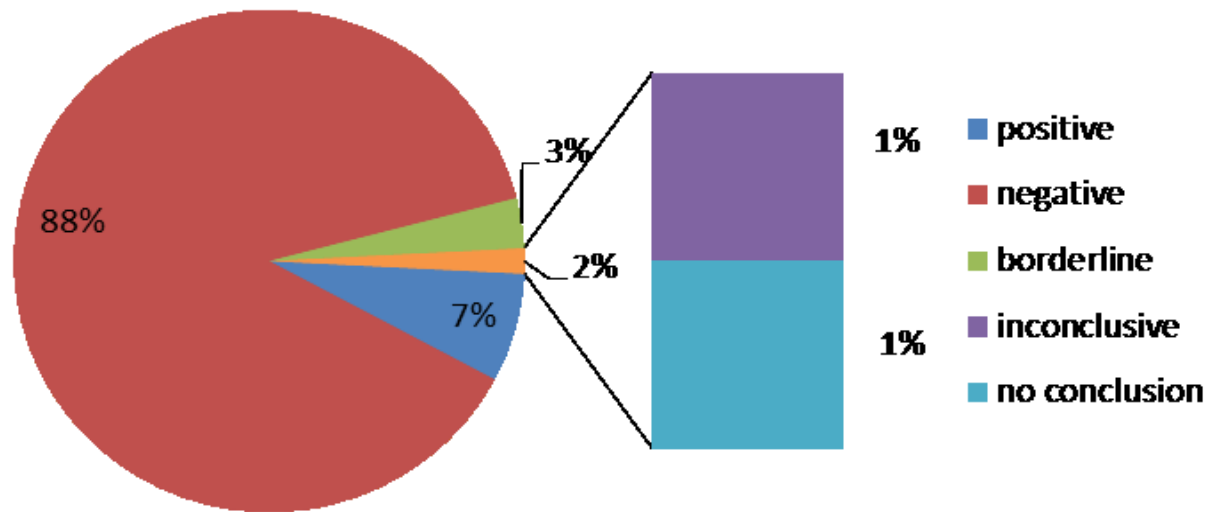
Overall

All positive



Overall

All negative



Qualitative tests

<u>Negative sample</u>	2011		2012		2013	
<u>Method</u>	N	%	N	%	N	%
Milenia Quickline HIT	3	67	14	50	15	100
Diamed PAGIA	71	58	66	33	60	98
Stago STic Expert	-	-	2	100	11	100
<u>Positive sample</u>	2011		2012		2013	
<u>Method</u>	N	%	N	%	N	%
Milenia Quickline HIT	3	100	14	36	15	73
Diamed PAGIA	71	97	66	80	62	100
Stago STic Expert	-	-	2	0	11	100

The mean OD-values and the between-laboratory variation for quantitative HIT methods for the positive HIT samples used in 2011 - 2013.

Method	2011			2012			2013		
	N	OD	CVb (%)	N	OD	CVb (%)	N	OD	CVb (%)
Genprobe PF4 IgG	-	-	-	-	-	-	3	2.05	-
GTI PF4 Enhanced	19	2.04	16.0	23	0.43	25.4	22	2.51	16.7
GTI PF4 IgG	41	1.96	23.8	38	0.33	39.0	35	2.45	23.1
Hyphen Zymutest IgGAM	8	1.94	-	5	0.32	-	6	1.36	-
Hyphen Zymutest IgG	26	1.78	20.8	27	0.20	34.0	32	1.51	36.6
Stago Asserachrom HPIA	22	2.44	18.4	22	0.51	21.3	14	2.51	23.3
Stago Asserachrom HPIA IgG	2	2.60	-	7	0.11	-	12	2.44	22.0
Technoclone Technozyme IgG	3	0.97	-	2	0.16	-	3	0.73	-



The mean OD/cut-off ratio values and the between-laboratory variation for quantitative HIT methods for the positive HIT samples used in 2011 - 2013.

Method	2011			2012			2013		
	N	Ratio	CVb (%)	N	Ratio	CVb (%)	N	ratio	CVb (%)
Genprobe PF4 IgG	-	-	-	-	-	-	3	5.1	-
GTI PF4 Enhanced	19	5.1	15.8	23	1.1	23.3	22	6.1	20.2
GTI PF4 IgG	41	4.9	24.0	38	0.8	38.6	35	6.0	24.2
Hyphen Zymutest IgGAM	8	3.6	-	5	0.7	-	6	1.4	-
Hyphen Zymutest IgG	26	4.8	31.5	27	0.5	36.8	32	4.0	44.0
Stago Asserachrom HPIA	22	5.1	25.1	22	1.0	19.1	14	4.8	17.8
Stago Asserachrom HPIA IgG	2	10.4	-	7	0.5	-	12	10.9	15.1
Technoclone Technozyme IgG	3	3.2	-	2	0.5	-	3	1.5	-

4T's pre-test probability

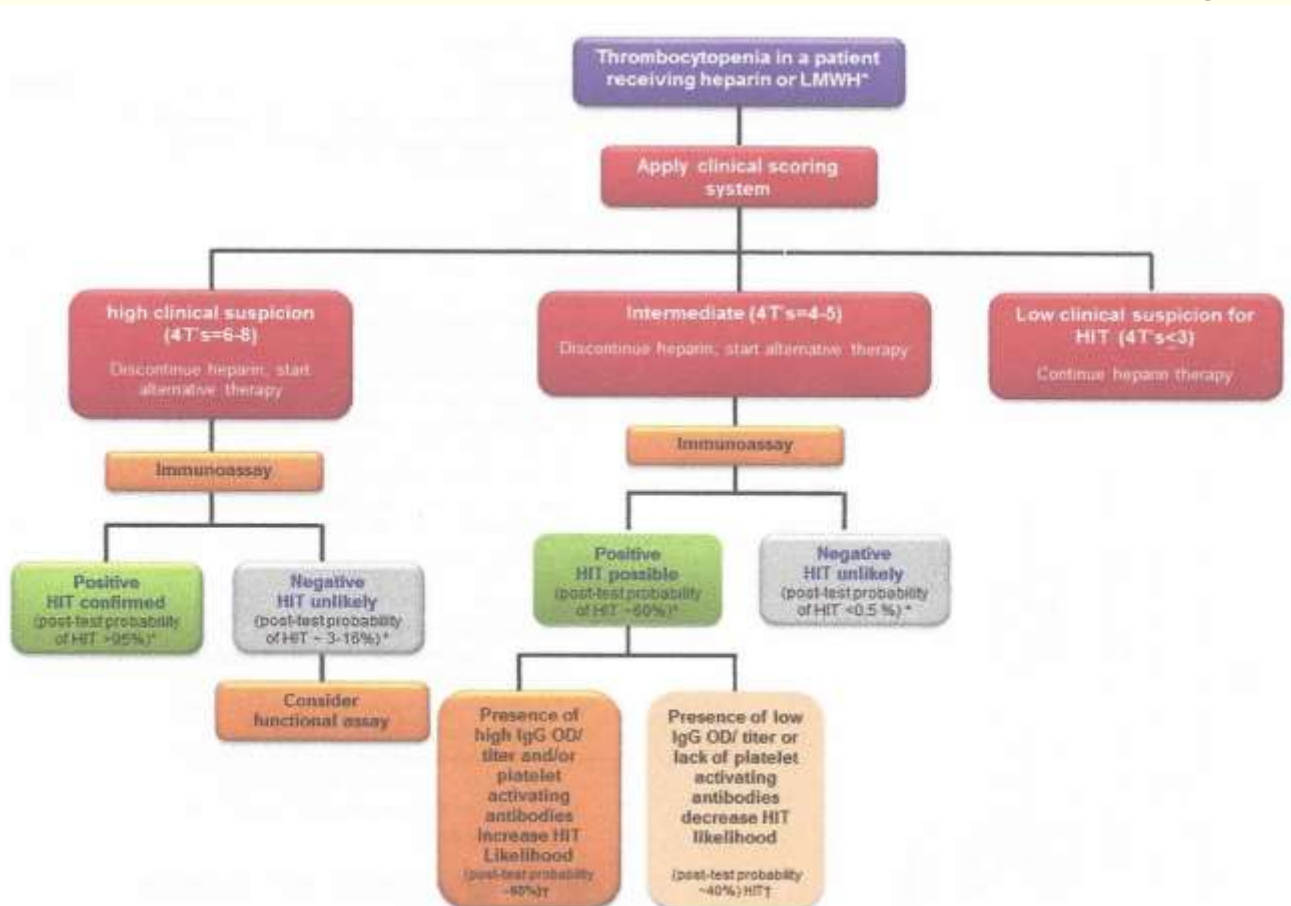


Figure 2. Diagnostic algorithm. Shown is our diagnostic approach for HIT using clinical and laboratory evaluation. *Based on Pouplard et al.⁴⁴ †Based on Nellen et al.⁵⁵

4T's pre-test probability

Reference result	Low	Moderate	High	Total
Positive HIT	0	9 (42.9%)	12 (57.1%)	21 (100%)
Negative HIT	42 (25.5%)	90 (54.5%)	33 (20.0%)	165 (100%)
Total	42 (22.6%)	99 (53.2%)	45 (24.2%)	186 (100%)

Performance of the 4T's score system classifying the risk for HIT

(Junqueira CCA 2011)

4T's pre-test probability

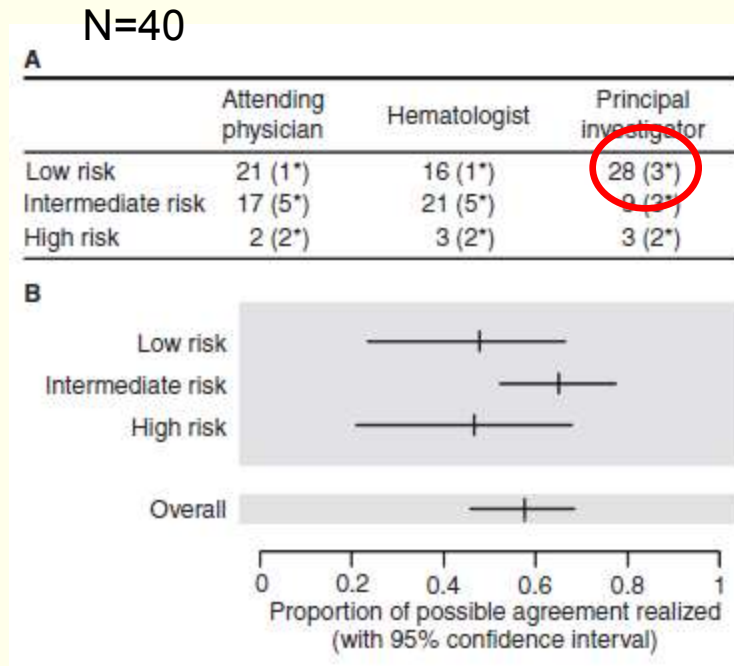
Table 1A. Pre-test probability for *in vitro* platelet-activating HIT antibodies according to the 4T score.

4T score		Hamilton ^a	Greifswald ^a	Tours ^a	Sidney ¹¹	Ghent ¹⁰	Giessen ¹²	Bern	Total	Probability %	95% CI
Low (0-3)	n/N	1/64	0/55	0/74	0/142	0/31	0/316	7(*)/859	8/1541	0.5	0.2-0.9
	%	1.6	0	0	0	0	0	0.8			
Int. (4-5)	n/N	8/28	11/139	14/129	5/92	4/62	9/130	50/358	101/938	10.8	8.8-12.8
	%	28.6	7.9	10.9	5.4	6.5	6.9	14.0			
High (6-8)	n/N	8/8	9/42	8/10	4/12	6/9	26/54	39/74	100/209	47.8	41.1-54.7
	%	100	21.4	80.0	33.3	66.7	48.1	52.7			
All	n/N	17/100	20/236	22/213	9/246	10/102	35/500	96/1291	209/2688	7.8	6.8-8.8
	%	17.0	8.5	10.3	3.7	9.8	7.0	7.4			

n = Patients with a positive functional assay for HIT antibodies; *N* = All patients evaluated for suspected HIT; (*) = See Table 1B.

(Nellen Haematologica 2012)

4T's pre-test probability



10.7% positive

48% agreement

65%

47%

(Nagler JTH 2011)

Conclusions

- The classification is in general acceptable.
- Positive: 97% correct.
- Negative: correct results between 88% and 97%! Thus false negative 3% - 12%!
- The effect of the used plasma on false positive or negative results is not clear.
- The results of a strong HIT sample are better than a weak HIT sample.

Conclusions

- The observed $CV_{\text{between-laboratory}}$ illustrates the need for standardisation.
- The harmonisation with the OD/cut-off ratio was not successful.
- The use of the 4T's (low) score in patient care may be a help in acute situations .