

Appendix: Supplementary Tables, Statistical Code and Calculations

Table S1 Model Comparisons and Variable Selection

MODEL (# of variables)	Full (10) *	Full _{LT} (10)*	Reduced _{LT} , A (8)*	Reduced _{LT} , B (6)*	Parsimonious _{LT} (5)*	ACR (4)
Included covariates that were not statistically significant	Sex, New headache, Temporal artery abnormality, Diplopia, CRP	Sex, New headache, Temporal artery abnormality, Diplopia, log ESR	New headache, Temporal artery abnormality, log ESR	Temporal artery abnormality		New headache (Age category omitted)
AUROC	.8084	.8196	.8185	.8163	.8164	.6339
p _{Hosmer-Lemeshow}	.3590	.5485	.1722	.0182	.8115	.2227
Brier score	.1381	.1313	.2434	.2426	.1335	.1792
p _{Spiegelhalter z-test}	.4833	.5811	<.001	<.001	.6662	.5213
AIC	480.6595	466.2297	462.7570	460.603	461.0216	576.4964
BIC	527.6611	513.2314	501.2129	490.5135	486.6589	593.5500
Internal validation AUROC		0.803 (95% CI 0.757, 0.849)			0.810 (95% CI 0.766, 0.854).	
External validation AUROC		Range 0.688, 0.824			Range 0.750, 0.845	

LT = log transformed covariates. The CRP and ESR were skewed distributions and log transformed for model fitting.

*The statistically significant predictors were: Age, Jaw claudication, Ischemic vision loss, Platelets, and CRP in the non-log transformed model. In the log transformed model lnCRP replaced the CRP and lnESR replaced the ESR

The Brier score has both a calibration and discrimination (sharpness) component. A statistically significant value of Spiegelhalter's z-test (evaluated at $\alpha=0.05$), indicates poor calibration. (1)

ACR= American College of Rheumatology non-histologic criteria. None of the patients with positive temporal artery biopsy were under age 50 years old and the age category was omitted on logistic regression.

Table S2 Model Performance for each prediction model at its optimal cutpoint (Liu method)

	Full Model	Parsimonious Model	ACR Model
ACR Model Optimal Cutpoint 0.294			
Sensitivity	0.68	0.65	0.47
Specificity	0.81	0.82	0.78
False Negative Rate	0.32	0.35	0.53
Misclassification rate	0.22	0.23	0.30
Parsimonious Model Optimal Cutpoint 0.265			
Sensitivity	0.70	0.73	0.54
Specificity	0.79	0.78	0.67
False Negative Rate	0.21	0.28	0.46
Misclassification rate	.23	0.23	0.35
Full Model Optimal Cutpoint 0.242			
Sensitivity	0.74	0.73	0.67
Specificity	0.77	0.77	0.49
False Negative Rate	0.25	0.27	0.32
Misclassification rate	0.24	0.24	0.46

Figure S1

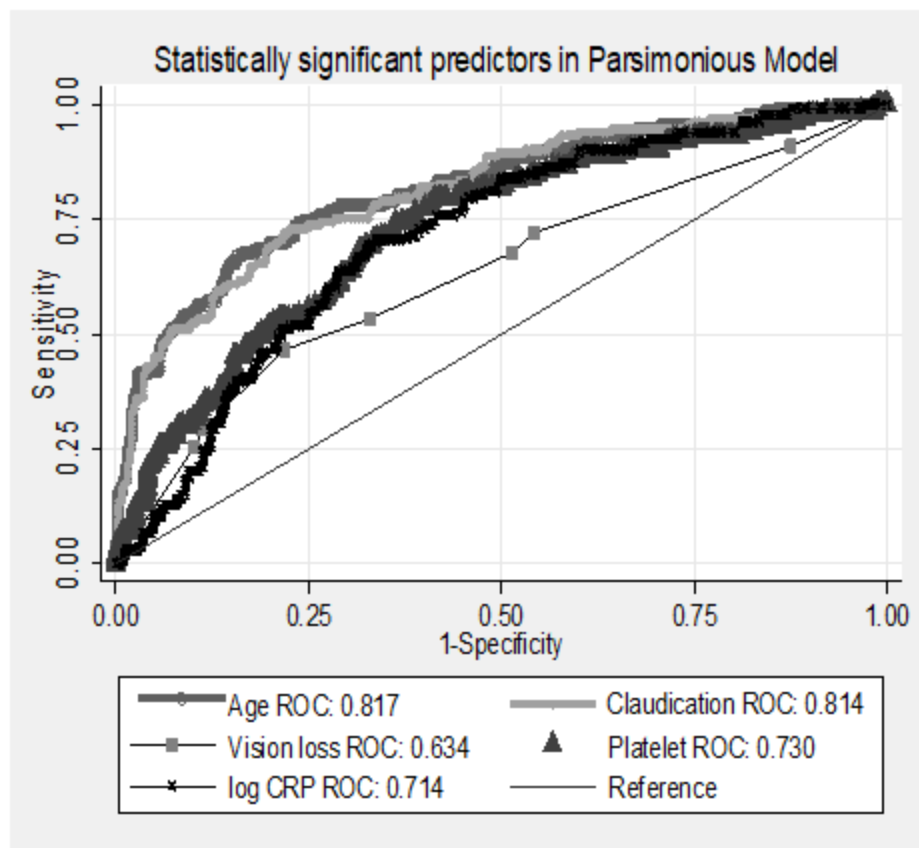


Table S3 Comparison of Prediction Rule Studies in the Literature

Author (Year)	N (positive biopsy events)	Statistically Significant Predictors	Odds Ratio
Gabriel (1995)	525 (172)	All claudication Synovitis TA Abn Px Highest ESR	4.55 0.31 2.55 1.01
Rodriguez-Valverde, (1997)	227 (90)	New headache TA Abn Px Jaw claudication Raised liver enzymes < 70 years old at disease onset	13.6 4.2 4.8 2.9 0.11
Rieck (2011)	82 (22)	Jaw claudication Weight loss	4.50 3.76
Gonzalez-Lopez (2013)	335 (81)	Jaw claudication New headache TA Abn Px Pain and stiffness in neck and shoulders Unintentional weight loss Age Biopsy Length ESR	4.6 4.4 2.8 2.3 1.33 1.085 1.079 1.042
De Lott (2015)	239 for logistic regression (?90)	Age Platelets	1.06 1.01
Grossman (2016)	224 (57) [included 25 biopsy negative GCA]	New headache Jaw claudication ESR Platelet count	6.0 4.5 1.5 1.74
Present study (2017)	530 (133)	Jaw Claudication Vision Loss Platelet LogCRP Age	4.0 2.7 1.005 1.35 1.04

GCA = giant cell arteritis

TA Abn Px = temporal artery abnormality on physical exam

COMMENTS ON THE GCA CALCULATOR

The calculator is meant to objectify decision-making when discussing management options with patients with suspected GCA. The calculator only predicts **biopsy-proven** GCA.

We encourage you to interpret the probability score with respect to the cutpoints. For scores lower than 15%, ask your patient, "Given GCA is a potentially blinding disease, and there is a _% chance you might have GCA, do you want to proceed with TABx and steroids, or do you want to continue observation?"

None of the 133 biopsy proven GCA patients had a probability score below 2.7%

7.5% of the patients with biopsy proven GCA had a normal platelet, and normal ESR and normal CRP level pre-steroid; the average probability score on this seronegative group was 11%.

Female gender and diplopia were NOT helpful predictors of GCA in this study. You will see the risk score goes down for females and patients with diplopia. More females had GCA than males, but more females also had negative biopsy. In this series 35% with biopsy proven GCA had vision loss. Perhaps the high incidence of vision loss made binocular diplopia unlikely and that may be why the diplopia variable performs this way on the calculator.

STATISTICAL PROGRAMS: Stata 14.2, JMP Pro 13

CODEBOOK FOR VARIABLES

VARIABLE NAME	MEANING		TYPE OF VARIABLE
<i>Outcome variable</i>			
<i>tabxneg0</i>	<i>Temporal artery biopsy pathology result</i>	<i>Positive =1 Negative=0</i>	<i>binary</i>
<i>Predictor variables</i>			
<i>age</i>	<i>Age in years</i>		<i>continuous</i>
<i>female1</i>	<i>Gender</i>	<i>Female=1 Male = 0</i>	<i>binary</i>
<i>newheadache</i>	<i>Recent onset headache</i>	<i>1= new headache 0= no new headache</i>	<i>binary</i>

taabnormality	Tender or pulseless temporal artery or scalp tenderness/nodule	1= present 0= absent	binary
Jawclaudication1	Jaw claudication + (tongue claudication)	1=claudication	binary
discrao	Permanent vision/field loss (disc edema, retinal artery occlusion, PION) In article = VL	1 = vision loss 0= no vision loss	binary
Diplopia1	Diplopia symptoms	1= diplopia present	binary
platelet			
lncrp	Natural log CRP + constant	Ln (CRP divided by ULN) +3.69	continuous
lnesr	Natural log Westergren ESR + constant	ln(ESR) + 4.61	continuous
length	Biopsy length in cm	Posthoc analysis (not a predictor)	continuous
f1530pr1	Probability of positive biopsy, full model		continuous
pabicpr1	Probability of positive biopsy, parsimonious model		continuous
acrpob1	Probability of positive biopsy ACR model		continuous
esrcat	ESR>=50 == 1 for ACR		binary
agecat	Age >=50 ==1 for ACR		binary

code3	region		Categorical string
code4	Numeric region code		categorical
nlbloodtabxpos1	Biopsy positive but Platelets<400, ESR<50 and CRP <=1		binary

METHOD SECTION

KATTAN NOMOGRAM CONSTRUCTION

Skewed data was normalized by the logarithmic function and constants were added to provide positive results for the Kattan nomogram. For the ESR the constant 4.61 was added to the logESR, and for the CRP the constant 3.69 was added to the logCRP so that there were no negative values for the later Kattan nomogram. For ease of use, the logarithmic transforms were converted back to ESR and CRP values in the nomogram scales.

RESULTS SECTION

TABLE 1

```
table1, by( tabxneg0) vars( age contn \ female1 bin \ newheadache bin \ taabnormality bin \ jawclaudication1 bin \platelet contn \ origesr conts \ crp conts \ discrao bin \ Diplopia1 bin \ length contn) saving(Table3GCA.xls)
```

UNIVARIATE LOGISTIC REGRESSION

```
foreach x of varlist age female1 newheadache taabnormality jawclaudication1 platelet origesr crp discrao Diplopia1 { logistic tabxneg0 `x' } *
```

"SERONEGATIVE" GCA

```
generate nlbloodtabxpos1 = 0
replace nlbloodtabxpos1 =1 if origesr<50 & crp <=1 & platelet<400 &tabxneg0==1
tabstat age female1 newheadache newheadache taabnormality jawclaudication1 discrao Diplopia1 length platelet origesr crp if tabxneg0==1, statistics( mean sd count ) by(nlbloodtabxpos1)
Summary statistics: mean, sd, N
by categories of: nlbloodtabxpos1
nlbloodtabxpos1 |      age      female1 newhea~e newhea~e taabno~y jawcla~1 discrao Diplop~1
length platelet origesr crp
-----+-----
0 | 77.06748 .6585366 .7642276 .7642276 .5121951 .4878049 .3577236
.0650407 1.915306 395 58.39443 13.77265
```


sum length, detail, if tabxneg0==0
length

Percentiles		Smallest			
1%	.5	.1			
5%	.8	.4			
10%	1	.4	Obs		376
25%	1.3	.5	Sum of Wgt.		376
50%	1.8		Mean		1.848005
		Largest	Std. Dev.		.6952717
75%	2.5	3.8			
90%	2.5	4.2	Variance		.4834027
95%	2.6	4.3	Skewness		.2796604
99%	3.8	4.6	Kurtosis		3.321012

sum length, detail, if tabxneg0==1
length

Percentiles		Smallest			
1%	.7	.6			
5%	.8	.7			
10%	1	.8	Obs		106
25%	1.5	.8	Sum of Wgt.		106
50%	2		Mean		1.922642
		Largest	Std. Dev.		.5876966
75%	2.5	2.6			
90%	2.5	2.7	Variance		.3453872
95%	2.6	2.8	Skewness		-.5285843
99%	2.8	3	Kurtosis		2.200076

CHOICE OF FULL MODEL TO MINIMIZE AIC AND BIC

Full model: nontransformed esr crp

Model	Obs	ll(null)	ll(model)	df	AIC	BIC
.	530	-298.5857	-229.3297	11	480.6595	527.6611

Full model: lnesr, crp

Model	Obs	ll(null)	ll(model)	df	AIC	BIC
.	530	-298.5857	-226.6329	11	475.2658	522.2674

Full model: esr, lncrp

Model	Obs	ll(null)	ll(model)	df	AIC	BIC
.	530	-298.5857	-222.7568	11	467.5137	514.5153

Full model: lnesr, lncrp

Model	Obs	ll(null)	ll(model)	df	AIC	BIC
.	530	-298.5857	-222.1149	11	466.2297	513.2314

In the non-transformed full model, the ESR was statistically significant ($p=0.029$ with $p_{MICE}=0.30$), but the CRP ($p=0.762$ with $p_{MICE}=0.651$) was not. However the full model with the log transformed CRP ($p=.003$) and log transformed ESR ($p=.273$) was chosen because it had lower AIC and BIC.

NO SPECIFICATION ERROR (Stata "linktest")

FULL MODEL

```
. logit tabxneg0 age female1 newheadache taabnormality jawclaudication1 platelet crp
origesr discrao Diplopia1, nolog
```

Logistic regression	Number of obs	=	530
	LR chi2(10)	=	138.51
	Prob > chi2	=	0.0000
Log likelihood = -229.32973	Pseudo R2	=	0.2319

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
age	.0465098	.0128504	3.62	0.000	.0213234	.0716961
female1	-.2353226	.2571522	-0.92	0.360	-.7393318	.2686865
newheadache	.2044438	.2854474	0.72	0.474	-.3550228	.7639105
taabnormality	.4003271	.2554037	1.57	0.117	-.1002551	.9009092
jawclaudication1	1.335526	.2592266	5.15	0.000	.8274509	1.843601
platelet	.0060248	.0010619	5.67	0.000	.0039435	.0081061
crp	.0028098	.0092628	0.30	0.762	-.015345	.0209645
origesr	.0089525	.0040991	2.18	0.029	.0009183	.0169866
discrao	.9951831	.2753072	3.61	0.000	.455591	1.534775
Diplopia1	-.0639864	.5051335	-0.13	0.899	-1.05403	.926057
_cons	-7.855003	1.121877	-7.00	0.000	-10.05384	-5.656165

```
. linktest, nolog
```

Logistic regression	Number of obs	=	530
	LR chi2(2)	=	138.71
	Prob > chi2	=	0.0000
Log likelihood = -229.23054	Pseudo R2	=	0.2323

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_hat	1.046251	.1490225	7.02	0.000	.7541728	1.33833
_hatsq	.0294055	.0662836	0.44	0.657	-.1005079	.1593189
_cons	-.0207729	.1574102	-0.13	0.895	-.3292911	.2877454

FULL MODEL WITH LOG TRANSFORMED ESR CRP

```
. logit tabxneg0 age female1 newheadache taabnormality jawclaudication1 platelet lncrp
lnesr discrao Diplopia1, nolog
Logistic regression
```

```
Number of obs      =      530
LR chi2(10)         =      152.94
Prob > chi2         =      0.0000
Pseudo R2          =      0.2561
```

```
Log likelihood = -222.11487
```

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
age	.0449871	.0131698	3.42	0.001	.0191748	.0707993
female1	-.1523935	.2610758	-0.58	0.559	-.6640926	.3593057
newheadache	.2306857	.2895042	0.80	0.426	-.3367321	.7981035
taabnormality	.3563223	.2609711	1.37	0.172	-.1551716	.8678162
jawclaudication1	1.296339	.2636562	4.92	0.000	.7795826	1.813096
platelet	.0050691	.0010637	4.77	0.000	.0029844	.0071538
lncrp	.2901259	.0980896	2.96	0.003	.0978738	.4823779
lnesr	.1870691	.170521	1.10	0.273	-.1471459	.5212841
discrao	1.03084	.2806157	3.67	0.000	.4808433	1.580836
Diplopia1	-.229284	.5020145	-0.46	0.648	-1.213214	.7546464
_cons	-9.96761	1.600932	-6.23	0.000	-13.10538	-6.829841

```
. linktest, nolog
```

```
Logistic regression
```

```
Number of obs      =      530
LR chi2(2)         =      154.36
Prob > chi2         =      0.0000
Pseudo R2          =      0.2585
```

```
Log likelihood = -221.40814
```

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_hat	1.124489	.1516177	7.42	0.000	.8273235	1.421654
_hatsq	.0723567	.0606377	1.19	0.233	-.0464911	.1912045
_cons	-.0515301	.1562692	-0.33	0.742	-.3578121	.2547519

A SMALL ODDS RATIOS MAY BE SEEMINGLY UNIMPORTANT, BUT PLATELETS WERE A CONTINUOUS COVARIATE with wide range. The odds ratio for platelets is **1.005** with β .0050691. Although a 1 unit change in platelets may be a small difference, and the odds ratio for platelets seemingly unimportant a 10 unit increase in platelets has effect $e^{(\beta_{\text{platelets}} \cdot 10)} = e^{(.0050691 \cdot 10)} = 1.05X$ increase in the odds ratio. A 50 unit increase in platelets results in a $e^{(.005691 \cdot 50)} = 1.29X$ increase in the odds.

PARSIMONIOUS MODEL

```
logit tabxneg0 age jawclaudication1 platelet lncrp discrao, nolog
```

```
Logistic regression
```

```
Number of obs      =      530
LR chi2(5)         =      148.15
Prob > chi2         =      0.0000
```

Log likelihood = -224.5108 Pseudo R2 = 0.2481

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
age	.0438666	.0129774	3.38	0.001	.0184314	.0693019
jawclaudication1	1.402289	.2527095	5.55	0.000	.9069877	1.897591
platelet	.0050816	.0010462	4.86	0.000	.003031	.0071321
lncrp	.3581129	.0800815	4.47	0.000	.2011559	.5150698
discrao	.9248225	.2686439	3.44	0.001	.3982902	1.451355
_cons	-8.49572	1.127081	-7.54	0.000	-10.70476	-6.286681

. linktest, nolog

Logistic regression	Number of obs	=	530
	LR chi2(2)	=	148.68
	Prob > chi2	=	0.0000
Log likelihood = -224.24784	Pseudo R2	=	0.2490

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_hat	1.073897	.1472921	7.29	0.000	.7852101	1.362585
_hatsq	.045486	.0627132	0.73	0.468	-.0774296	.1684017
_cons	-.0343638	.1566749	-0.22	0.826	-.341441	.2727135

ACR MODEL (5 subjects less than 50 years of age, all had negative TABx)

logit tabxneg0 agecat esrcat newheadache taabnormality, nolog

note: agecat != 1 predicts failure perfectly

agecat dropped and 5 obs not used

Logistic regression	Number of obs	=	525
	LR chi2(3)	=	25.77
	Prob > chi2	=	0.0000
Log likelihood = -284.24822	Pseudo R2	=	0.0434

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
agecat	0 (omitted)					
esrcat	.8195679	.2070725	3.96	0.000	.4137132	1.225423
newheadache	.0979034	.2451079	0.40	0.690	-.3824992	.5783061
taabnormality	.5792912	.2143856	2.70	0.007	.1591032	.9994792
_cons	-1.738102	.2369044	-7.34	0.000	-2.202426	-1.273778

linktest, nolog

Logistic regression	Number of obs	=	525
	LR chi2(2)	=	27.32
	Prob > chi2	=	0.0000
Log likelihood = -283.47458	Pseudo R2	=	0.0460

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
_hat	2.036413	.8596832	2.37	0.018	.3514652	3.721361
_hatsq	.5234275	.421919	1.24	0.215	-.3035185	1.350374

```

_cons | .3707679 .3752286 0.99 0.323 -.3646667 1.106203
-----

```

NO MULTICOLLINEARITY

```

collin age female1 newheadache taabnormality jawclaudication1 platelet crp origesr
discrao Diplopia1

```

(obs=530)

Collinearity Diagnostics

Variable	SQRT		Tolerance	R-Squared
	VIF	VIF		
age	1.02	1.01	0.9803	0.0197
female1	1.05	1.02	0.9549	0.0451
newheadache	1.10	1.05	0.9060	0.0940
taabnormality	1.15	1.07	0.8718	0.1282
jawclaudication1	1.09	1.05	0.9153	0.0847
platelet	1.19	1.09	0.8424	0.1576
crp	1.45	1.21	0.6880	0.3120
origesr	1.39	1.18	0.7220	0.2780
discrao	1.09	1.04	0.9168	0.0832
Diplopia1	1.02	1.01	0.9839	0.0161

```

Mean VIF      1.15

```

Eigenval		Cond Index
1	6.4979	1.0000
2	0.9639	2.5965
3	0.9080	2.6751
4	0.7584	2.9271
5	0.6696	3.1151
6	0.4741	3.7021
7	0.2660	4.9424
8	0.2211	5.4215
9	0.1496	6.5901
10	0.0831	8.8408
11	0.0082	28.0948

```

Condition Number      28.0948

```

Eigenvalues & Cond Index computed from scaled raw sscp (w/ intercept)

```

Det(correlation matrix) 0.4855

```

```

. collin age female1 newheadache taabnormality jawclaudication1 platelet lncrp lnesr
discrao Diplopia1

```

(obs=530)

Collinearity Diagnostics

Variable	SQRT		Tolerance	R-Squared
	VIF	VIF		
age	1.03	1.01	0.9740	0.0260
female1	1.03	1.02	0.9686	0.0314

newheadache	1.10	1.05	0.9080	0.0920
taabnormality	1.16	1.08	0.8653	0.1347
jawclaudication1	1.09	1.04	0.9180	0.0820
platelet	1.21	1.10	0.8231	0.1769
lncrp	1.68	1.30	0.5949	0.4051
lnesr	1.49	1.22	0.6724	0.3276
discrao	1.09	1.04	0.9199	0.0801
Diplopia1	1.02	1.01	0.9780	0.0220

Mean VIF 1.19

	Eigenval	Cond Index
1	7.2943	1.0000
2	0.9529	2.7668
3	0.9001	2.8468
4	0.6771	3.2822
5	0.4764	3.9131
6	0.2867	5.0440
7	0.2299	5.6334
8	0.0937	8.8239
9	0.0700	10.2054
10	0.0131	23.5941
11	0.0059	35.0522

Condition Number 35.0522

Eigenvalues & Cond Index computed from scaled raw sscp (w/ intercept)

Det(correlation matrix) 0.4313

PARSIMONIOUS MODEL

collin age jawclaudication1 platelet lncrp discrao

(obs=530)

Collinearity Diagnostics

Variable	SQRT		Tolerance	R- Squared
	VIF	VIF		
age	1.01	1.01	0.9869	0.0131
jawclaudication1	1.02	1.01	0.9796	0.0204
platelet	1.18	1.09	0.8475	0.1525
lncrp	1.16	1.08	0.8621	0.1379
discrao	1.03	1.01	0.9716	0.0284

Mean VIF 1.08

	Eigenval	Cond Index
1	4.4175	1.0000
2	0.7825	2.3760
3	0.6201	2.6690
4	0.0930	6.8934
5	0.0784	7.5068

```

        6      0.0085      22.7935
-----
Condition Number      22.7935
Eigenvalues & Cond Index computed from scaled raw sscp (w/ intercept)
Det(correlation matrix)  0.8271

```

ACR MODEL

```

collin agecat esrcat newheadache taabnormality
(obs=530)

```

```

Collinearity Diagnostics
              SQR
Variable      VIF VIF  Tolerance  R-
-----
      agecat      1.00   1.00   0.9955   0.0045
      esrcat      1.01   1.01   0.9854   0.0146
newheadache 1.06    1.03  0.9432    0.0568
taabnormality 1.06    1.03   0.9453   0.0547
-----

```

```

Mean VIF      1.03
              Cond
      Eigenval      Index
-----
      1      3.7179      1.0000
      2      0.5965      2.4965
      3      0.5034      2.7178
      4      0.1775      4.5764
      5      0.0046      28.3254
-----

```

```

Condition Number      28.3254
Eigenvalues & Cond Index computed from scaled raw sscp (w/ intercept)
Det(correlation matrix)  0.9365

```

There was NO specification error in our logistic regression models. There was no multicollinearity; the mean variance inflation factor (VIF) was 1.19, all of the predictor VIF were in the range of one with maximum 1.68 , and lowest observed tolerance 0.595 associated with the log CRP.

MULTIPLE IMPUTATION of non-log transformed data

```

mi set wide
mi register imputed platelet crp origesr newheadache taabnormality discrao Diplopia1
jawclaudication1
.
mi register regular tabxneg0 age female1
mi impute chained (regress) platelet (regress) crp (regress) origesr (logit)
newheadache (logit)taabnormality (logit) discrao
> (logit) Diplopia1 (logit) jawclaudication1 = tabxneg0 age female1, add(250)
rseed(4409)
note: variables discrao Diplopia1 contain no soft missing (.) values; imputing nothing
Conditional models:

```

```

newheadache: logit newheadache i.discrao i.Diplopia1 i.jawclaudication1
i.taabnormality platelet crp origesr tabxneg0
age female1
jawclaudicat~1: logit jawclaudication1 i.discrao i.Diplopia1 i.newheadache
i.taabnormality platelet crp origesr tabxneg0
age female1
taabnormality: logit taabnormality i.discrao i.Diplopia1 i.newheadache
i.jawclaudication1 platelet crp origesr tabxneg0
age female1
platelet: regress platelet i.discrao i.Diplopia1 i.newheadache
i.jawclaudication1 i.taabnormality crp origesr
tabxneg0 age female1
crp: regress crp i.discrao i.Diplopia1 i.newheadache i.jawclaudication1
i.taabnormality platelet origesr
tabxneg0 age female1
origesr: regress origesr i.discrao i.Diplopia1 i.newheadache i.jawclaudication1
i.taabnormality platelet crp
tabxneg0 age female1

```

Performing chained iterations ...

```

Multivariate imputation          Imputations =    250
Chained equations                added =    250
Imputed: m=1 through m=250      updated =          0
Initialization: monotone        Iterations = 2500
                                burn-in =    10

```

```

platelet: linear regression
crp: linear regression
origesr: linear regression
newheadache: logistic regression
taabnormality: logistic regression
discrao: logistic regression
Diplopia1: logistic regression
jawclaudicat~1: logistic regression

```

Variable	Observations per m			
	Complete	Incomplete	Imputed	Total
platelet	561	127	127	688
crp	530	158	158	688
origesr	530	158	158	688
newheadache	686	2	2	688
taabnormality	679	9	9	688
discrao	688	0	0	688
Diplopia1	688	0	0	688
jawclaudicat~1	683	5	5	688

(complete + incomplete = total; imputed is the minimum across m of the number of filled-in observations.)

```

. mi misstable patterns platelet crp origesr newheadache taabnormality
jawclaudication1 discrao Diplopia1

```

```

Missing-value patterns
(1 means complete)
      |   Pattern
Percent | 1 2 3 4      5 6
-----+-----
77%    | 1 1 1 1      1 1
      |
17%    | 1 1 1 0      0 0
3%     | 1 1 1 1      0 0
<1%    | 1 1 0 1      0 0
<1%    | 1 0 1 0      0 0
<1%    | 1 1 0 0      0 0
<1%    | 0 0 0 0      0 0
<1%    | 0 1 1 1      0 0
<1%    | 1 0 1 1      0 0
-----+-----
100%   |
Variables are (1) newheadache (2) jawclaudication1 (3) taabnormality (4) platelet
(5) crp (6) origesr
mi estimate:  logit tabxneg0 age female1 newheadache taabnormality jawclaudication1
platelet crp origesr discrao Diplopial
Multiple-imputation estimates      Imputations      =      250
Logistic regression                Number of obs    =      688
                                    Average RVI       =      0.0912
                                    Largest FMI       =      0.2232
DF adjustment:  Large sample      DF:    min      = 5,013.54
                                    avg          = 204,747.63
                                    max          = 632,370.74
Model F test:      Equal FMI      F( 10,313092.7) =      11.46
Within VCE type:   OIM            Prob > F        =      0.0000
-----+-----
tabxneg0 |   Coef.   Std. Err.   t      P>|t|   [95% Conf. Interval]
-----+-----
age |   .0522735   .0113708    4.60   0.000   .029987   .0745599
female1 |   .0268705   .2319645    0.12   0.908   -.4277741   .4815152
newheadache |   .0575915   .2500353    0.23   0.818   -.4324713   .5476543
taabnormality |   .4809197   .2290257    2.10   0.036   .0320287   .9298107
jawclaudication1 |   1.39079   .2254004    6.17   0.000   .949009   1.83257
platelet |   .0058186   .0010184    5.71   0.000   .0038221   .007815
crp |   .0041638   .0092029    0.45   0.651   -.0138769   .0222044
origesr |   .0088631   .0040743    2.18   0.030   .0008757   .0168505
discrao |   .9189811   .2453546    3.75   0.000   .4380926   1.39987
Diplopial |   .0395116   .4506416    0.09   0.930   -.8437314   .9227546
_cons |  -8.28233   1.007949   -8.22   0.000  -10.25789   -6.306771
-----+-----
logit tabxneg0 age female1 newheadache taabnormality jawclaudication1 platelet crp
origesr discrao Diplopial
Iteration 0:  log likelihood = -298.58568
Iteration 1:  log likelihood = -233.04312
Iteration 2:  log likelihood = -229.34022

```

Iteration 3: log likelihood = -229.32973

Iteration 4: log likelihood = -229.32973

Logistic regression	Number of obs	=	530
	LR chi2(10)	=	138.51
	Prob > chi2	=	0.0000
Log likelihood = -229.32973	Pseudo R2	=	0.2319

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
age	.0465098	.0128504	3.62	0.000	.0213234	.0716961
female1	-.2353227	.2571522	-0.92	0.360	-.7393318	.2686865
newheadache	.2044438	.2854474	0.72	0.474	-.3550228	.7639105
taabnormality	.4003271	.2554037	1.57	0.117	-.100255	.9009092
jawclaudication1	1.335526	.2592266	5.15	0.000	.8274508	1.843601
platelet	.0060248	.0010619	5.67	0.000	.0039435	.0081061
crp	.0028098	.0092628	0.30	0.762	-.015345	.0209645
origesr	.0089525	.0040991	2.18	0.029	.0009183	.0169866
discrao	.9951831	.2753072	3.61	0.000	.455591	1.534775
Diplopia1	-.0639863	.5051335	-0.13	0.899	-1.05403	.9260571
_cons	-7.855003	1.121877	-7.00	0.000	-10.05384	-5.656165

(MULTIPLE IMPUTATION CHAINED EQUATIONS OF LOG TRANSFORMED DATA IS usually **NOT** RECOMMENDED BY , BUT INCLUDED IN APPENDIX FOR COMPLETENESS SAKE)

MICE of log transformed data is not usually recommended, but performed on the log transformed full model to examine for trends. There was no change in the significance of the predictor variables in the log transformed full model; multiple imputation estimate for the temporal artery abnormality predictor was not statistically significant ($p_{original} = .172$, $p_{MICE} = .065$).

mi set wide

mi register imputed platelet lncrp lnesr newheadache taabnormality discrao Diplopia1 jawclaudication1

mi register regular tabxneg0 age female1

mi impute chained (regress) platelet (regress) lncrp (regress) lnesr (logit) newheadache (logit) taabnormality (logit) discrao (logit) Diplopia1 (logit) jawclaudication1 = tabxneg0 age female1, add(250) rseed(4409)

note: variables discrao Diplopia1 contain no soft missing (.) values; imputing nothing
Conditional models:

newheadache: logit newheadache i.discrao i.Diplopia1 i.jawclaudication1
i.taabnormality lnesr platelet lncrp tabxneg0
age female1

jawclaudicat~1: logit jawclaudication1 i.discrao i.Diplopia1 i.newheadache
i.taabnormality lnesr platelet lncrp tabxneg0
age female1

taabnormality: logit taabnormality i.discrao i.Diplopia1 i.newheadache
i.jawclaudication1 lnesr platelet lncrp tabxneg0

Model F test: Equal FMI F(10,328159.3) = 12.29
 Within VCE type: OIM Prob > F = 0.0000

tabxneg0	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
age	.0514132	.0117052	4.39	0.000	.0284713	.074355
female1	.1148088	.2367164	0.49	0.628	-.3491502	.5787677
newheadache	.0739943	.2562119	0.29	0.773	-.4281759	.5761644
taabnormality	.4321508	.234619	1.84	0.065	-.0277023	.892004
jawclaudication1	1.344632	.2293685	5.86	0.000	.8950734	1.79419
platelet	.0047802	.0010181	4.70	0.000	.0027844	.0067761
lncrp	.3254603	.095798	3.40	0.001	.1376466	.513274
lnesr	.1723798	.1546375	1.11	0.265	-.1307628	.4755223
discrao	.9623211	.2515404	3.83	0.000	.4693082	1.455334
Diplopia1	-.0911896	.4530914	-0.20	0.840	-.9792338	.7968546
_cons	-10.46421	1.454274	-7.20	0.000	-13.31468	-7.613738

logit tabxneg0 age female1 newheadache taabnormality jawclaudication1 platelet lncrp
 lnesr discrao Diplopia1

Iteration 0: log likelihood = -298.58568
 Iteration 1: log likelihood = -227.04763
 Iteration 2: log likelihood = -222.16089
 Iteration 3: log likelihood = -222.11488
 Iteration 4: log likelihood = -222.11486

Logistic regression Number of obs = 530
 LR chi2(10) = 152.94
 Prob > chi2 = 0.0000
 Log likelihood = -222.11486 Pseudo R2 = 0.2561

tabxneg0	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
age	.0449871	.0131698	3.42	0.001	.0191748	.0707993
female1	-.1523934	.2610758	-0.58	0.559	-.6640926	.3593057
newheadache	.2306857	.2895042	0.80	0.426	-.3367321	.7981035
taabnormality	.3563223	.2609711	1.37	0.172	-.1551716	.8678162
jawclaudication1	1.296339	.2636562	4.92	0.000	.7795826	1.813096
platelet	.0050691	.0010637	4.77	0.000	.0029844	.0071538
lncrp	.2901259	.0980896	2.96	0.003	.0978738	.482378
lnesr	.1870691	.170521	1.10	0.273	-.1471459	.5212841
discrao	1.03084	.2806157	3.67	0.000	.4808433	1.580836
Diplopia1	-.229284	.5020145	-0.46	0.648	-1.213214	.7546464
_cons	-9.96761	1.600932	-6.23	0.000	-13.10538	-6.82984

Multiple imputation analysis of the log transformed model: n=688,
 250 imputations

Predictor	β	Odds ratio (O.R.)	p value	95% confidence interval (O.R.)	β Multiple imputation estimates	P Multiple imputation estimates

Age	0.045	1.046	0.001	1.019, 1.074	0.052	<.001
Gender (female)	-0.152	0.859	0.559	0.514, 1.432	0.114	0.628
New headache	0.231	1.259	0.426	0.714, 2.221	0.078	0.761
Jaw claudication	1.296	3.656	<0.001	2.181, 6.129	1.342	<0.001
TA abnormality	0.356	1.428	0.172	0.856, 2.382	0.430	0.067
Vision Loss	1.031	2.803	<0.001	1.617, 4.859	0.967	<0.001
Diplopia	-0.229	0.795	0.648	0.297, 2.127	-0.090	0.842
lnESR	0.187	1.206	0.273	0.863, 1.684	0.167	0.280
lnCRP	0.290	1.337	0.003	1.103, 1.620	0.331	0.001
Platelets	0.005	1.005	<0.001	1.003, 1.007	0.005	<0.001
Constant	-9.967				-10.450	

TA abnormality: temporal artery abnormality on clinical exam

lnESR: natural logarithm of ESR

lnCRP: natural logarithm CRP

BOOTSTRAP SAMPLING (3000 random samples) OF PARSIMONIOUS MODEL

logit tabxneg0 age jawclaudication1 platelet lncrp discrao, vce (bootstrap, reps(3000)

bca seed(1))

estat bootstrap

INTERNAL VALIDATION PARSIMONIOUS MODEL

cvAUROC tabxneg0 age jawclaudication1 platelet lncrp discrao, kfold(10) seed(3)

1-fold.....

2-fold.....

3-fold.....

4-fold.....

5-fold.....

6-fold.....

7-fold.....

8-fold.....

9-fold.....

10-fold.....

(530 real changes made)

	ROC		-Asymptotic Normal--	
Obs	Area	Std. Err.	[95% Conf. Interval]	
530	0.8102	0.0224	0.76634	0.85397

INTERNAL VALIDATION FULL MODEL

```

cvAUROC tabxneg0 female1 age newheadache taabnormality
jawclaudication1 platelet lnesr lncrp discrao, kfold(10) seed(1)
cvAUROC tabxneg0 female1 age newheadache taabnormality jawclaudication1 platelet lnesr
lncrp discrao Diplopia1, kfold(10) seed
> (2)
1-fold.....
2-fold.....
3-fold.....
4-fold.....
5-fold.....
6-fold.....
7-fold.....
8-fold.....
9-fold.....
10-fold.....
(530 real changes made)

```

	Obs	Area	ROC Std. Err.	-Asymptotic Normal-- [95% Conf. Interval]
	530	0.8030	0.0233	0.75726 0.84875

EXTERNAL VALIDATION further examples

Full model; Combined centers below

Full model: Toronto below

Full model: Swiss below

Parsimonious model: Combined centers, below

External Validation: Comparison with the development data of the distribution of important variables (demographics, predictors and outcome with ANOVA.

```

by code3, sort : tabstat Age female1 New_Headache TA_tender_noPulse Jaw_claudication
CRP Platelets Vision_Loss ESR Diplopia length, statistics( mean sd count )
Combined

```

stats	Age	female1	New_He~e	TA~Pulse	Jaw_cl~n	CRP	Platel~s
Vision~s	ESR	Diplopia	length				
mean	73.04762	.5873016	.7619048	.4761905	.3492063	5.18452	381.5079
sd	10.24133	.4962739	.4293388	.5034444	.4805484	1.518077	139.7956
N	63	63	63	63	63	63	63

```

Kingston
stats |      Age  female1  New_He~e  TA~Pulse  Jaw_cl~n      CRP  Platel~s
Vision~s  ESR  Diplopia      length

```

```

-----+-----
-----
      mean | 74.43605 .6686047 .75 .3953488 .2674419 5.307306 317.6105
.2325581 8.343498 .0930233 1.756977
      sd | 9.499245 .4720892 .434277 .490353 .4439171 1.657388 117.5335
.4236963 .868971 .2913131 .5978599
      N | 172 172 172 172 172 172 172
172 172 172
-----

```

Ottawa

```

stats |      Age  female1 New_He~e TA~Pulse  Jaw_cl~n      CRP  Platel~s
Vision~s      ESR  Diplopia length
-----+-----
      mean | 74.36219 .7058824 .7815126 .2016807 .210084 3.541939 315.0168
.2436975 7.546964 .0252101 2.5
      sd | 9.659166 .4575717 .4149671 .4029517 .4090905 1.534551 119.9266
.4311275 1.430981 .1574255 0
      N | 119 119 119 119 119 119 119
119 119 119

```

Rochester_MN

```

stats |      Age  female1 New_He~e TA~Pulse  Jaw_cl~n      CRP  Platel~s
Vision~s      ESR  Diplopia length
-----+-----
      mean | 74.21154 .6923077 .6923077 .1730769 .1538462 4.553688 279.5192
.1153846 8.10026 .0576923 1.317308
      sd | 10.15437 .4660414 .4660414 .3820047 .3643213 1.310443 94.99731
.3226025 1.139259 .2354355 .4869759
      N | 52 52 52 52 52 52 52
52
-----

```

Toronto

```

stats |      Age  female1 New_He~e TA~Pulse  Jaw_cl~n      CRP  Platel~s
Vision~s      ESR  Diplopia length
-----+-----
      mean | 72.66935 .6935484 .6774194 .5080645 .2822581 4.312429 280.2742
.0967742 7.8404 .0241935 1.607917
      sd | 10.47701 .4628898 .4693602 .5019631 .4519242 1.621985 107.6076
.2968494 1.034101 .154273 .7713623
      N | 124 124 124 124 124 124 124
124 124 120
-----

```

```

by tabxneg0, sort : tabstat Age female1 New_Headache TA_tender_noPulse
Jaw_claudication CRP Platelets Vision_Loss ESR Diplopia length, statistics( mean sd
count ) by(code3)

```

Negative Biopsy Group

Summary statistics: mean, sd, N

by categories of: code3

code3	Age	female1	New_He~e	TA~Pulse	Jaw_cl~n	CRP	Platel~s
Vision~s	ESR	Diplopia	length				
-----+-----							

Combined	67.83333	.5416667	.6666667		.375	.1666667	4.714693
323.7083	.4166667	8.215517	.0833333	1.916667			
	11.84563	.5089774	.4815434	.4945354	.3806935	1.613385	114.5727
.5036102	.8071274	.2823299	.2041241				
	24	24	24	24	24	24	24
24	6						
-----+-----							

Kingston	73.24286	.6928571	.7357143	.3785714	.1857143	5.104099	303.3857
.2142857	8.299645	.0928571	1.734286				
	9.733035	.4629656	.4425354	.4867726	.3902723	1.644053	108.3706
.4117993	.8720117	.2912743	.6051067				
	140	140	140	140	140	140	140
140	140	140	140				
-----+-----							

Ottawa	73.23478	.673913	.7934783	.1630435	.173913	3.134447	282.3261
.2282609	7.308337	.0217391	2.5				
	9.928618	.4713482	.4070274	.3714295	.3811116	1.322775	92.46765
.4220114	1.51303	.1466296	0				
	92	92	92	92	92	92	92
92							
-----+-----							

Rochester_MN	73.86842	.6842105	.7368421	.1578947	.0526316	4.329098	272.5
.1052632	7.989262	.0263158	1.307895				
	10.50912	.4710691	.4462583	.369537	.2262943	1.257937	96.22321
.3110117	1.210942	.1622214	.469837				
	38	38	38	38	38	38	38
38	38						
-----+-----							

Toronto	72.67961	.6990291	.6699029	.4563107	.2427184	4.056551	266.9417
.0679612	7.726733	.0194175	1.6085				
	10.95554	.460923	.4725473	.5005232	.4308227	1.628432	96.77626
.25291	1.071258	.1386618	.8055068				
	103	103	103	103	103	103	103
103	103	103	100				
-----+-----							

Total	72.82771	.6801008	.7279597	.3274559	.1838791	4.278151	287.3224
.1813602	7.886487	.0503778	1.848005				

		10.34455	.4670258	.4455721	.4698773	.3878744	1.703687	102.1441
.3858025		1.189804	.2189994	.6952717				
		397	397	397	397	397	397	397
397		397	397	376				

Positive Biopsy Group

Summary statistics: mean, sd, N

by categories of: code3

code3	Age	female1	New_He~e	TA~Pulse	Jaw_cl~n	CRP	Platel~s
Vision~s	ESR	Diplopia	length				

Combined	76.25641	.6153846	.8205128	.5384615	.4615385	5.473644	
417.0769	.5641026	8.408749	.025641	2			
		7.645838	.4928641	.3887764	.5050354	.5050354	1.399769
.5023561	.7727799	.1601282	0				143.2898
		39	39	39	39	39	39
13							

Kingston	79.65625	.5625	.8125	.46875	.625	6.196337	
379.8438	.3125	8.535355	.09375	1.85625			
		6.198904	.5040161	.3965578	.5070073	.4918694	1.424984
.4709291	.8420514	.2961446	.563364				136.4897
		32	32	32	32	32	32
32							

Ottawa	78.2037	.8148148	.7407407	.3333333	.3333333	4.930431	426.4074
.2962963	8.360062	.037037	2.5				
		7.654585	.3958474	.4465761	.4803845	.4803845	1.404883
.4653216	.626882	.1924501	0				136.6799
		27	27	27	27	27	27
27							

Rochester_MN	75.14286	.7142857	.5714286	.2142857	.4285714	5.16329	298.5714
.1428571	8.40154	.1428571	1.342857				
		9.428738	.4688072	.5135526	.4258153	.5135526	1.298283
.3631365	.8857189	.3631365	.5487248				92.28527
		14	14	14	14	14	14
14							

Toronto	72.61905	.6666667	.7142857	.7619048	.4761905	5.567447	345.6667
.2380952	8.39791	.047619	1.605				
		7.933954	.4830459	.46291	.4364358	.5117663	.815159
.4364358	.5752944	.2182179	.5880163				134.3244

		21	21	21	21	21	21	21	21	21	21
20											
-----+-----											

Total		76.7782	.6616541	.7593985	.481203	.4736842	5.519391	386.2632			
.3533835		8.426856	.0601504	1.922642							
		7.824779	.4749357	.4290648	.5015356	.5011947	1.375809	138.6938			
.4798278		.7398071	.2386642	.5876966							
		133	133	133	133	133	133	133			
133		133	133	106							

```

foreach x of varlist age female1 newheadache taabnormality
jawclaudication1 platelet origesr crp discrao Diplopia1 length {
oneway `x' code3, bonferroni
}
*
foreach x of varlist age female1 newheadache taabnormality jawclaudication1 platelet
origesr crp discrao Diplopia1 length {
2.
. oneway `x' code3, bonferroni
3.
. }

```

Analysis of Variance					
Source	SS	df	MS	F	Prob > F
Between groups	309.98749	4	77.4968724	0.79	0.5340
Within groups	51702.6105	525	98.4811628		

```

Total      52012.598    529    98.3224914
Bartlett's test for equal variances:  chi2(4) =   1.7275   Prob>chi2 = 0.786
      Comparison of AGE by code3
      (Bonferroni)

```

Row Mean=					
Col Mean	Combined	Kingston	Ottawa	Roches..	
-----+-----					
Kingston	1.38843				
	1.000				
Ottawa	1.31457	-.073861			
	1.000	1.000			
Roches..	1.16392	-.224508	-.150647		
	1.000	1.000	1.000		
Toronto	-.378264	-1.76669	-1.69283	-1.54218	
	1.000	1.000	1.000	1.000	

Analysis of Variance					
Source	SS	df	MS	F	Prob > F

```

-----
Between groups      .66318155    4    .165795387    0.75    0.5560
Within groups      115.517951   525    .220034191
-----
Total              116.181132   529    .219624068
Bartlett's test for equal variances:  chi2(4) =    0.6108  Prob>chi2 = 0.962
Comparison of SEX(female) by code3
(Bonferroni)

```

```

Row Mean-|
Col Mean |   Combined   Kingston     Ottawa   Roches..
-----+-----
Kingston |   .081303
          |       1.000
          |
Ottawa   |   .118581     .037278
          |       1.000     1.000
          |
Roches.. |   .105006     .023703   -.013575
          |       1.000     1.000     1.000
          |
Toronto  |   .106247     .024944   -.012334   .001241
          |       1.000     1.000     1.000     1.000

```

```

Analysis of Variance
Source          SS          df          MS          F          Prob > F
-----
Between groups   .847271494    4    .211817874    1.09    0.3615
Within groups   102.171596   525    .194612565
-----

```

```

Total          103.018868   529    .194742661
Bartlett's test for equal variances:  chi2(4) =    2.3152  Prob>chi2 = 0.678
Comparison of NEWHEADACHE by code3
(Bonferroni)

```

```

Row Mean-|
Col Mean |   Combined   Kingston     Ottawa   Roches..
-----+-----
Kingston |   -.011905
          |       1.000
          |
Ottawa   |   .019608     .031513
          |       1.000     1.000
          |
Roches.. |   -.069597   -.057692   -.089205
          |       1.000     1.000     1.000
          |
Toronto  |   -.084485   -.072581   -.104093   -.014888
          |       1.000     1.000     0.665     1.000

```

```

Analysis of Variance
Source          SS          df          MS          F          Prob > F
-----
Between groups   8.56420742    4    2.14105185    9.82    0.0000

```

Within groups 114.424472 525 .217951375

Total 122.988679 529 .232492777

Bartlett's test for equal variances: chi2(4) = 11.1540 Prob>chi2 = 0.025

Comparison of **taabnormal~y** by code3

(Bonferroni)

Row Mean-|

Col Mean | Combined Kingston Ottawa Roches..

-----+-----

Kingston | -.080842

 | 1.000

 |

Ottawa | -.27451 -.193668

 | 0.002 0.005

 |

Roches.. | -.303114 -.222272 -.028604

 | 0.006 0.028 1.000

 |

Toronto | .031874 .112716 .306384 .334988

 | 1.000 0.409 0.000 0.000

Analysis of Variance

Source SS df MS F Prob > F

Between groups 1.44865439 4 .362163596 1.91 0.1077

Within groups 99.6532324 525 .189815681

Total 101.101887 529 .191118879

Bartlett's test for equal variances: chi2(4) = 5.5112 Prob>chi2 = 0.239

Comparison of **jawclaudic~1** by code3

(Bonferroni)

Row Mean-|

Col Mean | Combined Kingston Ottawa Roches..

-----+-----

Kingston | -.081764

 | 1.000

 |

Ottawa | -.139122 -.057358

 | 0.409 1.000

 |

Roches.. | -.19536 -.113596 -.056238

 | 0.170 1.000 1.000

 |

Toronto | -.066948 .014816 .072174 .128412

 | 1.000 1.000 1.000 0.750

Analysis of Variance

Source SS df MS F Prob > F

Between groups 490529.653 4 122632.413 9.00 **0.0000**

Within groups 7155506.27 525 13629.5358

Total 7646035.92 529 14453.7541
 Bartlett's test for equal variances: $\chi^2(4) = 10.0430$ Prob> $\chi^2 = 0.040$
 Comparison of **platelet** by code3
 (Bonferroni)

Row Mean-|
 Col Mean | Combined Kingston Ottawa Roches..
 -----+-----
 Kingston | -63.8975
 | 0.002
 |
 Ottawa | -66.4911 -2.59366
 | 0.003 1.000
 |
 Roches.. | -101.989 -38.0912 -35.4976
 | 0.000 0.397 0.680
 |
 Toronto | -101.234 -37.3363 -34.7426 .754963
 | 0.000 0.069 0.208 1.000

Analysis of Variance

Source	SS	df	MS	F	Prob > F
Between groups	56924.9564	4	14231.2391	15.10	0.0000
Within groups	494873.465	525	942.616123		

Total 551798.421 529 1043.0972
 Bartlett's test for equal variances: $\chi^2(4) = 43.4064$ Prob> $\chi^2 = 0.000$
 Comparison of **origesr** by code3
 (Bonferroni)

Row Mean-|
 Col Mean | Combined Kingston Ottawa Roches..
 -----+-----
 Kingston | 3.82676
 | 1.000
 |
 Ottawa | -21.4612 -25.2879
 | 0.000 0.000
 |
 Roches.. | -5.79117 -9.61793 15.67
 | 1.000 0.483 0.022
 |
 Toronto | -15.5368 -19.3636 5.92435 -9.74566
 | 0.011 0.000 1.000 0.552

Analysis of Variance

Source	SS	df	MS	F	Prob > F
Between groups	11197.2915	4	2799.32288	17.29	0.0000
Within groups	85022.0439	525	161.94675		

Total 96219.3355 529 181.889103
 Bartlett's test for equal variances: $\chi^2(4) = 174.8649$ Prob> $\chi^2 = 0.000$

Comparison of **crp** by code3
(Bonferroni)

Row Mean-				
Col Mean	Combined	Kingston	Ottawa	Roches..
-----+-----				
Kingston	4.82371			
	0.103			
Ottawa	-6.68107	-11.5048		
	0.008	0.000		
Roches..	-4.13833	-8.96204	2.54274	
	0.832	0.000	1.000	
Toronto	-3.80594	-8.62966	2.87512	.332386
	0.538	0.000	0.789	1.000

Analysis of Variance

Source	SS	df	MS	F	Prob > F

Between groups	7.75825082	4	1.9395627	12.05	0.0000
Within groups	84.5228813	525	.160995964		

Total	92.2811321	529	.174444484		

Bartlett's test for equal variances: $\chi^2(4) = 32.3925$ Prob> $\chi^2 = 0.000$

Comparison of **DiscRAO** by code3
(Bonferroni)

Row Mean-				
Col Mean	Combined	Kingston	Ottawa	Roches..
-----+-----				
Kingston	-.275378			
	0.000			
Ottawa	-.264239	.011139		
	0.000	1.000		
Roches..	-.392552	-.117174	-.128313	
	0.000	0.656	0.549	
Toronto	-.411162	-.135784	-.146923	-.01861
	0.000	0.042	0.045	1.000

Analysis of Variance

Source	SS	df	MS	F	Prob > F

Between groups	.473271773	4	.118317943	2.38	0.0503
Within groups	26.0474829	525	.049614253		

Total	26.5207547	529	.050133752		

Bartlett's test for equal variances: $\chi^2(4) = 79.0289$ Prob> $\chi^2 = 0.000$

Comparison of **Diplopia1** by code3
(Bonferroni)

```

Row Mean-|
Col Mean |   Combined   Kingston   Ottawa   Roches..
-----+-----
Kingston |   .045404
      |   1.000
      |
Ottawa |  -.022409  -.067813
      |   1.000    0.110
      |
Roches.. |  .010073  -.035331  .032482
      |   1.000    1.000    1.000
      |
Toronto |  -.023425  -.06883  -.001017  -.033499
      |   1.000    0.090    1.000    1.000

```

```

                        Analysis of Variance
Source                SS                df                MS                F                Prob > F
-----+-----
Between groups        73.7444151    4    18.4361038        60.96 0.0000
Within groups        144.25787    477    .302427401
-----+-----

```

```

Total                218.002285    481    .453227204
Bartlett's test for equal variances:  chi2(3) = 61.1587  Prob>chi2 = 0.000
note: Bartlett's test performed on cells with positive variance:
      1 multiple-observation cells not used

```

Comparison of **length** by code3
(Bonferroni)

```

Row Mean-|
Col Mean |   Combined   Kingston   Ottawa   Roches..
-----+-----
Kingston |  -.216707
      |   1.000
      |
Ottawa |   .526316   .743023
      |   0.001    0.000
      |
Roches.. |  -.656377  -.439669  -1.18269
      |   0.000    0.000    0.000
      |
Toronto |  -.365768  -.14906  -.892083  .290609
      |   0.073    0.231    0.000    0.016

```

```

foreach x of varlist age female1 newheadache taabnormality
jawclaudication1 platelet origesr crp discrao  Diplopia1 {
  anova `x' code4
}

```

★

```

Number of obs =          530    R-squared      = 0.0060
Root MSE      = 9.92377  Adj R-squared = -0.0016
Source | Partial SS      df      MS      F      Prob>F
-----+-----

```

```

age | 309.98749      4  77.496872      0.79  0.5340
      |
      code4 | 309.98749      4  77.496872      0.79  0.5340
      |
Residual | 51702.61      525  98.481163
-----+-----
      Total | 52012.598      529  98.322491
      Number of obs =      530  R-squared      = 0.0057
      Root MSE      = .469078 Adj R-squared = -0.0019
Source | Partial SS      df      MS      F      Prob>F
-----+-----
      Sex | .66318155      4  .16579539      0.75  0.5560
      |
      code4 | .66318155      4  .16579539      0.75  0.5560
      |
Residual | 115.51795      525  .22003419
-----+-----
      Total | 116.18113      529  .21962407
      Number of obs =      530  R-squared      = 0.0082
      Root MSE      = .441149 Adj R-squared = 0.0007
Source | Partial SS      df      MS      F      Prob>F
-----+-----
      HA | .84727149      4  .21181787      1.09  0.3615
      |
      code4 | .84727149      4  .21181787      1.09  0.3615
      |
Residual | 102.1716      525  .19461256
-----+-----
      Total | 103.01887      529  .19474266
      Number of obs =      530  R-squared      = 0.0696
      Root MSE      = .466853 Adj R-squared = 0.0625
Source | Partial SS      df      MS      F      Prob>F
-----+-----
      TA | 8.5642074      4  2.1410519      9.82  0.0000
      |
      code4 | 8.5642074      4  2.1410519      9.82  0.0000
      |
Residual | 114.42447      525  .21795137
-----+-----
      Total | 122.98868      529  .23249278
      Number of obs =      530  R-squared      = 0.0143
      Root MSE      = .435678 Adj R-squared = 0.0068
Source | Partial SS      df      MS      F      Prob>F
-----+-----
      Claud | 1.4486544      4  .3621636      1.91  0.1077
      |
      code4 | 1.4486544      4  .3621636      1.91  0.1077
      |
Residual | 99.653232      525  .18981568
-----+-----

```

	Total		101.10189		529	.19111888			
			Number of obs =		530	R-squared		=	0.0642
			Root MSE		116.746	Adj R-squared		=	0.0570
Source		Partial SS		df		MS	F		Prob>F
-----+									
	Plat		490529.65		4	122632.41		9.00	0.0000
	code4		490529.65		4	122632.41		9.00	0.0000
Residual		7155506.3		525		13629.536			
-----+									
	Total		7646035.9		529	14453.754			
			Number of obs =		530	R-squared		=	0.1032
			Root MSE		30.7021	Adj R-squared		=	0.0963
Source		Partial SS		df		MS	F		Prob>F
-----+									
	ESR		56924.956		4	14231.239		15.10	0.0000
	code4		56924.956		4	14231.239		15.10	0.0000
Residual		494873.46		525		942.61612			
-----+									
	Total		551798.42		529	1043.0972			
			Number of obs =		530	R-squared		=	0.1164
			Root MSE		12.7258	Adj R-squared		=	0.1096
Source		Partial SS		df		MS	F		Prob>F
-----+									
	CRP		11197.292		4	2799.3229		17.29	0.0000
	code4		11197.292		4	2799.3229		17.29	0.0000
Residual		85022.044		525		161.94675			
-----+									
	Total		96219.335		529	181.8891			
			Number of obs =		530	R-squared		=	0.0841
			Root MSE		.401243	Adj R-squared		=	0.0771
Source		Partial SS		df		MS	F		Prob>F
-----+									
	Vision		7.7582508		4	1.9395627		12.05	0.0000
	code4		7.7582508		4	1.9395627		12.05	0.0000
Residual		84.522881		525		.16099596			
-----+									
	Total		92.281132		529	.17444448			
			Number of obs =		530	R-squared		=	0.0178
			Root MSE		.222743	Adj R-squared		=	0.0104
Source		Partial SS		df		MS	F		Prob>F
-----+									
Diplopia		.47327177			4	.11831794		2.38	0.0503

code4		.47327177	4	.11831794	2.38 0.0503
Residual		26.047483	525	.04961425	
-----+-----					
Total		26.520755	529	.05013375	

STATA NOMOGRAM

```
logit tabxneg0 CRP_divide_ULN Platelets Vision_Loss Jaw_claudication Age
nomolog, title(Nomogram: Probability of Giant Cell Arteritis) varlblsize(2.8)
vli1(Vision_Loss,0,1,1,0) vli4(Jaw_claudication,0,1,1,0) vli5(Age,40,100,10,0)
vli6(Platelets,50,950,75,0) vli9(CRP_divide_by_ULN,0,8.11,1,1) prlabsize(3.5)
```

CALIBRATION PLOT are visual representation of H-L statistic.

```
drop prob
drop probgroup
logit tabxneg0 age female1 newheadache taabnormality jawclaudication1 platelet lncrp
lnesr discrao Diplopia1
predict prob
egen probgroup=cut(prob), at(0(0.1)1)
tab probgroup tabxneg0
preserve
collapse (mean) tabxneg0, by(probgroup)
replace probgroup=probgroup + 0.05
scatter tabxneg0 probgroup || line probgroup probgroup, legend(order(1 "Observed" 2
"Predicted"))
1 newheadache taabnormality jawclaudication1 platelet lncrp lnesr discrao Diplopia1
lroc
predict xb1, xb
logit tabxneg0 age jawclaudication1 platelet lncrp discrao
lroc
predict xb2, xb
logistic tabxneg0 agecat esrcat newheadache taabnormality
lroc
predict xb3, xb
roccomp tabxneg0 xb1 xb2 xb3, graph summary
roccomp tabxneg0 xb1 xb2 xb3, graph summary
```

		ROC		-Asymptotic Normal--	
	Obs	Area	Std. Err.	[95% Conf. Interval]	
xb1	525	0.8174	0.0223	0.77377	0.86111
xb2	525	0.8142	0.0221	0.77080	0.85755
xb3	525	0.6339	0.0287	0.57753	0.69018

n=525 (in the ACR model 5 patients under the age of 50 years were excluded)

ACR = American College of Rheumatology Classification Criteria (non-histologic)

```
drop xb xb2 xb3 xb4 xb5
```

```

logistic tabxneg0 age
predict xb1, xb
logit tabxneg0 jawclaudication1
lroc
predict xb2, xb
logistic tabxneg0 discrao
lroc
predict xb3, xb
logistic tabxneg0 platelet
lroc
predict xb4, xb
logistic tabxneg0 lncrp
lroc
predict xb5, xb
roccomp tabxneg0 xb1 xb2 xb3 xb4 xb5, graph summary

```

Bootstrap Sensitivity Analysis: Full model

```

logistic tabxneg0 age female1 newheadache jawclaudication1 platelet lnesr lncrp discrao
Diplopial

```

```

Logistic regression      Number of obs      =      526
                        LR chi2(9)          =      150.06
                        Prob > chi2         =      0.0000
Log likelihood = -222.3942      Pseudo R2      =      0.2523

```

	tabxneg0	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
	age	1.04388	.0136856	3.28	0.001	1.017398	1.071051
	female1	.8514999	.2223184	-0.62	0.538	.5104393	1.420447
	newheadache	1.365738	.3870027	1.10	0.271	.7837297	2.379953
	jawclaudication1	3.979413	1.027158	5.35	0.000	2.399433	6.599778
	platelet	1.005126	.0010682	4.81	0.000	1.003034	1.007221
	lnesr	1.173762	.2118964	0.89	0.375	.8239766	1.672035
	lncrp	1.362775	.1355529	3.11	0.002	1.12139	1.65612
	discrao	2.622504	.7265376	3.48	0.001	1.5237	4.513701
	Diplopial	.7751479	.3885454	-0.51	0.611	.2902132	2.07039
	_cons	.0000968	.0001336	-6.70	0.000	6.48e-06	.0014462

```

logistic tabxneg0 age female1 newheadache jawclaudication1 platelet lnesr lncrp discrao
Diplopial, vce (bootstrap, reps(5000) bca seed(1))

```

```

                        Number of obs      =      526
                        Replications        =      5,000
                        Wald chi2(9)        =      90.23
                        Prob > chi2         =      0.0000
Log likelihood = -222.3942      Pseudo R2      =      0.2523

```

		Observed	Bootstrap			Normal-based	
	tabxneg0	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]	
	age	1.04388	.0135409	3.31	0.001	1.017675	1.07076
	female1	.8514999	.2350384	-0.58	0.560	.495711	1.462651
	newheadache	1.365738	.4293089	0.99	0.321	.7375625	2.528924
	jawclaudication1	3.979413	1.074401	5.12	0.000	2.344246	6.755147
	platelet	1.005126	.0010727	4.79	0.000	1.003025	1.00723
	lnesr	1.173762	.1960574	0.96	0.337	.8460601	1.628393
	lncrp	1.362775	.1277916	3.30	0.001	1.133977	1.637736

```

discrao | 2.622504 .7398522 3.42 0.001 1.508614 4.55884
Diplopial | .7751479 .4196151 -0.47 0.638 .2682866 2.239599
_cons | .0000968 .0001394 -6.42 0.000 5.77e-06 .0016263
-----
Bootstrap Sensitivity Analysis: Parsimonious model
logistic tabxneg0 age jawclaudication1 platelet lncrp discrao
Logistic regression Number of obs = 526
LR chi2(5) = 147.61
Prob > chi2 = 0.0000
Log likelihood = -223.62022 Pseudo R2 = 0.2481
-----
tabxneg0 | Odds Ratio Std. Err. z P>|z| [95% Conf. Interval]
-----+-----
age | 1.044307 .0135879 3.33 0.001 1.018012 1.071281
jawclaudication1 | 4.080527 1.03364 5.55 0.000 2.483694 6.704009
platelet | 1.00508 .0010511 4.85 0.000 1.003022 1.007142
lncrp | 1.430682 .1142496 4.48 0.000 1.223401 1.673082
discrao | 2.487281 .6682512 3.39 0.001 1.469044 4.211288
_cons | .0002163 .0002437 -7.49 0.000 .0000238 .0019693
logistic tabxneg0 age jawclaudication1 platelet lncrp discrao, vce (bootstrap, reps(5000)
Logistic regression Number of obs = 526
Replications = 5,000
Wald chi2(5) = 93.78
Prob > chi2 = 0.0000
Log likelihood = -223.62022 Pseudo R2 = 0.2481
-----
| Observed Bootstrap Normal-based
tabxneg0 | Odds Ratio Std. Err. z P>|z| [95% Conf. Interval]
-----+-----
age | 1.044307 .0130375 3.47 0.001 1.019064 1.070175
jawclaudication1 | 4.080527 1.051293 5.46 0.000 2.462724 6.761094
platelet | 1.00508 .001026 4.96 0.000 1.003071 1.007093
lncrp | 1.430682 .1129918 4.53 0.000 1.225511 1.670202
discrao | 2.487281 .6674884 3.40 0.001 1.469927 4.208757
_cons | .0002163 .0002465 -7.40 0.000 .0000232 .0020197
-----

```

NOMOGRAM CONSIDERATIONS

In this paper, there is only a nomogram for the parsimonious model.

A nomogram of the full model is available for readers interested in the graphic visualization of the importance of all 10 variables.

lnCRP	CRP	lnESR	ESR
0.00112	0.025	0.00483	0.01
1.35187	0.096508	3.34377	0.281892
2.70262	0.372552	6.68271	7.94633
4.05337	1.438168	10.0217	224.001
5.40412	5.551787		
6.75487	21.43167		
8.10562	82.73315		

$\ln\text{CRP} = \log\text{CRP} + 3.69$ and $\ln\text{ESR} = \log\text{ESR} + 4.61$

The addition of constants was performed to avoid non-negative values, as the nomogram cannot otherwise be generated. The values are transformed back to ESR and CRP.