



RISK STRATIFICATION AND SCORING SYSTEM MODELS IN APS

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Maastricht, Sept 2018**

Biomarker Vs Risk Factor

Thrombosis and/or PM



aPL testing



APS



NO APS

Biomarker Vs Risk Factor

aPL testing



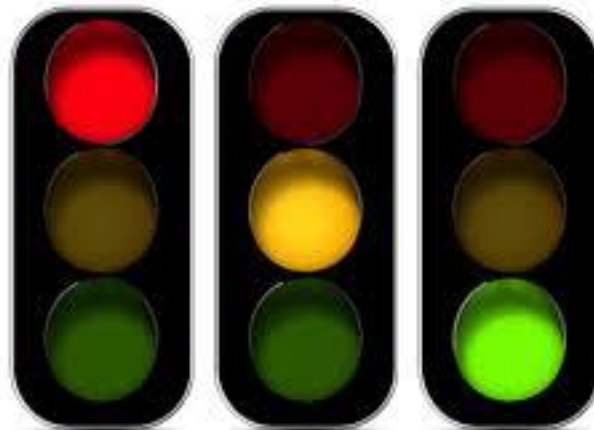
Risk of thrombosis and/or PM

Biomarker Vs Risk Factor

aPL testing



Risk of thrombosis and/or PM



How do we assess the risk of aPL-related manifestations?

- Full thrombophilia screen
- Activity of the autoimmune diseases
- Other cardiovascular risk factors
- Presence of aPL
 - LA is the strongest risk factor

Galli et al. Blood 2003

- Double or **triple** positivity ↑ the risk

Pengo et al. JTH 2010

Quantify the risk for patients

- When high risk is high enough?



SCORE SYSTEMS IN APS

Ann Rheum Dis 2011;**70**:1517-1518 doi:10.1136/ard.2010.145177

Risk Scale for the diagnosis of antiphospholipid syndrome

Savino Sciascia¹, Domenico Cosseddu², Barbara Montaruli², Anna Kuzenko¹,
Maria Tiziana Bertero¹

		aCL+	aCL-
LA positive	aβ2GPI +	High risk OR>9	Medium risk OR 5-9
	aβ2GPI -	Medium risk OR 5-9	Low risk OR 1-5
LA negative	aβ2GPI +	Medium risk OR 5-9	Low risk OR 1-5
	aβ2GPI -	Low risk OR 1-5	Low risk OR 1-5

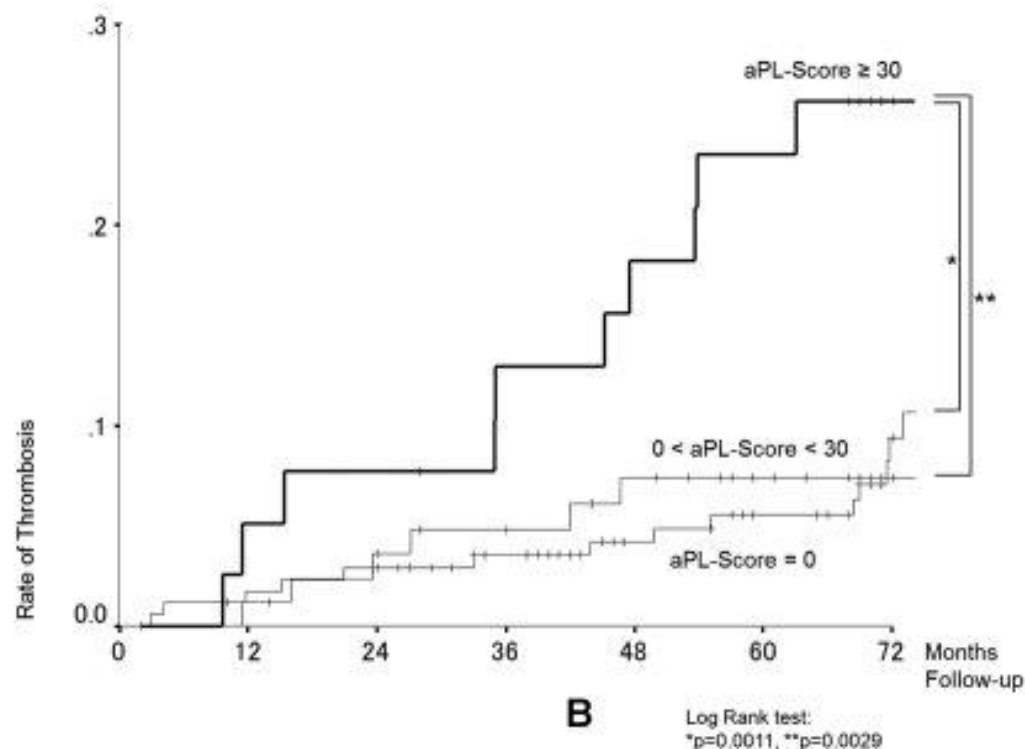
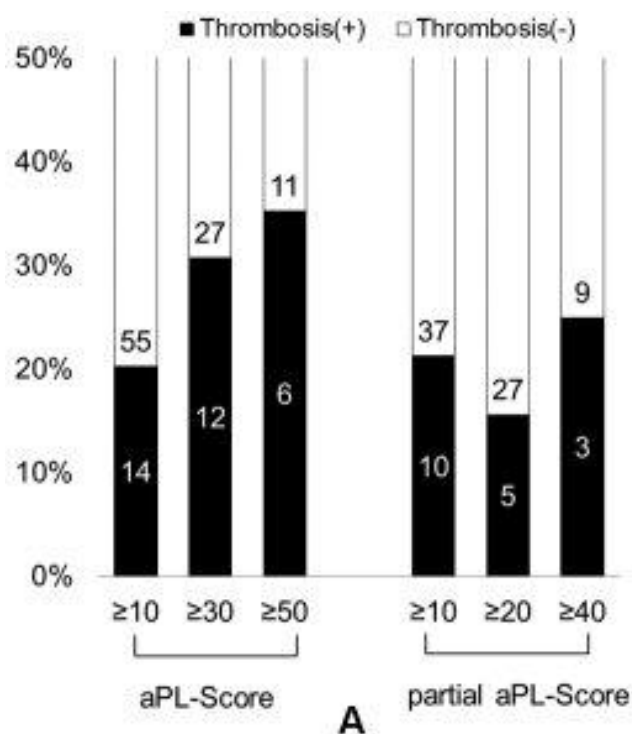
Methods for LA test	aCL and aβ2GPI titre			
	NEGATIVE < 10 U	LOW 10-30 U	MEDIUM 30-50 U	HIGH >50 U
SCT	Low risk OR 1-5	Low risk OR 1-5	Medium risk OR 5-9	High risk OR >9
KCT	Low risk OR 1-5	Medium risk OR 5-9	Medium risk OR 5-9	High risk OR >9
DRVVT	Medium risk OR 5-9	Medium risk OR 5-9	High risk OR >9	High risk OR >9
PTT-LA \ STACLOT LA	Medium risk OR 5-9	Medium risk OR 5-9	High risk OR >9	High risk OR >9

SCORE SYSTEMS IN APS

ARTHRITIS & RHEUMATISM
Vol. 64, No. 2, February 2012, pp 504-512

Efficacy of the Antiphospholipid Score for the Diagnosis of Antiphospholipid Syndrome and Its Predictive Value for Thrombotic Events

Kotaro Otomo, Tatsuya Atsumi, Olga Amengual, Yuichiro Fujieda, Masaru Kato, Kenji Oku, Tetsuya Horita, Shinsuke Yasuda, and Takao Koike



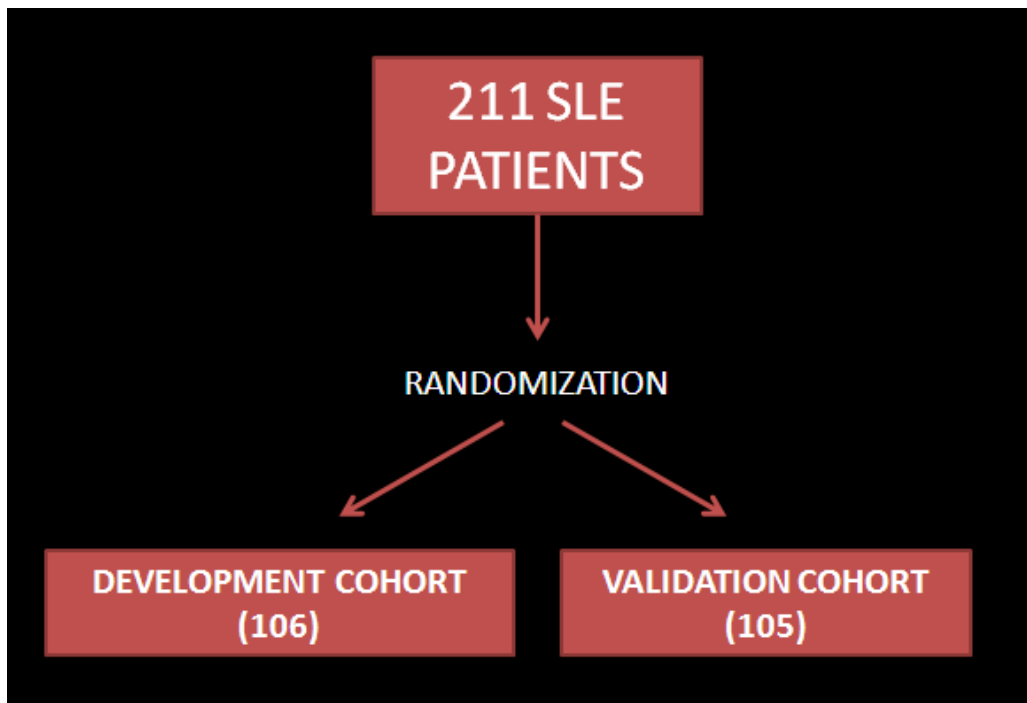
GAPSS: aim

- To develop a **risk** score (Global APS Score or GAPSS) derived from the combination of **independent risk of thrombosis and pregnancy loss**, taking into account:
 - **aPL profile** (criteria and non-criteria aPL),
 - **conventional cardiovascular risk factors**
 - **SLE autoimmune antibodies profile**

To validate this score by testing GAPSS in a separate cohort of patients.

Randomisation

- Patients were randomly divided in 2 sets.
- Computer-generated randomized list of patients filtered by the criterion of the diagnosis in order to equally distribute the diseases prevalence (SLE and APS, SLE and aPL positivity or SLE alone)



To confirm the efficacy of randomization, the prevalence of the variables in the 2 sets were computed and **no statistical difference were found**

Results

Univariate model

DEVELOPMENT
COHORT (n=106)

Characteristic	OR	CI [95%]	p
Conventional thrombotic risk factor ≥ 1	1.84	0.782-4.253	NS
Smoking	0.823	0.353-1.920	NS
Oral Contraceptive pill	0.558	0.160-1.950	NS
Hyperlipemia	2.492	1.28-5.918	0.036
Arterial hypertension	1.831	1.099-8.280	0.035
Diabetes	1.831	0.81-21.938	NS
Hormone replacement therapy	3.55	0.655-13.23	NS
dsDNA	1.63	0.738-3.59	NS
ENA	1.304	1.127-2.780	0.039
RO	0.471	0.188-9.178	NS
LA	1.885	0.315-7.482	NS
RNP	1.324	1.116-6.09	0.047
Sm	0.369	0.124-2.0979	NS
LA	1.885	1.116-8.507	0.031
aCL IgG/IgM	3.998	1.987-10.448	0.023
a β_2 GPI IgG/IgM	3.98	1.462-10.892	0.049
aPT IgG/IgM	2.778	1.037-7.47	0.034
aPS/PT IgG/IgM	2.133	1.368-7.128	0.006
aPrS IgG	1.424	0.177-8.22	NS
aPE IgG/IgM	1.997	0.457-2.193	

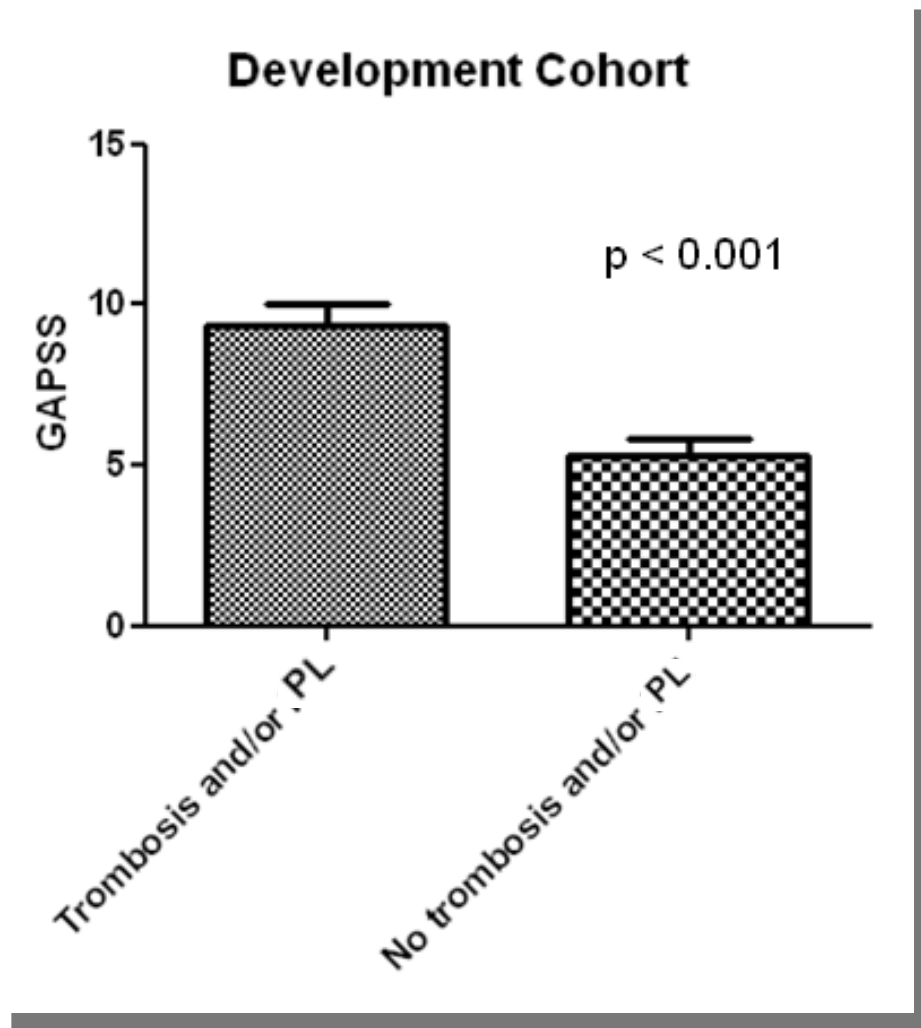
Development and validation of GAPSS

To calculate GAPSS, we assigned **each of the six variables** identified in the development cohort as independent risk factors for thrombosis and/or pregnancy morbidity, **a number of points that was proportional to its regression coefficient**

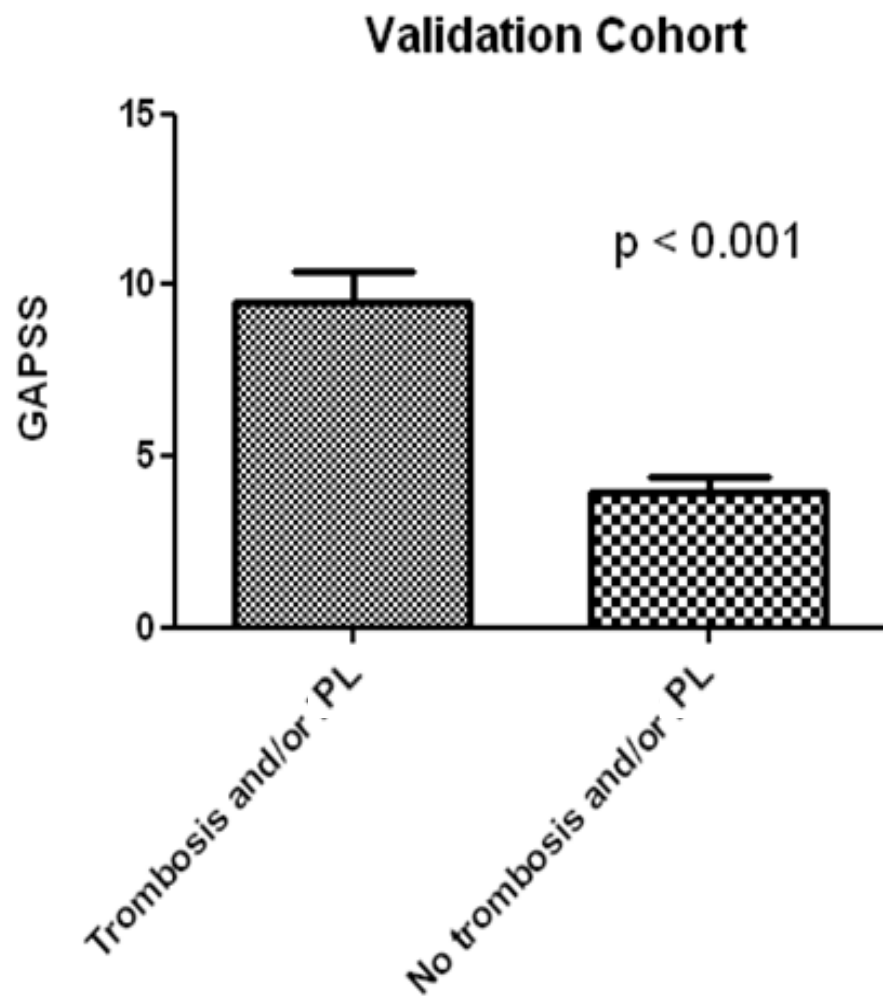
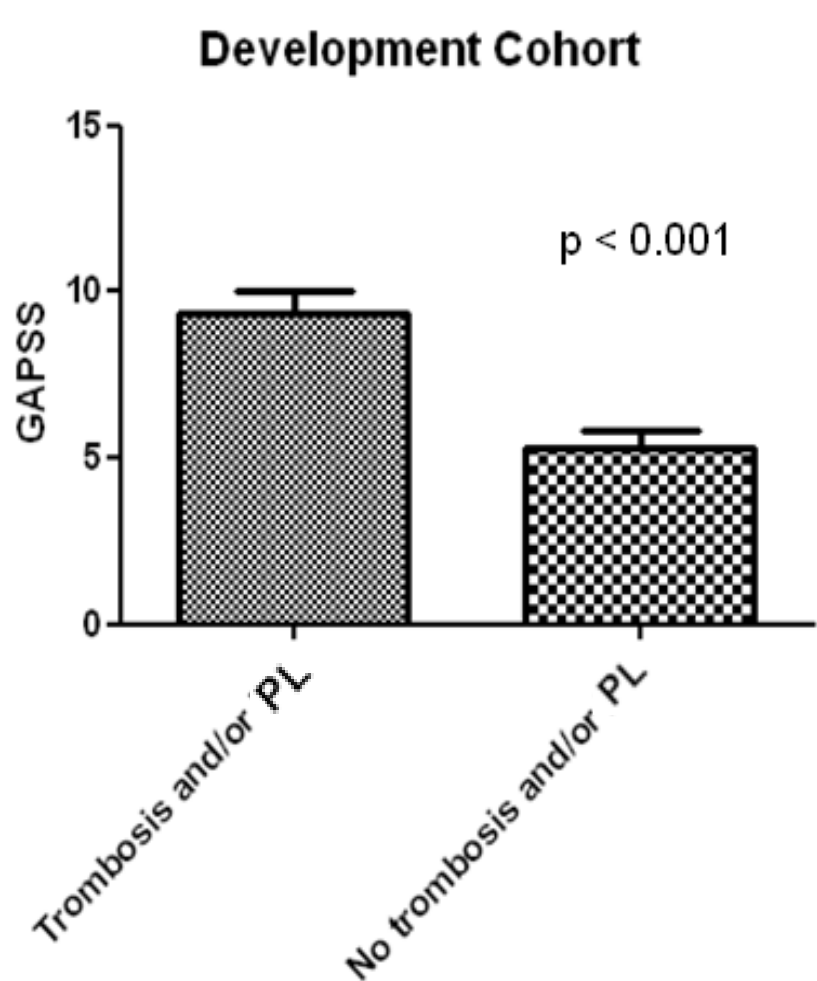
	β Coefficient	GAPSS*
Hyperlipidemia	1.73	3
Arterial hypertension	0.54	1
aCL IgG/IgM	2.63	5
Anti- β 2GPI IgG/IgM	2.02	4
aPS/PT IgG/IgM	1.78	3
LA	2.35	4

*Assignment of points to risk factors was based on a linear transformation of the corresponding β regression coefficient by using the formula $GAPSS = [\beta_x / \beta_{min}]$, where β_x is the β regression coefficient for the variable X and β_{min} is the lowest β value among the significant variables in the whole population after multivariate analysis. For example, in this cohort, the GAPSS for hyperlipidemia is 3, as $GAPSS = [\beta_{hyperlipidemia} / \beta_{arterial hypertension}] = [1.73 / 0.54] = 3.20 = 3$, when rounded to the nearest integer.

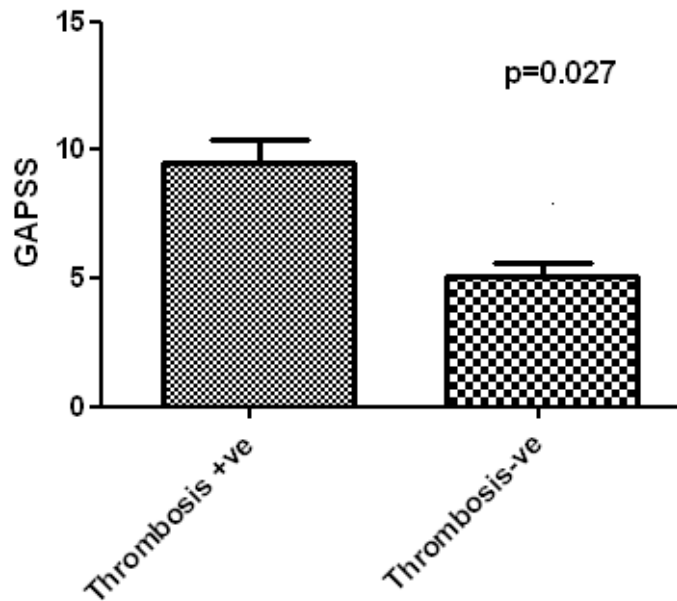
Development and validation of GAPSS



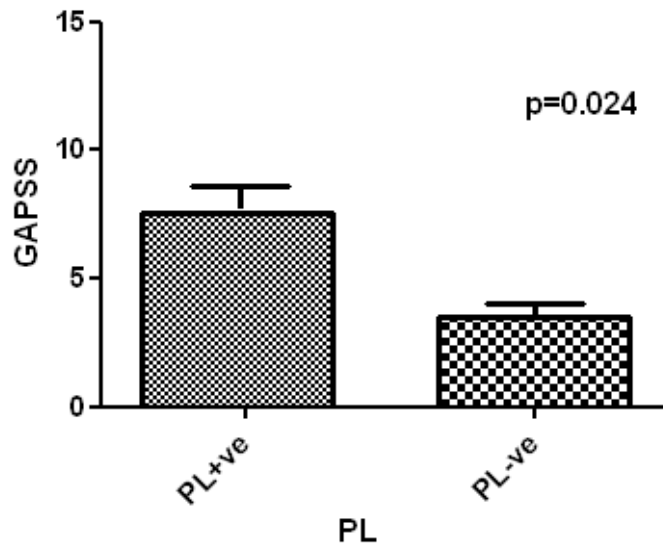
Development and validation of GAPSS



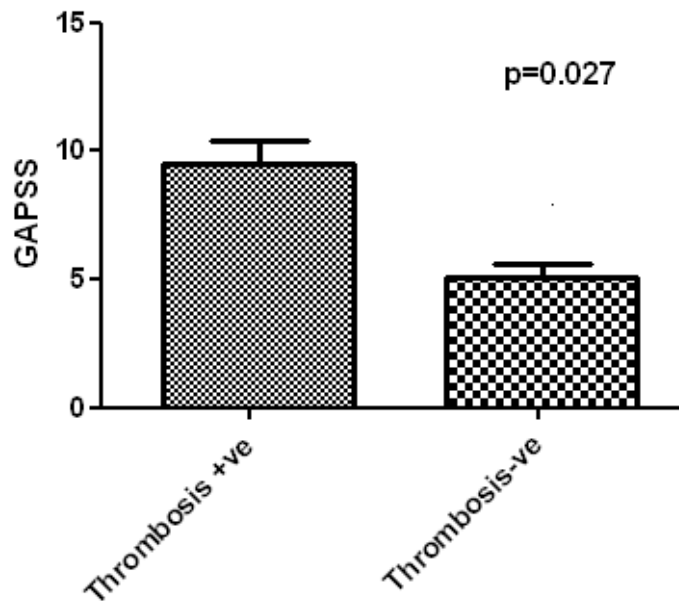
Development Cohort Thrombosis



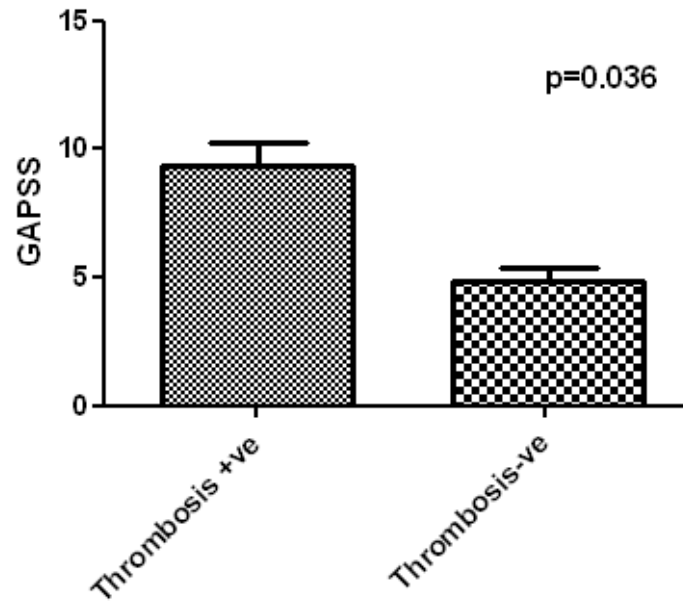
Development Cohort PL



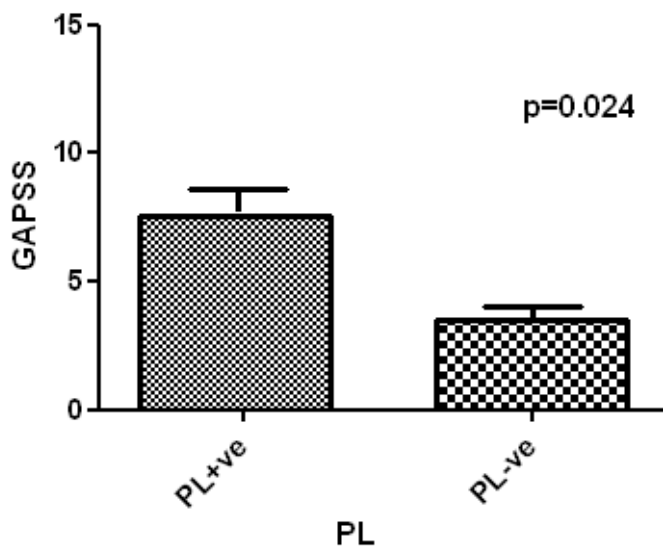
Development Cohort Thrombosis



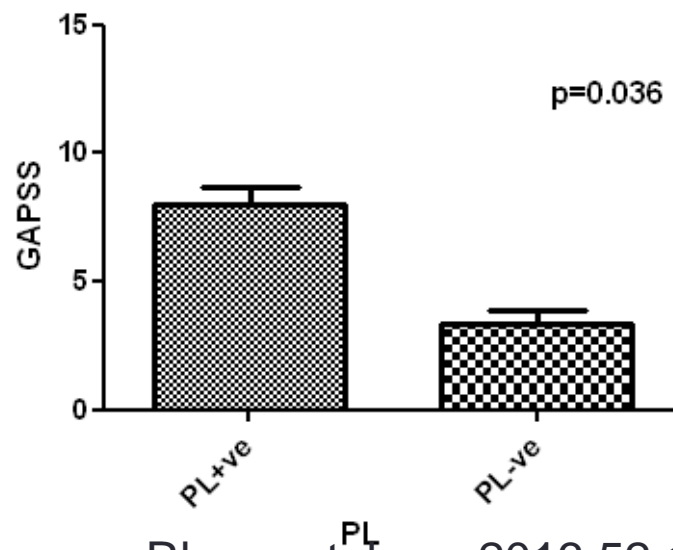
Validation Cohort Thrombosis



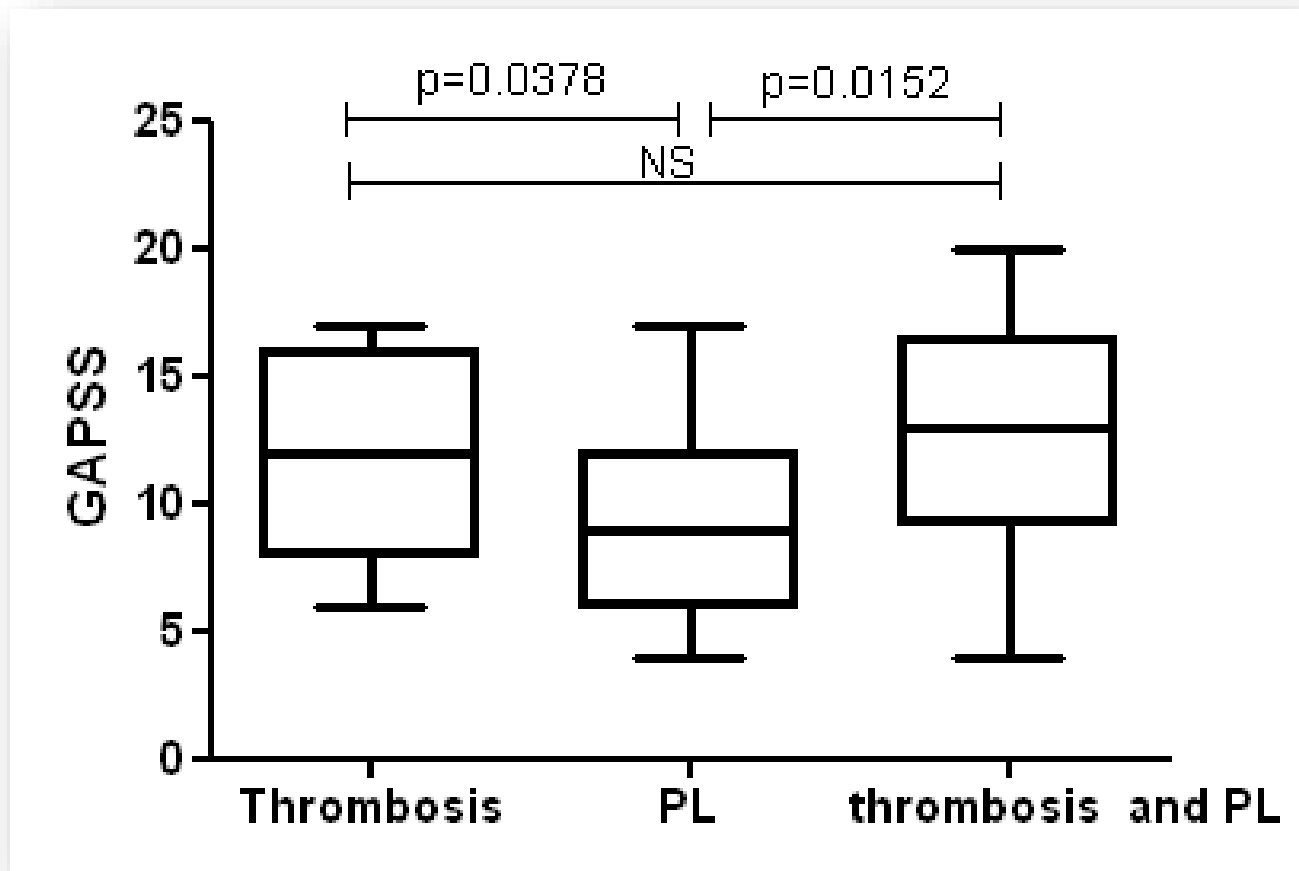
Development Cohort PL



Validation Cohort PL

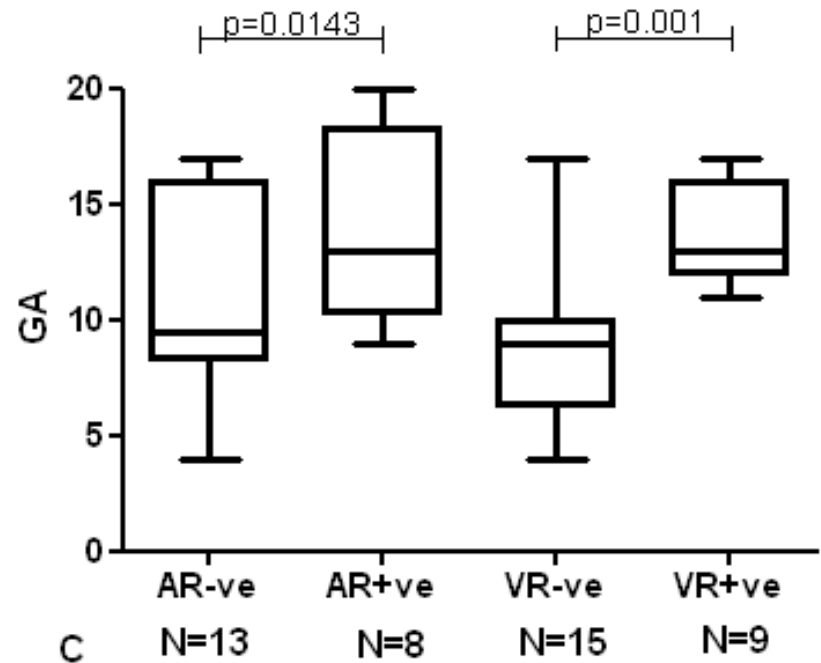
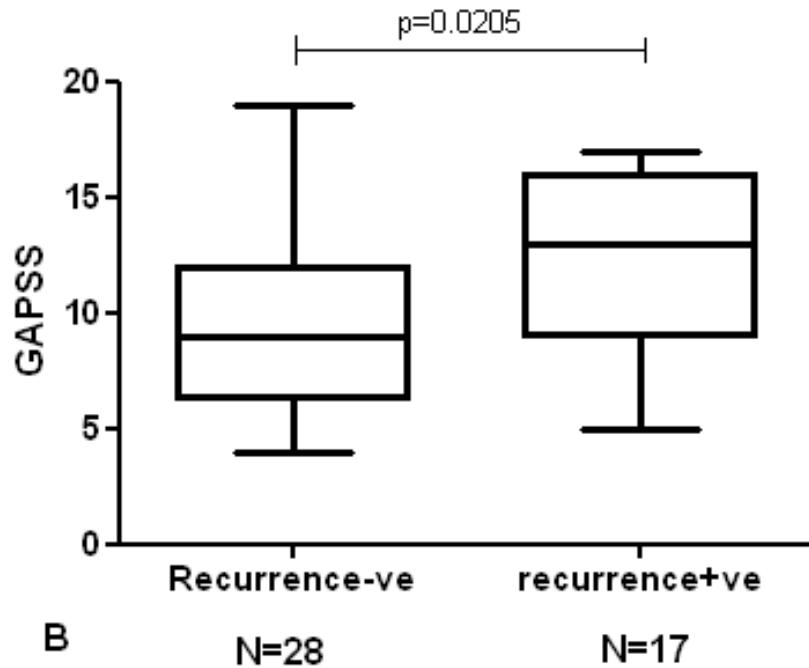


Clinical relevance of the in a cohort of primary APS patients (N=62)



Higher values of GAPSS were showed in patients who experienced thrombosis compared to those with pregnancy loss alone

PAPS with thrombotic recurrences showed higher values of GAPSS compared to those without



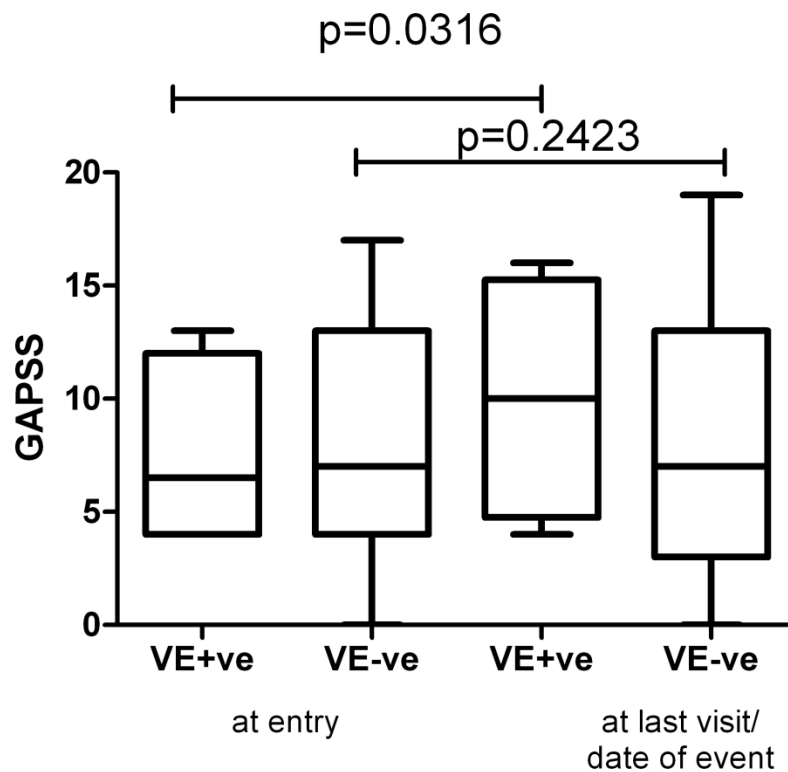
AR= arterial recurrences

VR= venous recurrences

	Sensitivity (%)	Specificity (%)	OR	[95%IC]
Cut off 5	100	8.3	1.78	1.345-2.336
Cut off 7	100	29.2	1.85	1.375-2.490
Cut off 8	100	16.7	2.00	1.429-2.799
Cut off 9	100	33.3	7.01	1.783-63.21
Cut off 10	100	54.2	8.5	2.001-75.81
Cut off 11	94.1	78.0	18.27	3.74-114.05
Cut off 12	88.2	78.0	20.64	3.92-185.92
Cut off 15	35.3	83.3	21.64	3.89-189.56

GAPSS values ≥ 11 are strongly associated with higher risk of recurrences

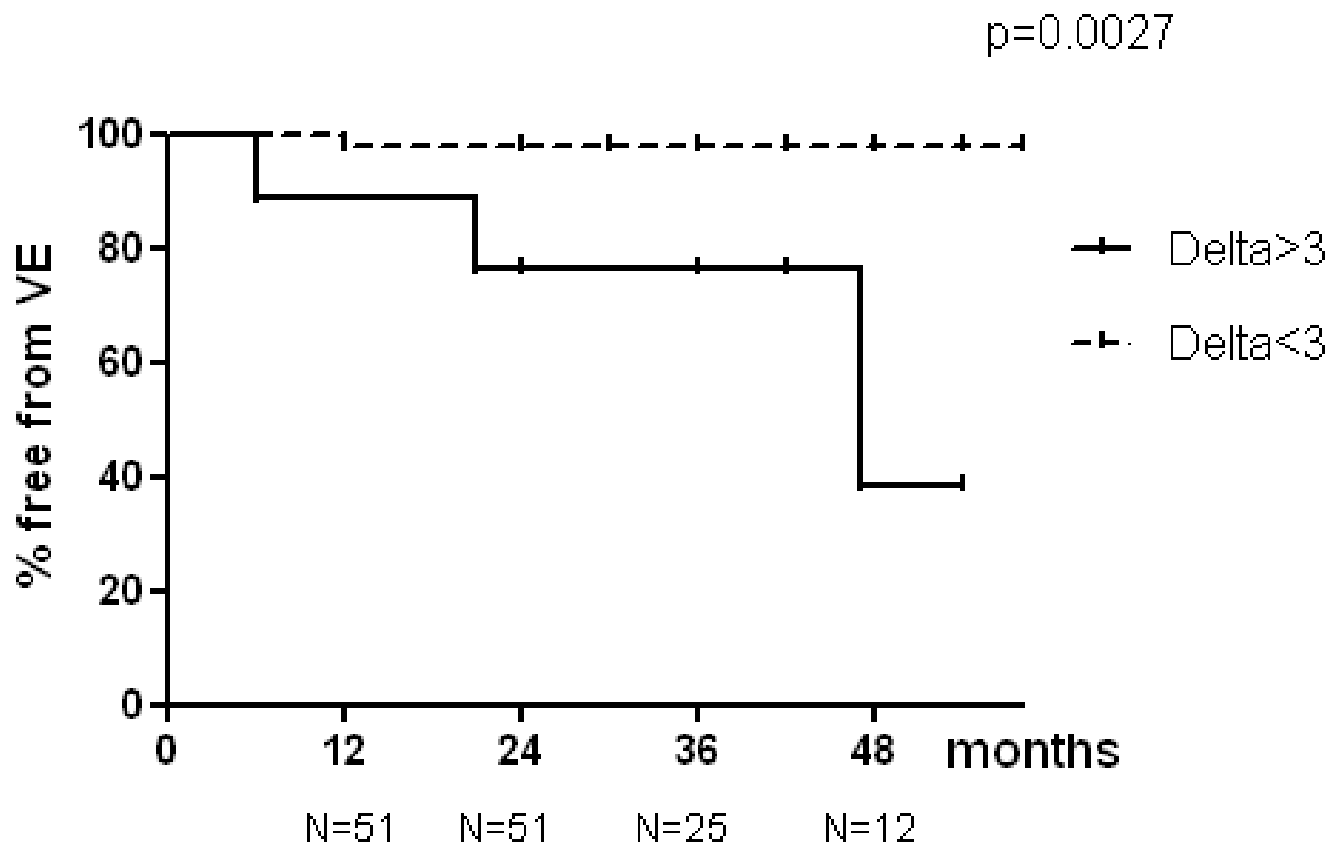
Validation of GAPSS in a prospective cohort (n=51)



An increase in the GAPSS (entry vs. last visit) was seen in patients who experienced thrombosis (n=4)

No changes were observed in those without thrombotic event (n=47)

Validation of GAPSS in a prospective cohort (n=51)



The cumulative proportion of thrombosis-free individuals was higher in the patients whose GAPSS was not increased by ≥ 3 points (p=0.002)

Validity of the global anti-phospholipid syndrome score to predict thrombosis: a prospective multicenter cohort study

Validity of the global anti-phospholipid syndrome score to predict thrombosis: a prospective multicentre cohort study

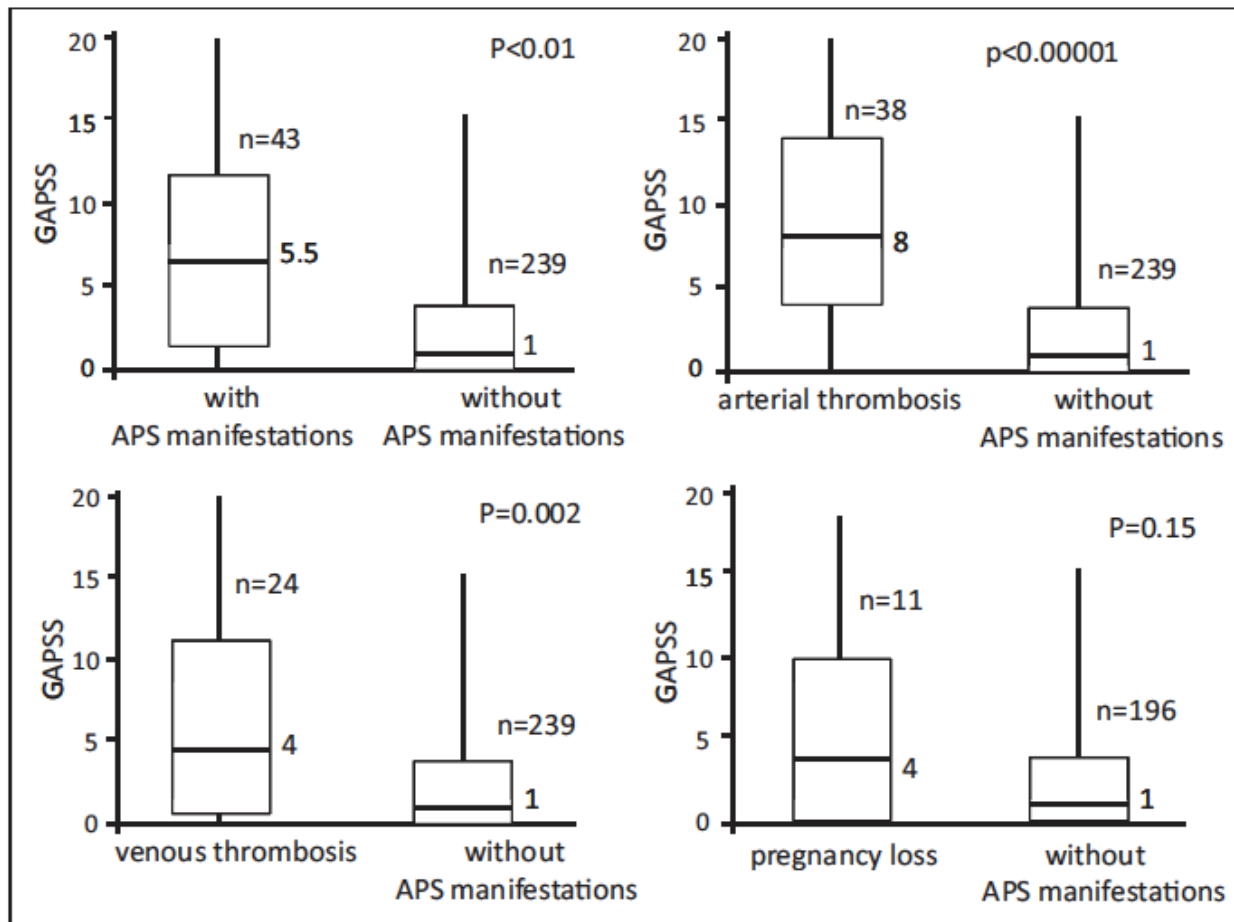
TABLE 2

Prediction of thrombosis using GAPSS according to different cut-off values in univariate survival analysis

GAPSS cut-off value	Frequency of thrombosis in patients with a positive GAPSS, n/N (%)	Frequency of thrombosis in patients with a negative GAPSS, n/N (%)	Univariate analysis HR (95% CI)	P-value
>10	8/51 (16)	8/86 (9)	1.73 (0.63, 4.79)	0.29
>12	7/34 (21)	9/103 (9)	2.48 (0.89, 6.92)	0.08
>16	3/5 (60)	13/132 (10)	6.86 (1.90, 24.77)	0.003

GAPSS: global APS score; HR: hazard ratio.

An independent validation of the Global Anti-Phospholipid Syndrome Score in a Japanese cohort of patients with autoimmune diseases



STUDY	YEAR	STUDY DESIGN	AIM	NUMBER OF PATIENTS	PATIENTS' CHARACTERISTICS
Sciascia et al.	2013	Cross-Sectional	To validate the first GAPSS score with a validation cohort	105	SLE
Sciascia et al.	2014	Prospective	To prospectively and independently validate GAPSS, with a follow-up of mean 32.94 (SD 12.06) months	51	SLE aPL positive patients
Zuily et al.	2015	Prospective	To investigate the validity of the global APS score (GAPSS) to predict thrombosis in patients with autoimmune diseases, followed up for a mean duration of 43.1 (S.D. 20.7) months	137	patients with aPL and/or SLE
Oku et al.	2015	Retrospective	To validate the GAPSS independently	282	41 APS (17 PAPS) patients, 88 SLE without APS, 50 rheumatoid arthritis, 16 Sjögren's syndrome, 21 systemic sclerosis, 10 polymyositis/ dermatomyositis and 56 other autoimmune diseases
Sciascia et al.	2015	Retrospective	To evaluate the clinical relevance of the global APS score (GAPSS) in a cohort of primary APS patients	62	PAPS patients
Zigon et al.	2016	Retrospective	To evaluate association of different risk factors with thrombosis; and b) to apply GAPSS on a large cohort of unselected Slovenian patients	585	Systemic Autoimmune Diseases
Sciascia et al.	2016	Retrospective	To evaluate the clinical utility of the GAPSS with the help of APS ACTION Registry	550	APS Patients
Zu et al.	2016	Retrospective	To evaluate the clinical relevance of aGAPSS in a Chinese cohort	89	89 APS Patients
Fernandez Mosteirín et al.	2017	Retrospective	To independently validate the aGAPSS to predict thrombosis in a cohort of patients with APS and/or autoimmune disease	319	PAPS diagnosed in 130 patients and 89 SAPS patients, and 100 patients with autoimmune disease without APS
Radin et al.	2017	Retrospective	To investigate the validity of aGAPSS in young patients with myocardial infarction	83	APS Patients

APS Task Force on Laboratory Diagnostic and Trends (Rio, 2013)

	Risk Scale for APS Diagnosis	aPL-S	GAPSS
Year	2011	2013	2013
APS Risk assessment	Yes	Yes	Yes
Thrombotic risk assessment	No	Yes	Yes
PM risk assessment	No	Yes	Yes
aPL			
LA	Yes~	Yes~	Yes#
aCL	Yes	Yes	Yes
aβ2GPI	Yes	Yes	Yes
aPS/PT	No	Yes~	Yes~
Cardiovascular Risk Factors	No	No	Yes*
Approach	Semi-quantitative	Quantitative	Quantitative

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RISK ASSESMENT

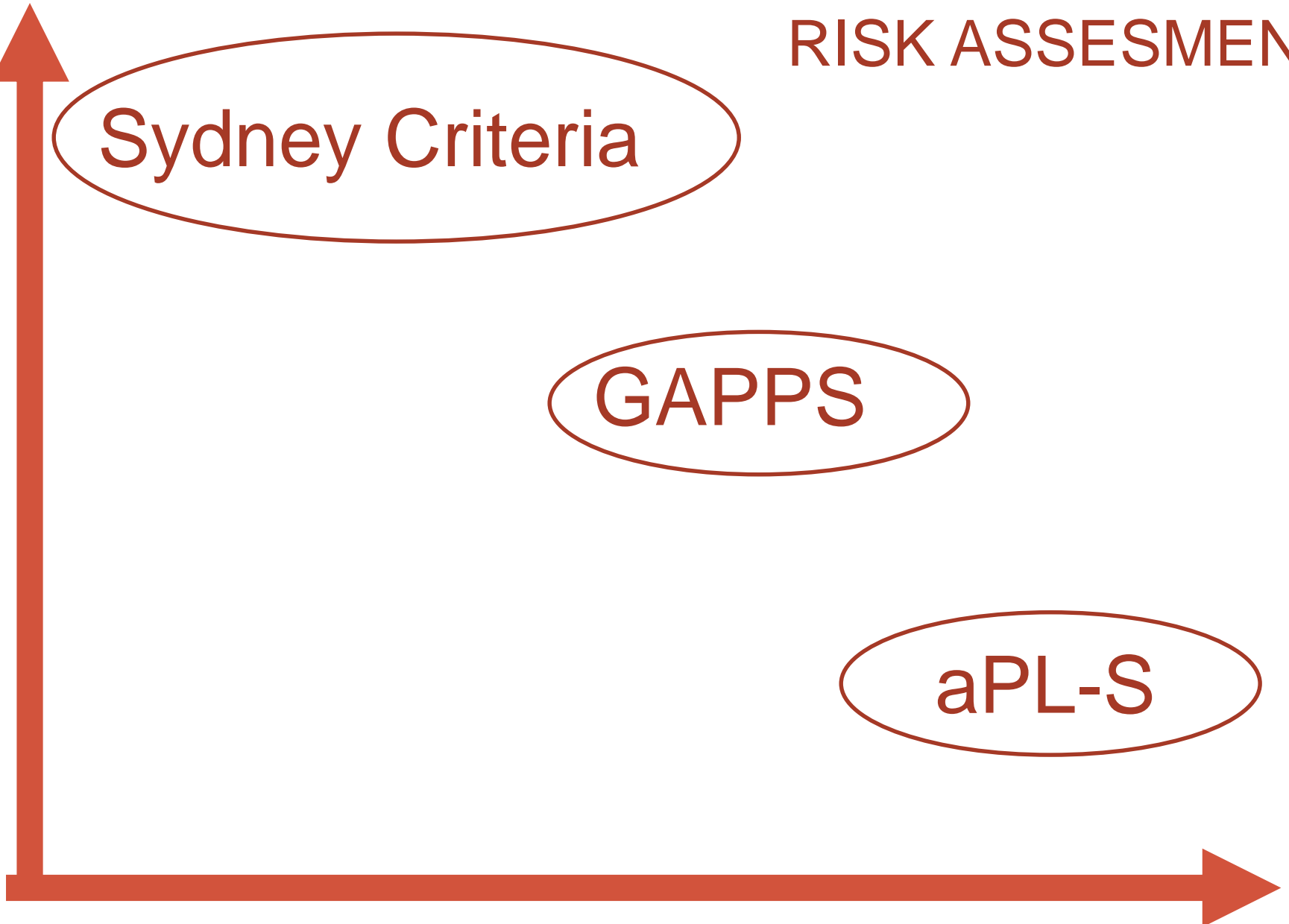
FEASIBILITY

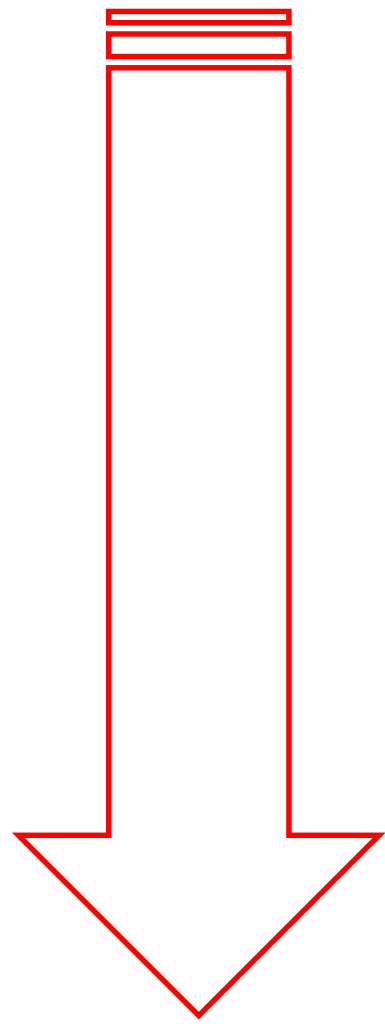
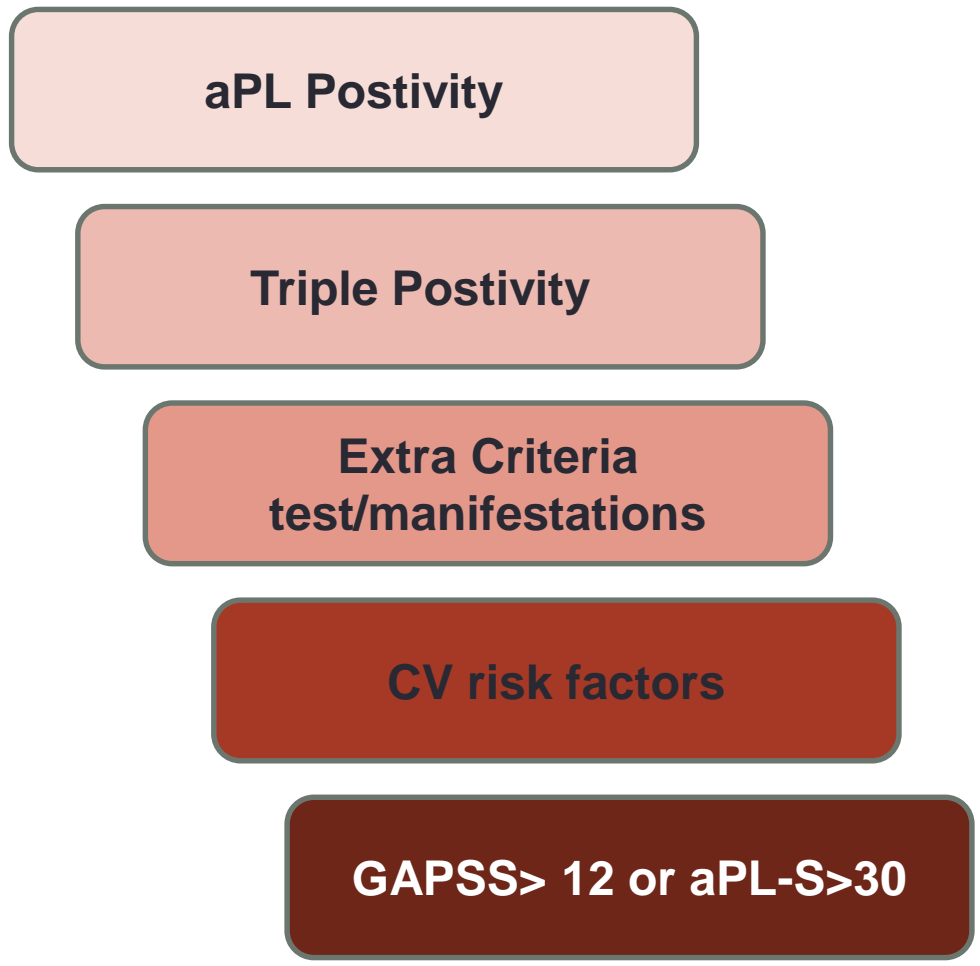
Sydney Criteria

GAPPS

aPL-S

SPECIFICITY

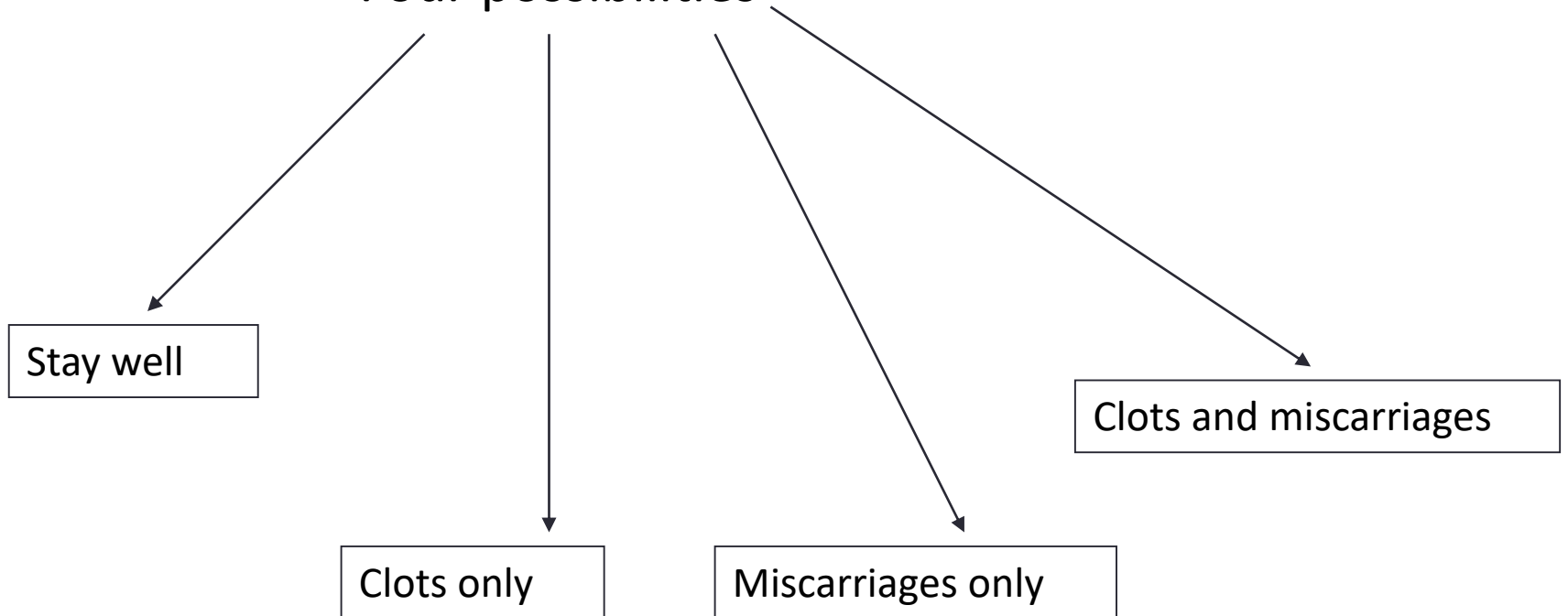




HIGH RISK

Positive aPL tests

Four possibilities



THERE IS CURRENTLY NO TEST TO PREDICT ACCURATELY WHICH GROUP YOU
WILL BE IN

Conclusion 1: Positive aPL tests

Five

~~Four~~ possibilities

Impact on prognosis and outcomes

Stay well

Clots only

Miscarriages only

Clots and miscarriages