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

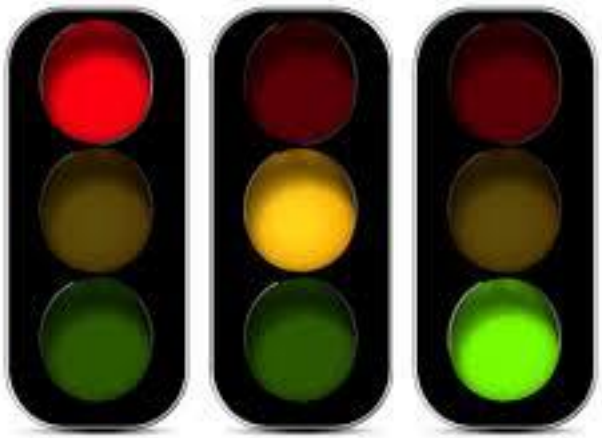
Risk of thrombosis and/or PM

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 a. Blood 2003

  - Double or triple positivity ⇧ the risk

Pengo et al. JTH 2010

Quantify the risk for patients

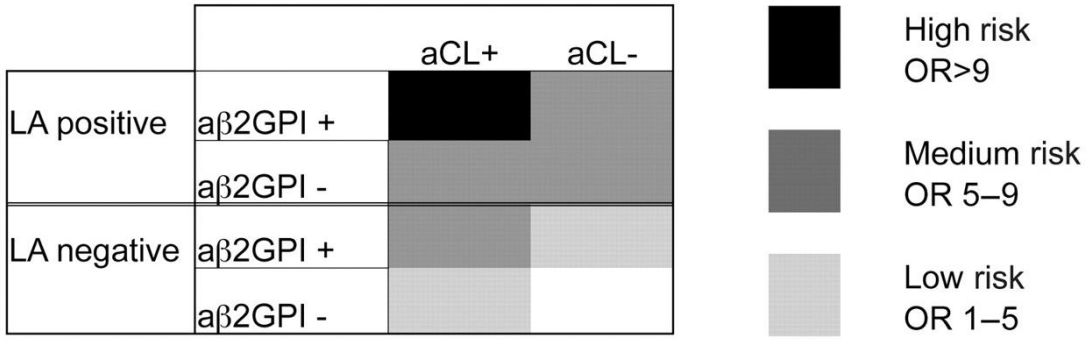
- When high risk is high enough?

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 Sciascia[1], Domenico Cosseddu[2], Barbara Montaruli[2], Anna Kuzenko[1], Maria Tiziana Bertero[1]



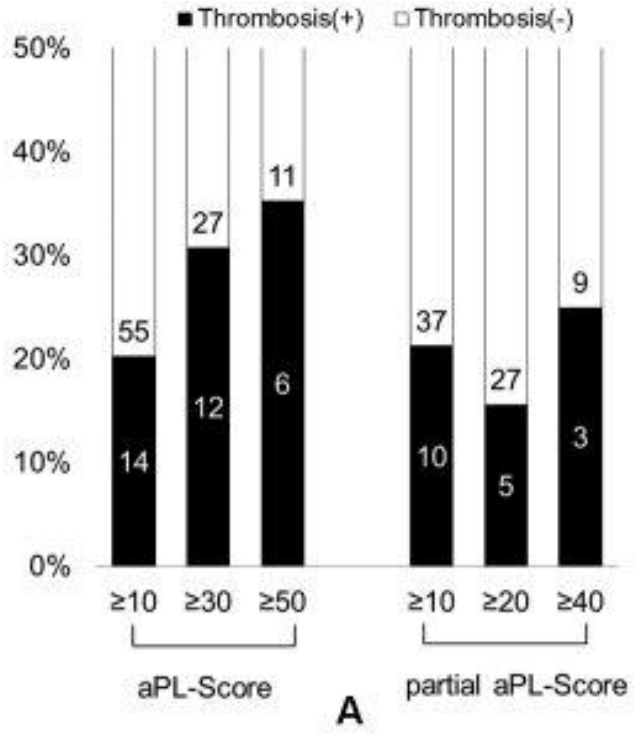
Methods for LA test	aCL and aβ2GPI titre: NEGATIVE < 10 U	LOW 10–30 U	MEDIUM 30–50 U	HIGH >50 U
SCT				
KCT				
DRVVT				
PTT-LA \ STACLOT LA				

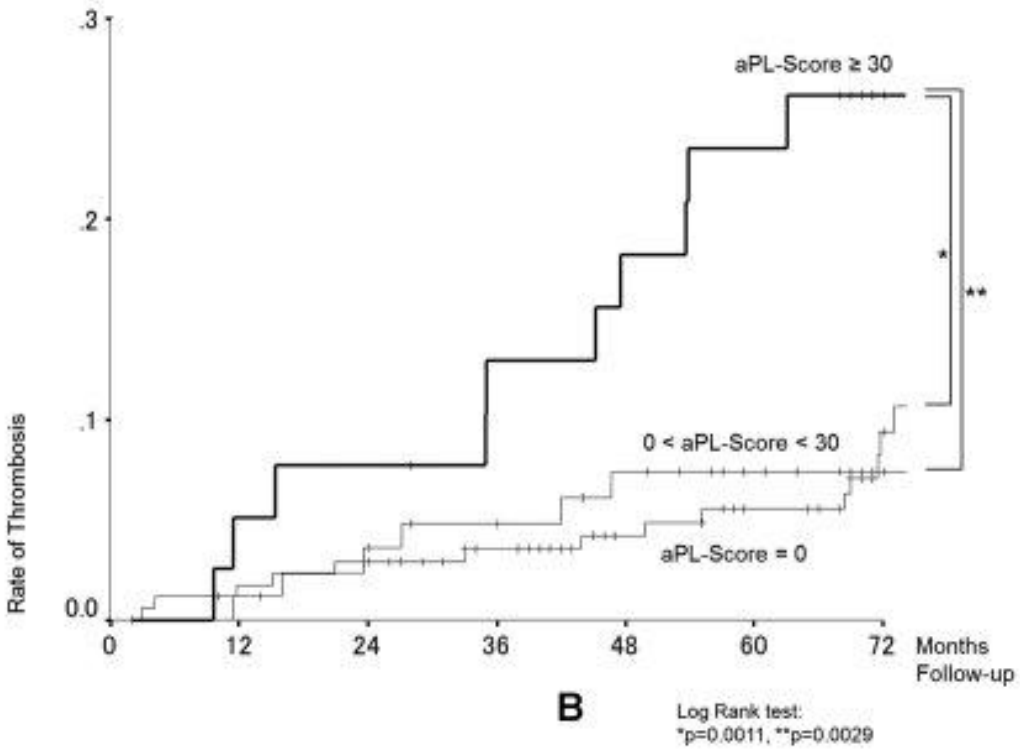
SCORE SYSTEMS IN APS

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

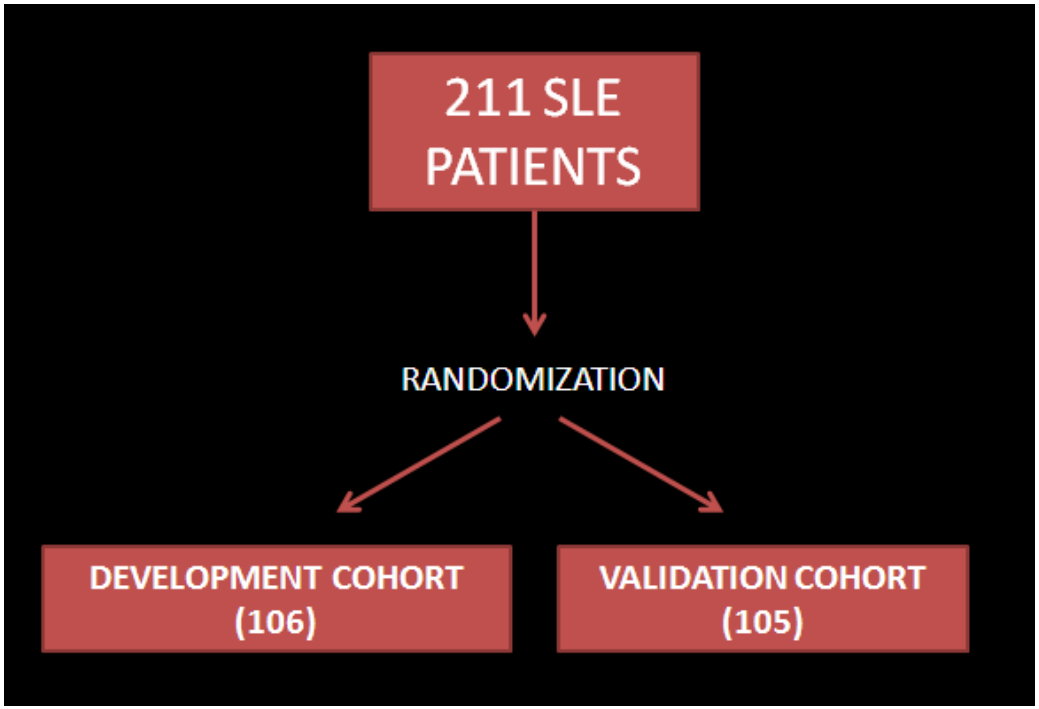
- To develop a risk score (Global APS Score or GAPSS) derived from the combination of independent risk of thrombosis and pregnancy loss, taking into account:
  - aPL profile (criteria and non-criteria aPL),
  - conventional cardiovascular risk factors
  - SLE autoimmune antibodies profile

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

Sciascia S, Rheumatology. 2013;52:1397-403

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

DEVELOPMENT COHORT (n=106)

	OR	CI [95%]		p
Characteristic				
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
aβ_2GPI 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

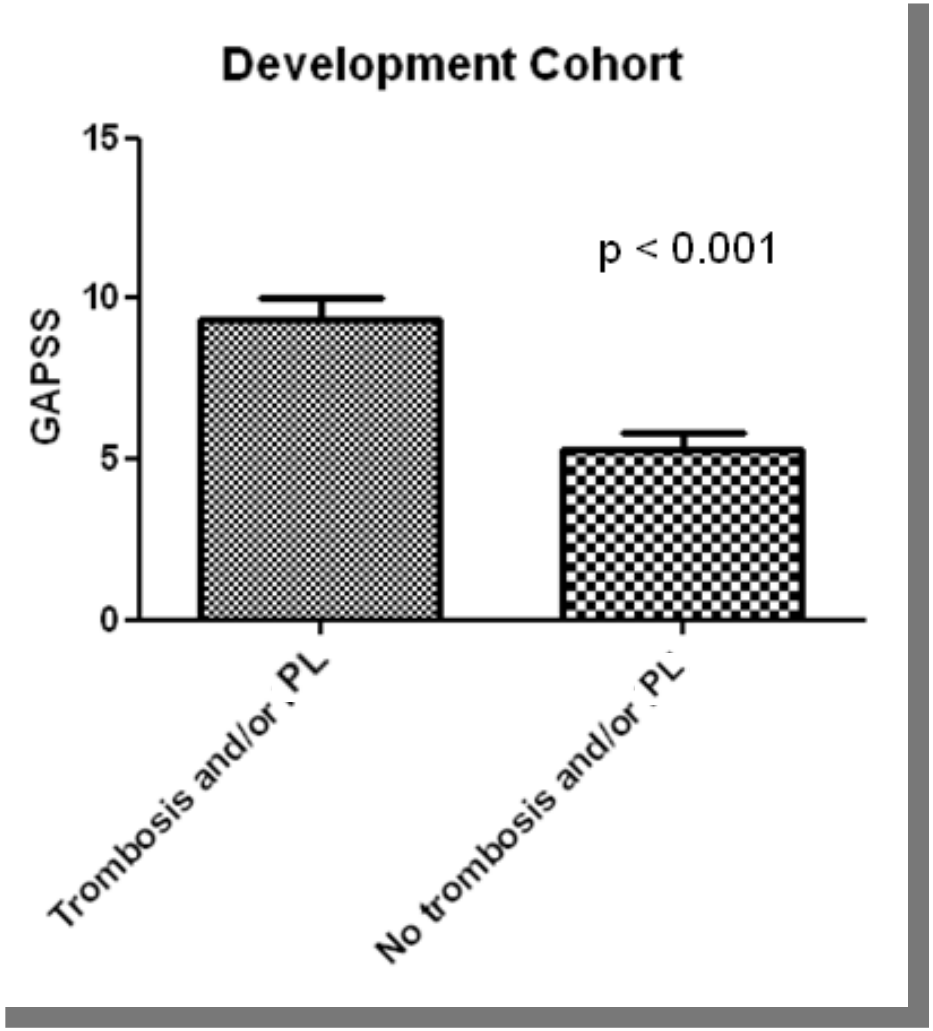
To calculate GAPSS, we assigned each of the six variables identified in the development cohort as independent risk factors for thrombosis and/or pregnancy morbidity, a number of points that was proportional to its regression coefficient

	β Coefficient	GAPSS*
Hyperlipidemia	1.73	3
Arterial hypertension	0.54	1
aCL IgG/IgM	2.63	5
Anti-β2GPI 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.

Rheumatology. 2013;52:1397-403

Development and validation of GAPSS



Rheumatology. 2013;52:1397-403

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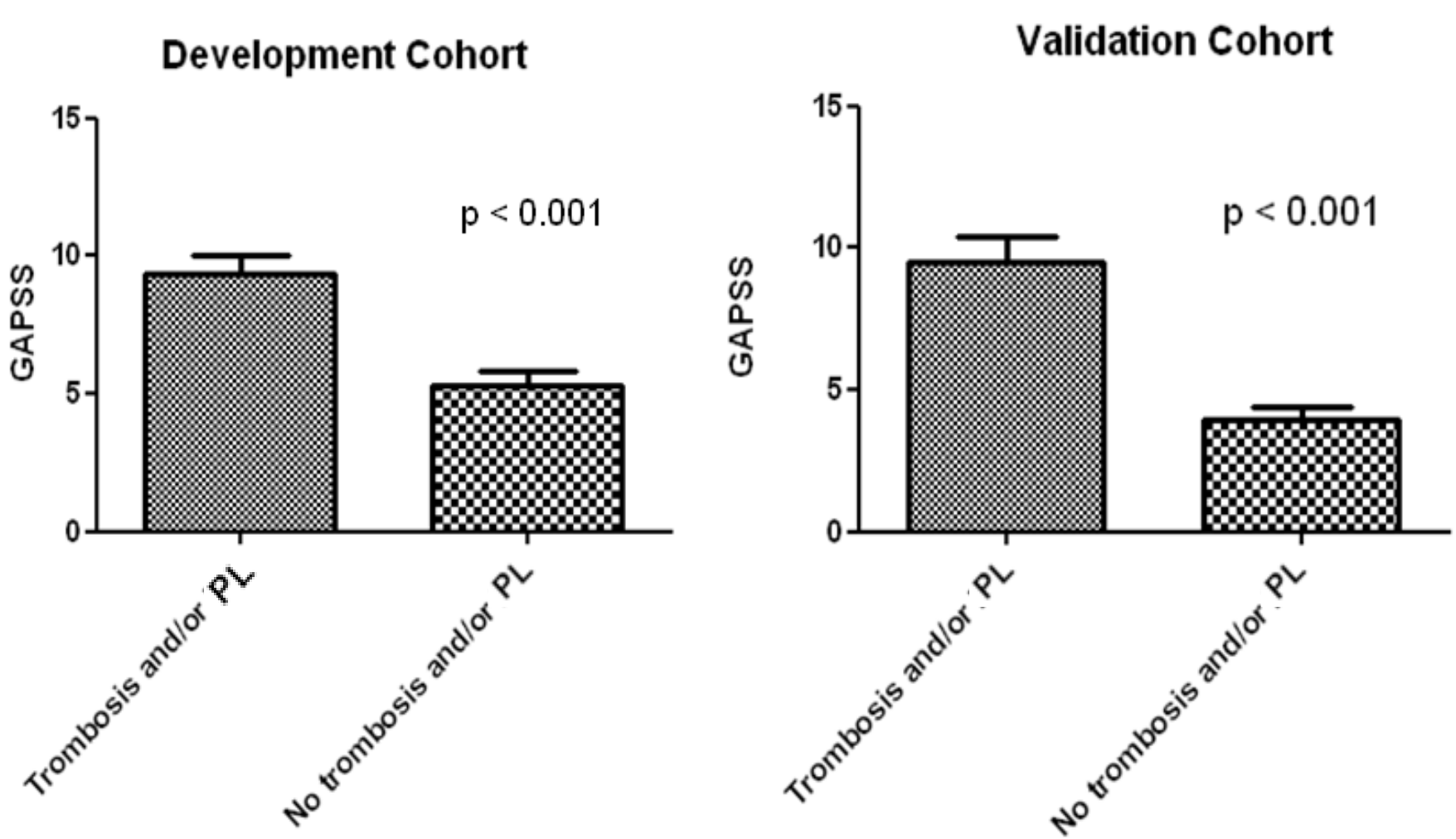
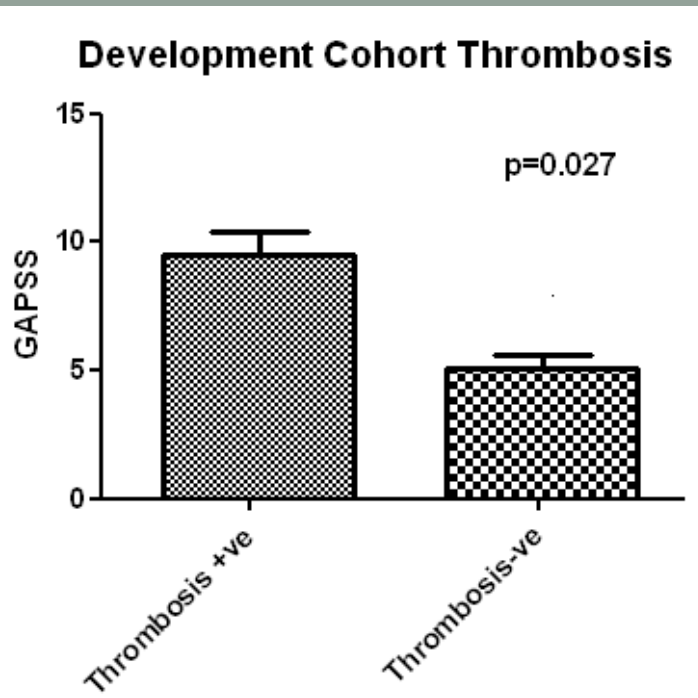
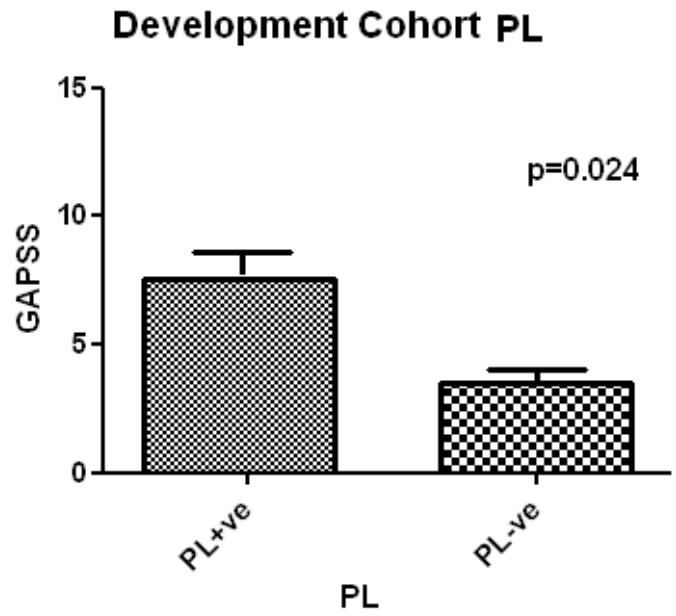
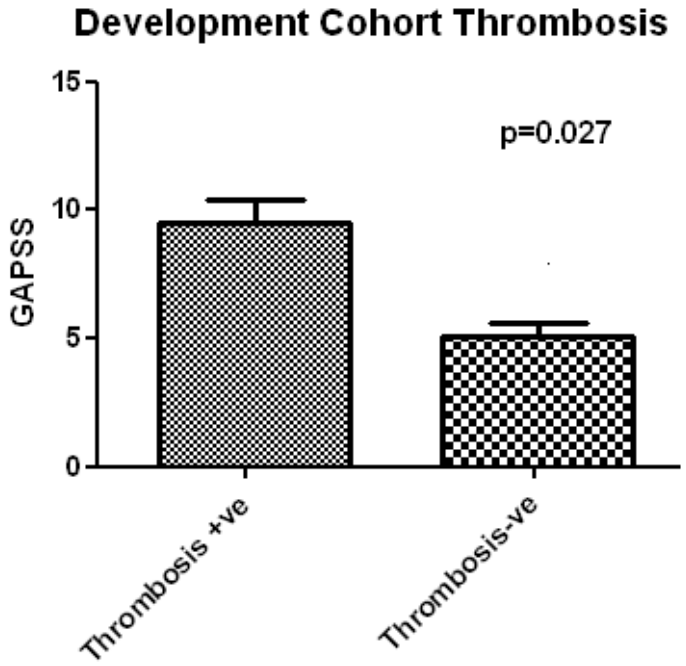


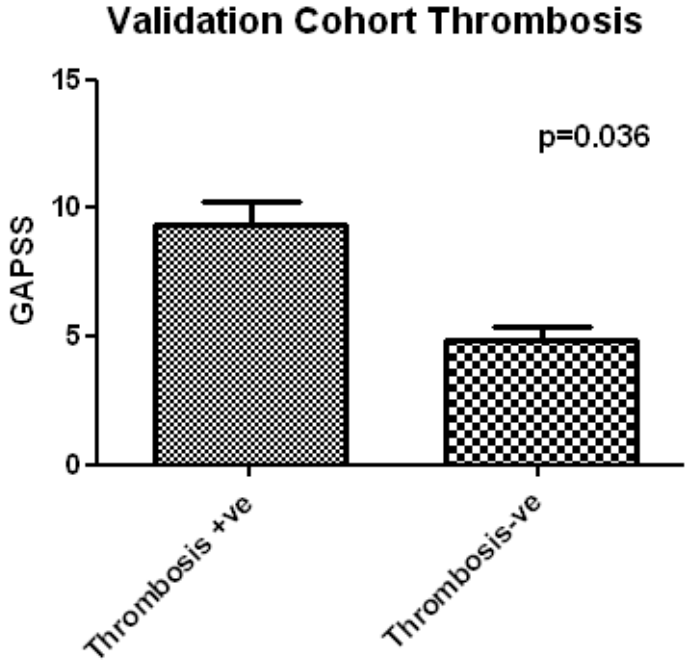
Rheumatology. 2013;52:1397-403

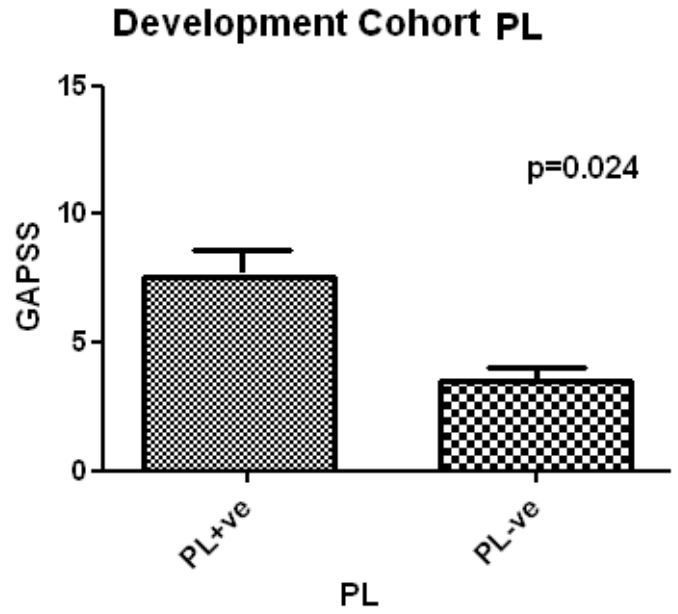


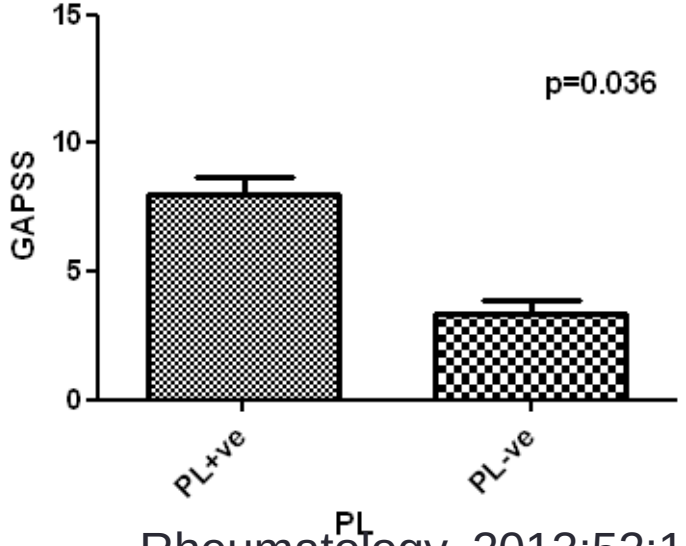


Rheumatology. 2013;52:1397-403



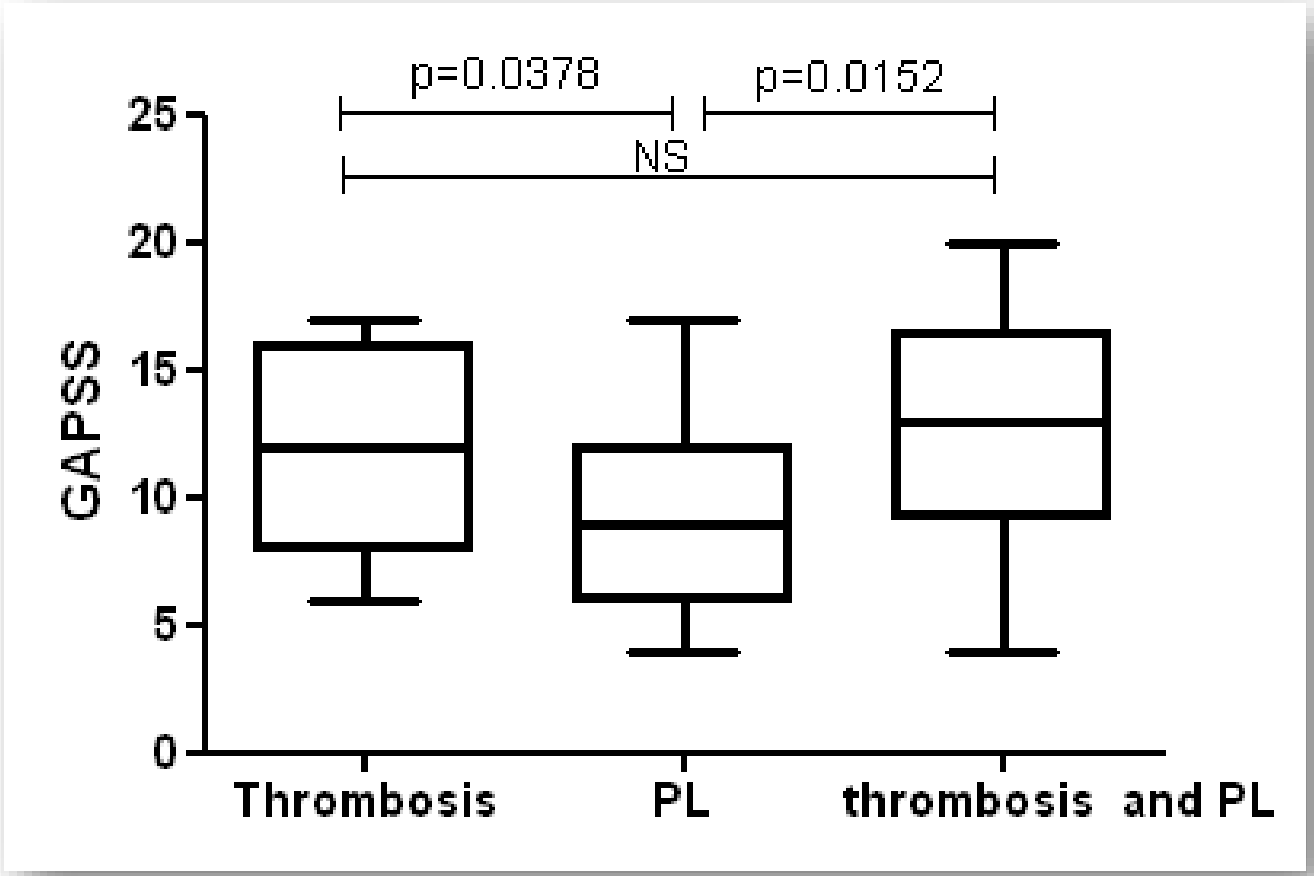






Rheumatology. 2013;52:1397-403

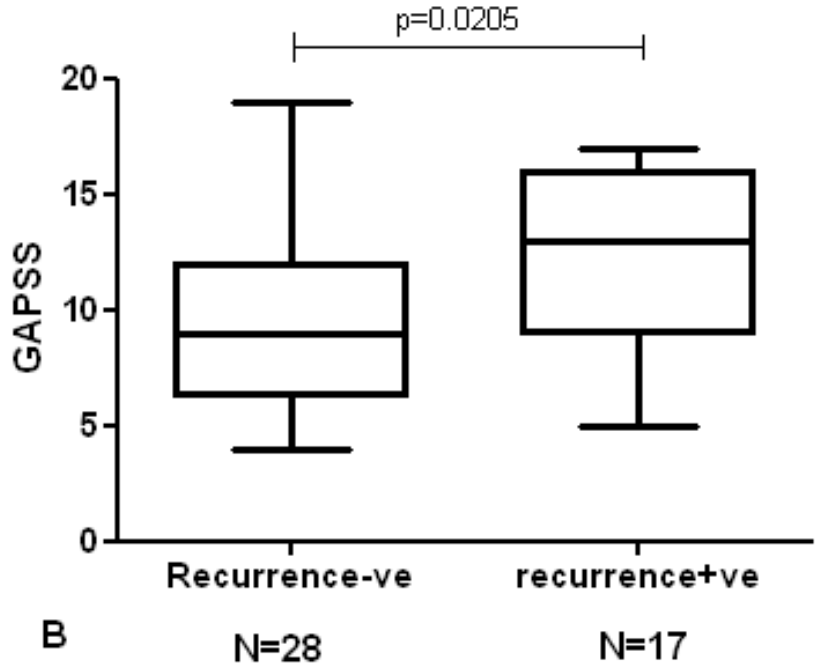
Clinical relevance of the in a cohort of primary APS patients (N=62)

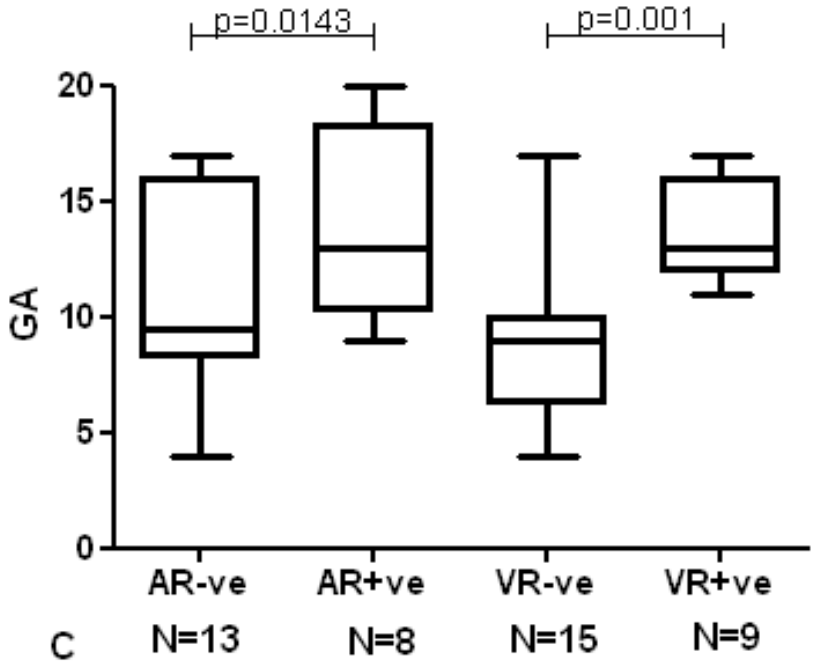


Higher values of GAPSS were showed in patients who experienced thrombosis compared to those with pregnancy loss alone

Rheumatology. 2015;54:134-8

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





AR= arterial recurrences

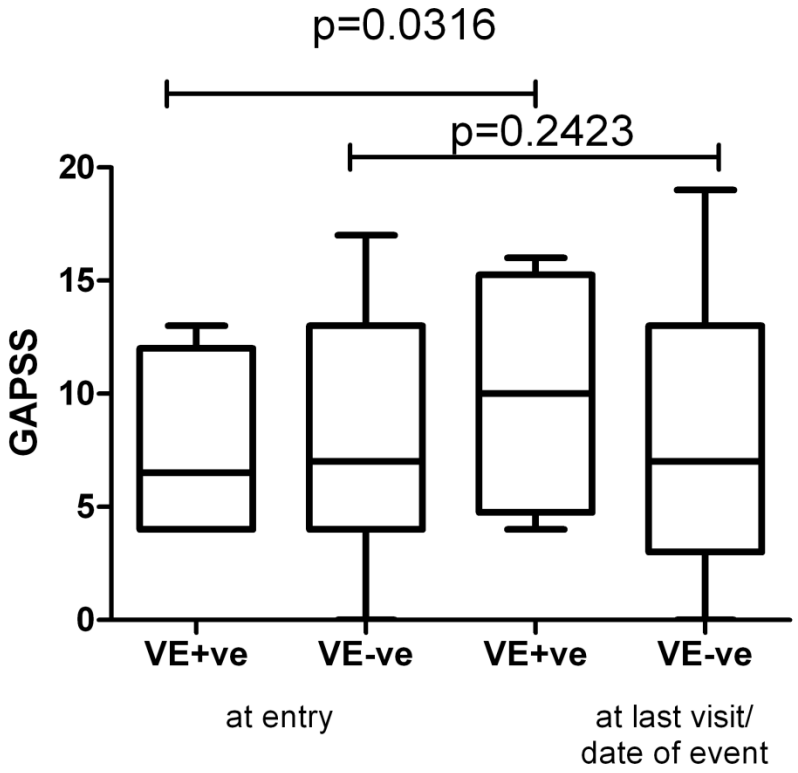
VR= venous recurrences

Rheumatology. 2015;54:134-8

	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)

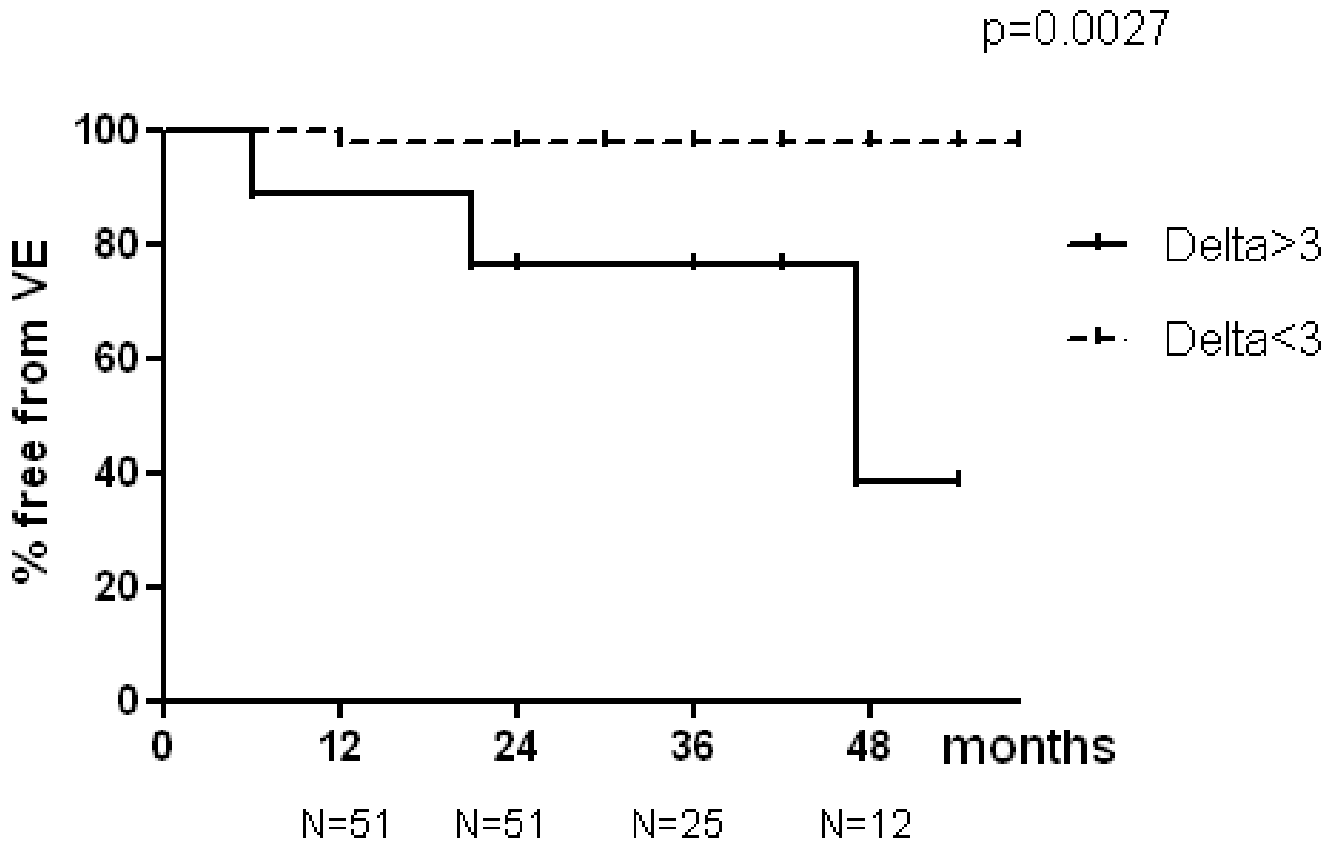


An increase in the GAPSS (entry vs. last visit) was seen in patients who experienced thrombosis (n=4)

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

Arthritis Care Res. 2014;66:1915-20

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)

Arthritis Care Res. 2014;66:1915-20

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

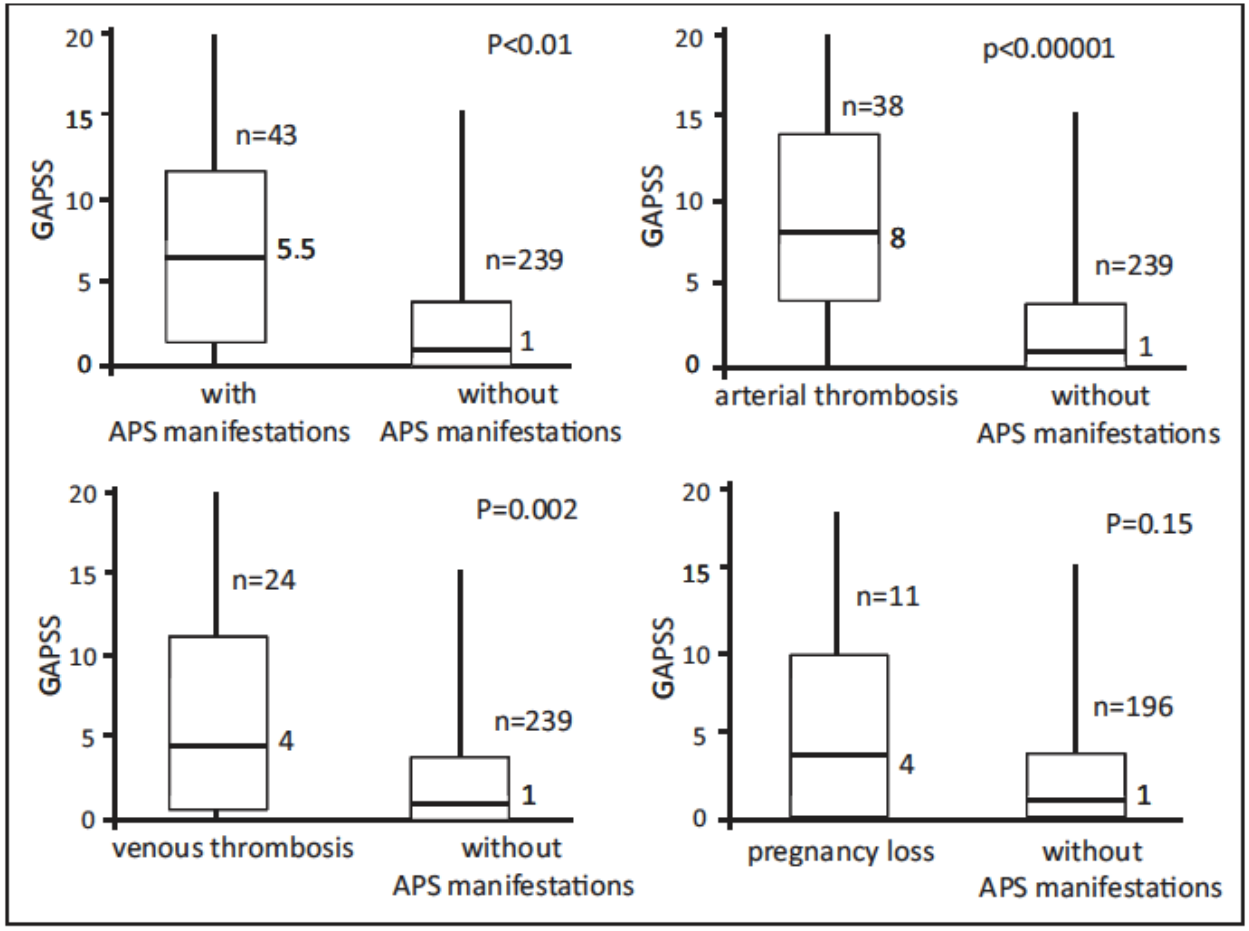
TABLE 2
Prediction of thrombosis using GAPSS according to different cut-off values in univariate survival analysis

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.

Zuily S. Rheumatology. 2015;54:2071-5.

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



Oku, K et al. Lupus. 2015;24:774-5.

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 revalence of aGAPSS in a chinese cohort	89	89 APS Patients
Fernandez Mosteirin 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

Sciascia & Bertolaccini, Rheumatology 2017

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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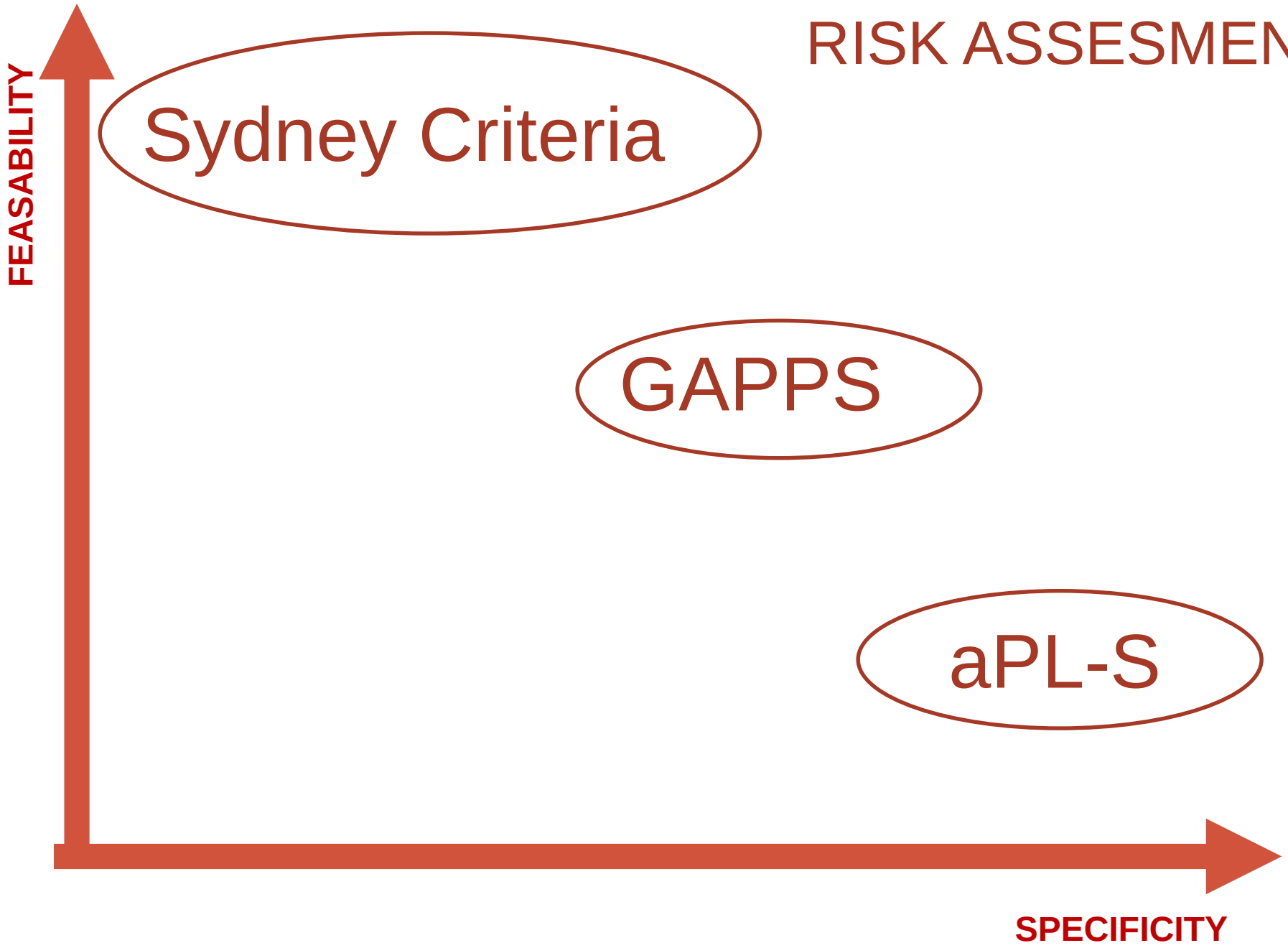
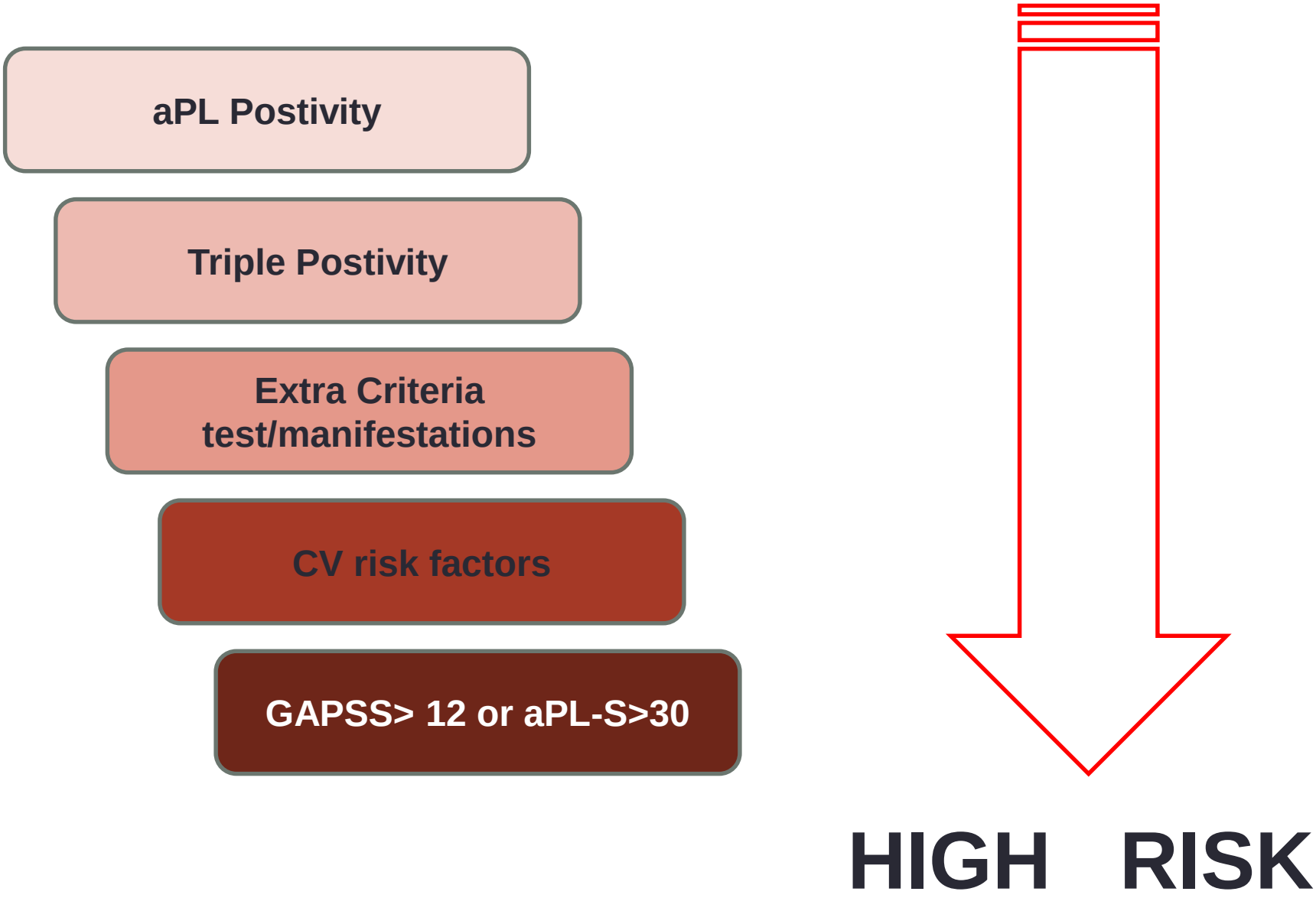
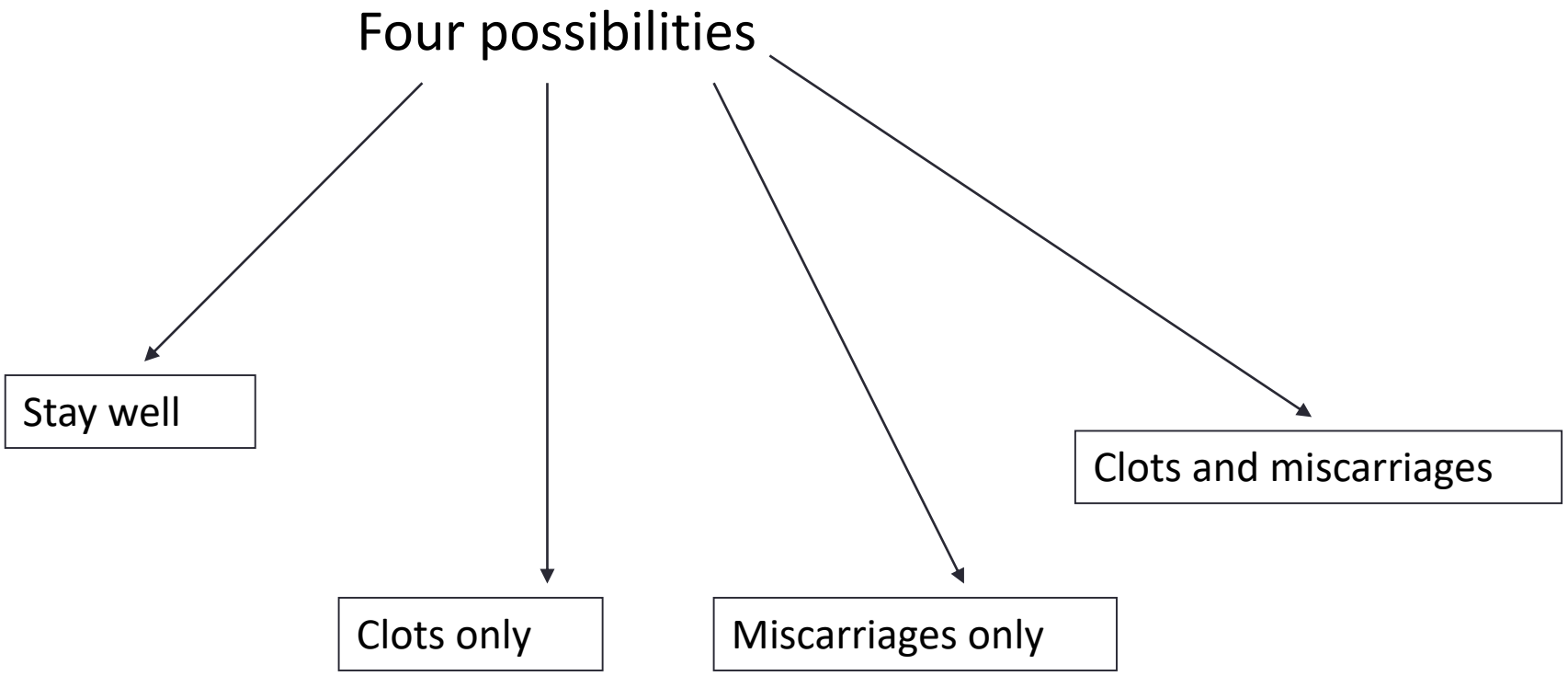
RISK ASSESMENT




aPL Postivity
Triple Postivity
Extra Criteria
test/manifestations
CV risk factors
GAPSS> 12 or aPL-S>30
HIGH RISK

Positive aPL tests



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

Conclusion 1: Positive aPL tests