



# Regression and Clinical prediction models

Session 21  
Presenting results

Pedro E A A Brasil  
[pedro.brasil@ini.fiocruz.br](mailto:pedro.brasil@ini.fiocruz.br)  
2018





# Session objective

- In this session, the students will be introduced to several formats that will allow the user to estimate absolute risk individually for a patient of interest.





# Introduction

- Epidemiologic regression analyses commonly concentrate on estimation of relative effects.
  - Hazard ratios and odds ratios
- Various presentation formats are possible for prediction models and for decision rules
- Prediction vs Decision
  - presentation as a decision rule may lead more easily to a wide application of a model



# Introduction

- Additional results may increase the confidence of users that the tool will improve their decisions.
  - Calibration plots
    - Accuracy of results; how close the predicted values are from the observed values
  - Reclassification tables
    - Net reclassification Improvement and Integrated discrimination improvement indicate correct changes of subjects risk categories in model updating.





# Introduction

- Additional results may increase the confidence of users that the tool will improve their decisions.
  - Decision curves
    - Trade-off of wrong/correct classifications at different thresholds are improved with the tool/model
  - Decision limits/thresholds
    - Graphs/tables with accuracies with different decision limits including their rationale and weights
  - External or temporal validation
    - Reproducible results across different populations



# What users want?

## Users' Guide for an Article About Interpreting Diagnostic Test Results

### Are the results valid?

- Did participating patients present a diagnostic dilemma?
- Did investigators compare the test to an appropriate, independent reference standard?
- Were those interpreting the test and reference standard blind to the other results?
- Did investigators perform the same reference standard to all patients regardless of the results of the test under investigation?

### What are the results?

- What likelihood ratios were associated with the range of possible test results?

### How can I apply the results to patient care?

- Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?
- Are the study results applicable to the patients in my practice?
- Will the test results change my management strategy?
- Will patients be better off as a result of the test?



# Introduction

**Table 18.1** Some examples of presentation formats for clinical prediction models and clinical decision rules

Rule	Characteristics	Pros	Cons	Example
<i>Prediction models</i>				
Regression formula	Simple, follows directly from analysis	Can be implemented in computerized format	Leaves work to the user; difficult to calculate confidence intervals	Predicted response dose, formula in abstract <sup>209</sup>
Spreadsheet	Includes exact calculations, exact 95% confidence intervals	Standard software, familiar to many	Needs user to open specific file	Survival after surgery for lung cancer <sup>36</sup>
Prognosis program	Includes exact calculations, exact 95% confidence intervals	Easy to download and install	Needs user to get acquainted with specific software	Oncologiq ( <a href="http://oncologiq.nl/">http://oncologiq.nl/</a> )
Nomogram	Includes quite exact calculations, approximate 95% confidence intervals	Quite exact predictions	Difficult to understand at first sight	Prostate cancer recurrence <sup>226</sup>
Score chart	Includes approximate calculations, approximate 95% confidence intervals	Easy to understand	Approximate predictions	DRASTIC prediction rule for renal artery stenosis <sup>243</sup>
Table	Includes averaged calculations, approximate 95% confidence intervals can be added	Very easy to understand and use	Predictions by predictor combination; continuous predictors have to be categorized	Framingham risk equation to identify candidates of statin therapy <sup>487</sup>
Specific formats	Based on specific interest of audience	Should appeal specifically to target audience	Less easy to understand for non-target audience	Relevance of pre- and post-chemotherapy mass size in testicular cancer prediction example <sup>419</sup>
<i>Decision rules</i>				
Regression tree	Simple, large groups	Very easy to understand and use	Unstable if based on limited data Continuous predictors have to be categorized	Goldman diagnostic index for acute MI <sup>142</sup>
Score chart rule	Score based on highly rounded coefficients	Rule simple to understand	Inaccurate predictions	CT rule for minor head injury <sup>391</sup>
Survival by group	Simple, large groups	Very easy to understand and use	Stable but cut-offs based on distribution of risk rather than decision-analytic considerations	IGCC classification for testicular cancer <sup>5</sup>
Meta-model tree	Simple, large groups	Very easy to understand and use		Testicular cancer group with >70% benign tissue <sup>418</sup>

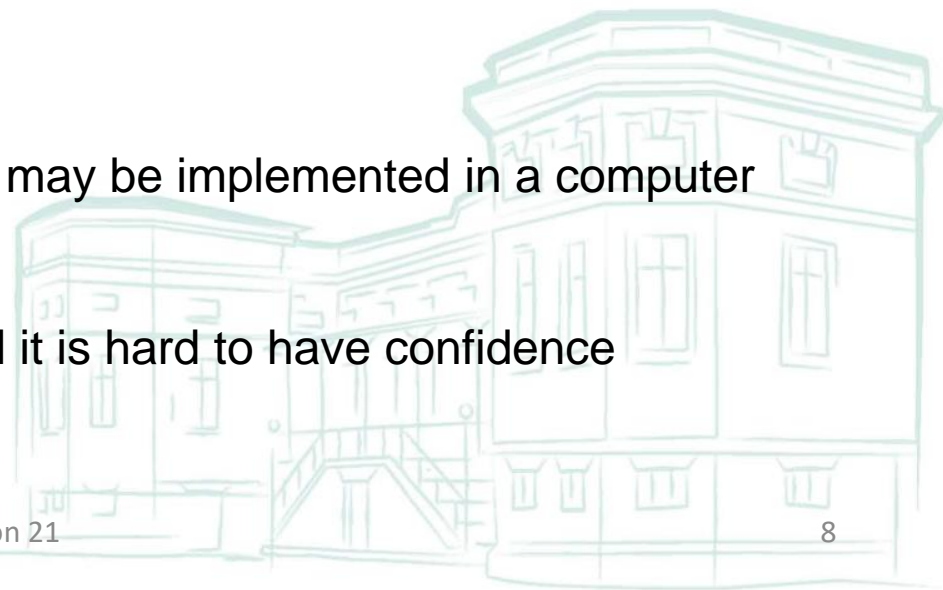


# Formula

**Box 18.1** Regression formula for prediction of the individual follicle-stimulating hormone threshold <sup>209</sup>

FSH response dose = 4 body mass index (in kg/m<sup>2</sup>) + 32 clomiphene citrate resistance (yes = 1 or no = 0) + 7 initial free insulin-like growth factor-I (in ng/mL) + 6 initial serum FSH level (in IU/L) – 51

- Simple and easy to construct, and may be implemented in a computer program.
- Leave all the work for the user and it is hard to have confidence intervals estimate.







# Digital calculators

- There are some websites with this sort of tool.
  - MELD score and mortality for liver disease
    - <http://www.mayoclinic.org/medical-professionals/model-end-stage-liver-disease/meld-score-90-day-mortality-rate-alcoholic-hepatitis>
  - Colon cancer 5 year survival probability
    - <https://www.mskcc.org/nomograms/colorectal/overall-survival-probability>
- May be intuitive for most users.
- User must download file and have the appropriate software.

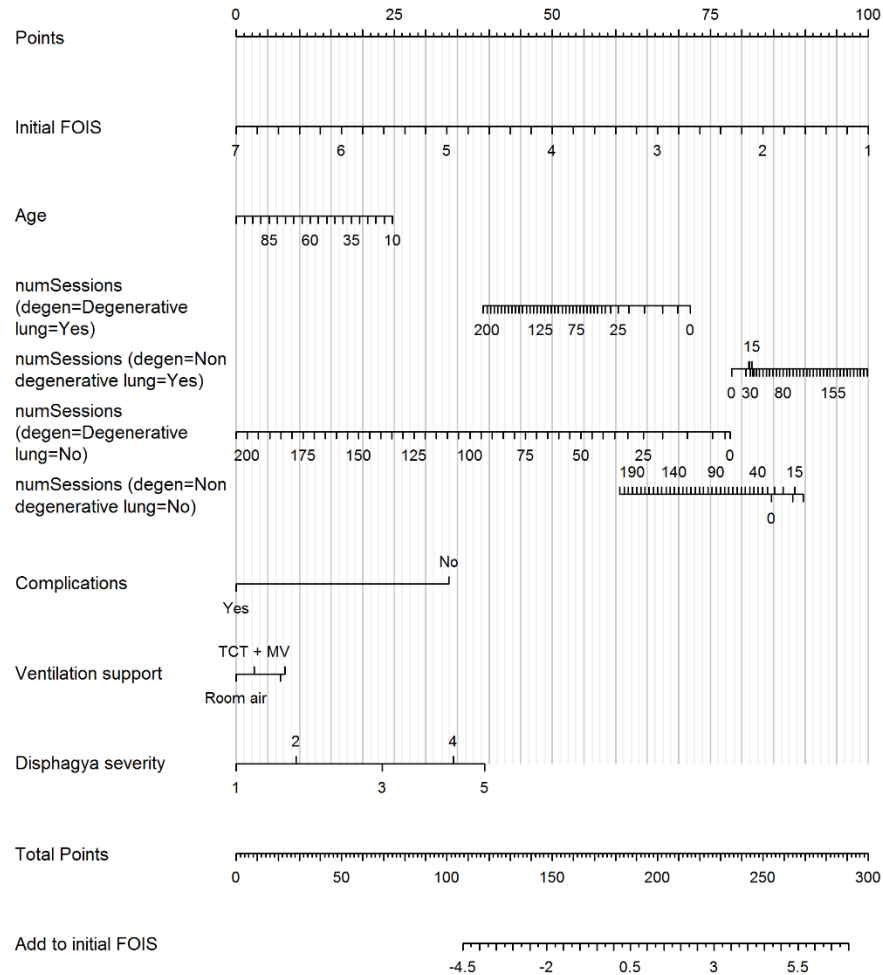


# Digital calculators

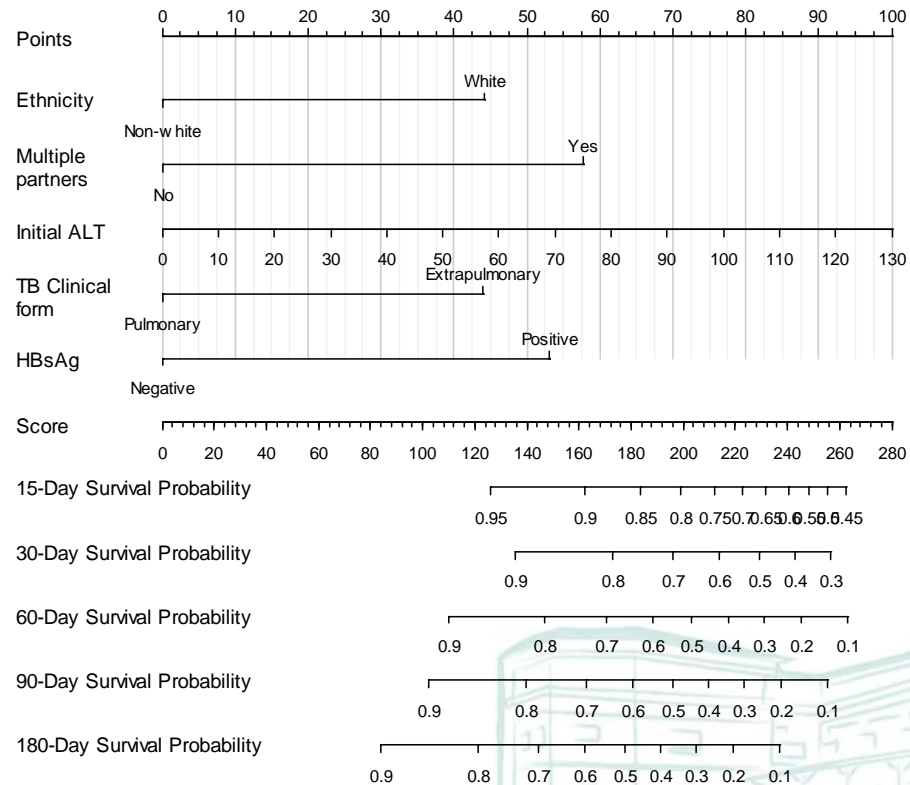
- Shiny apps let users interact with your data analysis.
  - It's a R library that turn R codes into a web page.
  - Requires a server with Rstudio and Shiny app installed
  - <https://shiny.ipec.fiocruz.br/pedrobrasil/>
  - <https://shiny.rstudio.com/>
- May be intuitive for most users.
- User must be connected to the internet



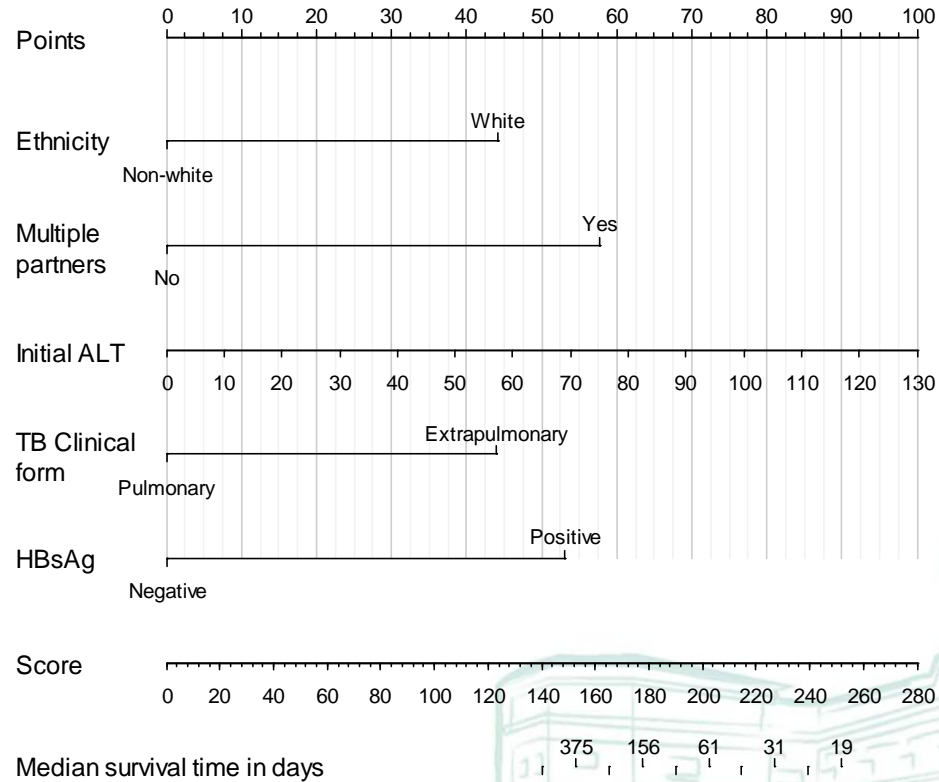
# Nomogram



# Nomogram



# Nomogram

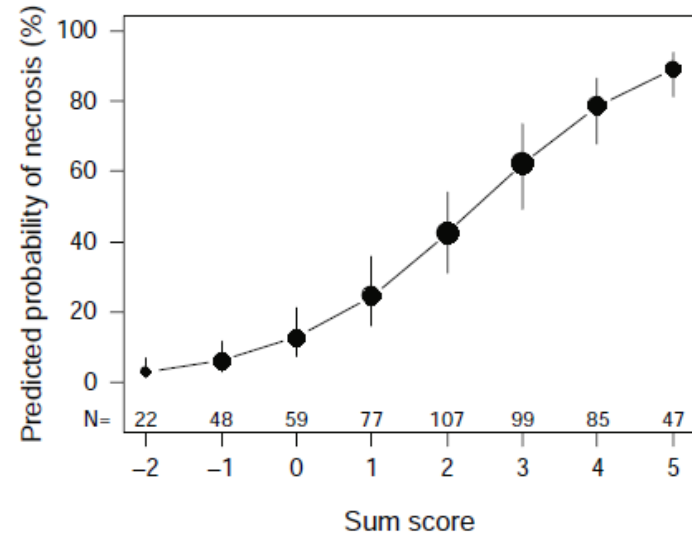


# Score chart

Table 18.2 Score chart for estimation of the probability of benign tissue after chemotherapy for metastatic testicular cancer with continuous predictors

Characteristic	Scores	Sum score
Primary tumor		
Teratoma elements	1	
Prechemotherapy tumor markers		
AFP elevated	1	
HCG elevated	1	
LDH times normal		
Values	0.6    1    1.6    2.5    4    6	
Scores <sup>a</sup>	-0.5   0    0.5    1    1.5   2	
Postchemotherapy size (mm)		
Values	<5    10    20    40    70	
Scores <sup>a</sup>	+0.5   0    -0.5   -1    -1.5	
Reduction in size		
Values	Increase   0%    50%    100%	
Scores <sup>a</sup>	-1    0    1    2	
Total score (add all)		....
Probability of benign tissue and		...%
95% CI from Fig. 18.2		[...% - ...%]

<sup>a</sup>Intermediate scores can be estimated with linear interpolation



- Easy to understand and use
- Approximate predictions.
- The second step may be represented either by a table or a graph.



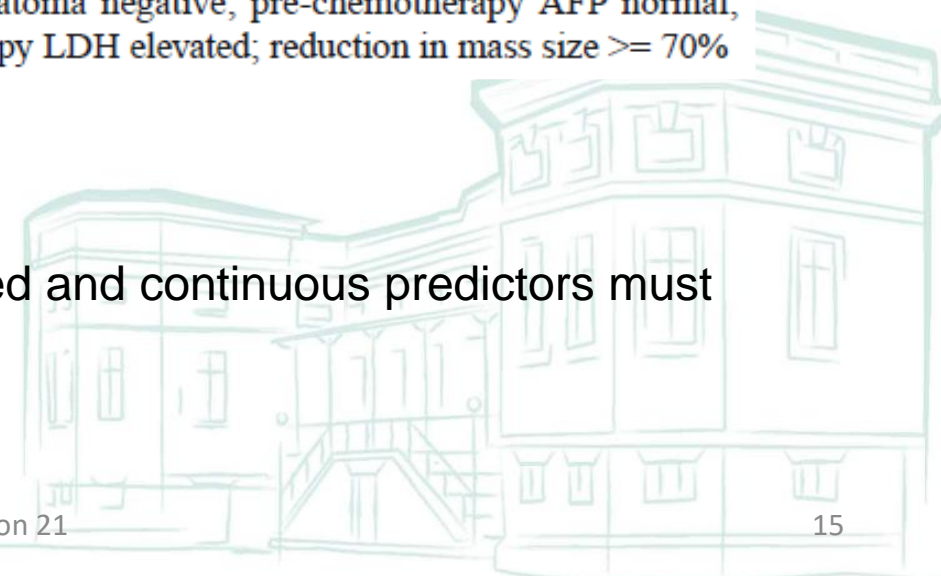
# Decision table

**Table 18.3** Probability of benign tissue in relation to the sum of five favourable characteristics and mass size for the testicular cancer case study

Residual mass size (mm)	Sum of favourable characteristics <sup>a</sup>					
	0	1	2	3	4	5
0–9			$p > 60\%$	$p > 70\%$	$p > 80\%$	Follow-up $p > 90\%$
10–19	Resection					
20–29				$p > 60\%$		
30–49					$p > 70\%$	$p > 80\%$
$\geq 50$ or increased mass	$p \leq 60\%$					

<sup>a</sup>Sum of five characteristics: primary tumor teratoma negative; pre-chemotherapy AFP normal; Pre-chemotherapy HCG normal; Pre-chemotherapy LDH elevated; reduction in mass size  $\geq 70\%$

- Easy to understand and use
- Some predictors must be combined and continuous predictors must be categorized.



# Flow chart

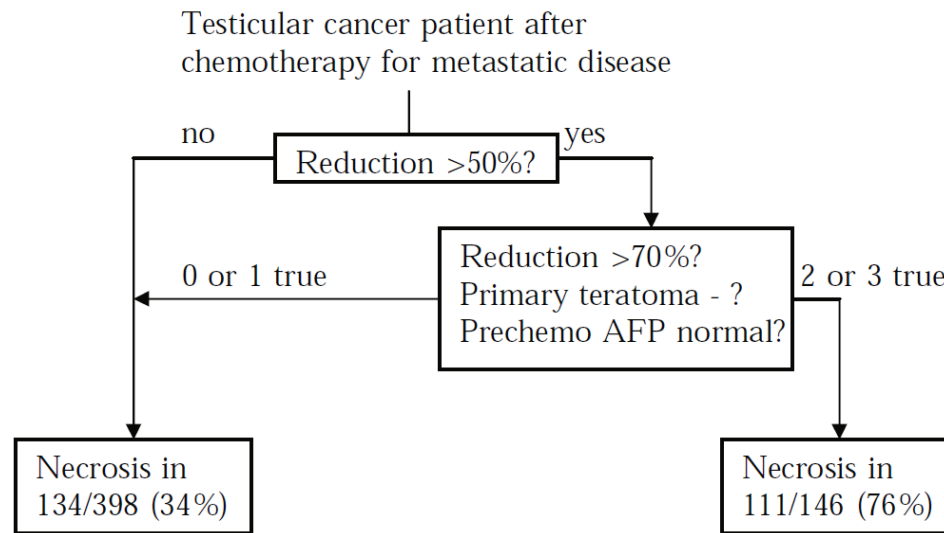


Fig. 18.5 Decision rule for patients with testicular cancer <sup>418</sup>

- Easy to understand and use
- Unstable if based on limited data. Usually is outperformed by other methods.

# Flow chart + risk table

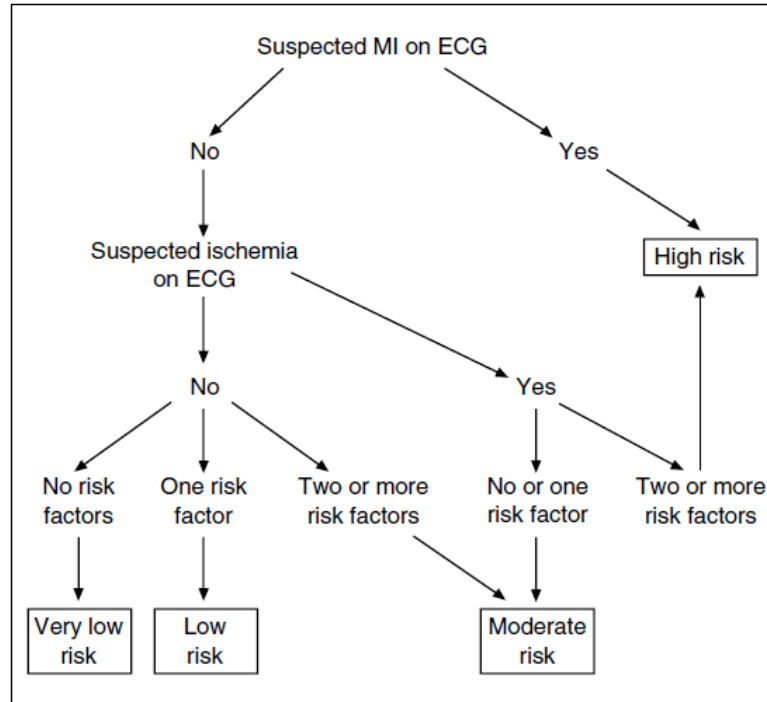


Figure 1. Derivation of the Four Initial Risk Groups on the Basis of Data Available at the Time of Presentation in the Emergency Department.

Myocardial infarction (MI) was suspected if the electrocardiogram (ECG) showed ST-segment elevation of 1 mm or more or pathologic Q waves in two or more leads, and these findings were not known to be old. Ischemia was suspected if the ECG showed ST-segment depression of 1 mm or more or T-wave inversion in two or more leads, and these findings were not known to be old. Risk factors included systolic blood pressure below 110 mm Hg, rales heard above the bases bilaterally on physical examination, and known unstable ischemic heart disease, defined as a worsening of previously stable angina, the new onset of postinfarction angina or angina after a coronary-revascularization procedure, or pain that was the same as that associated with a prior myocardial infarction. The difference between each adjacent pair of risk groups was significant ( $P < 0.001$ ).

# Continuation

Table 4. Rate of First Major Event According to the Level of Risk Identified in the Emergency Department.

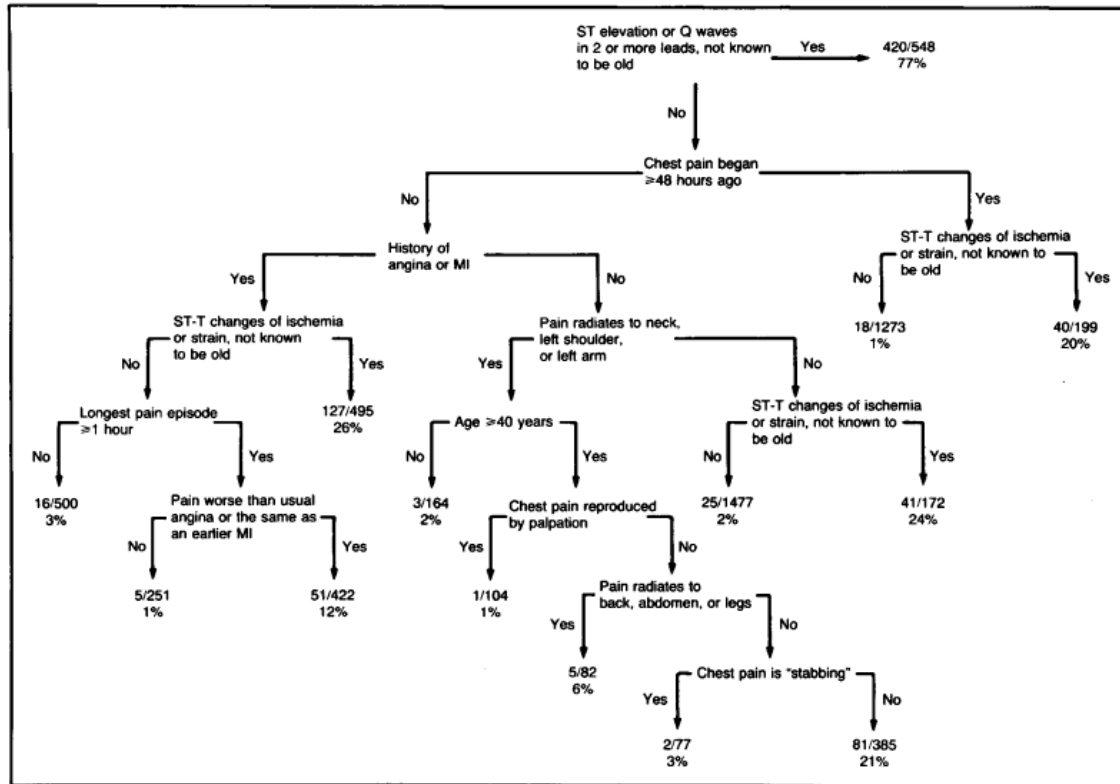
RISK*	FIRST MAJOR EVENT									
	≤12 HOURS		>12–24 HOURS		>24–48 HOURS		>48–72 HOURS		0–72 HOURS	
	Derivation Set	Validation Set	Derivation Set	Validation Set	Derivation Set	Validation Set	Derivation Set	Validation Set	Derivation Set	Validation Set
	<i>number of patients/total number (percent)</i>									
High	125/1034 (12.1)	24/317 (7.6)	36/909 (4.0)	10/293 (3.4)	39/873 (4.5)	9/283 (3.2)	22/834 (2.6)	8/273 (2.9)	222/1034 (21.5)	51/317 (16.1)
Moderate	55/1949 (2.8)	9/845 (1.1)	36/1894 (1.9)	18/836 (2.2)	32/1858 (1.7)	22/818 (2.7)	35/1826 (1.9)	17/795 (2.1)	158/1949 (8.1)	66/845 (7.8)
Low	11/1511 (0.7)	5/918 (0.5)	14/1500 (0.9)	11/912 (1.2)	11/1485 (0.7)	10/901 (1.1)	19/1473 (1.3)	10/891 (1.1)	55/1511 (3.6)	36/918 (3.9)
Very low	5/6188 (0.1)	4/2596 (0.2)	12/6182 (0.2)	5/2592 (0.2)	18/6170 (0.3)	5/2586 (0.2)	13/6152 (0.2)	1/2580 (0)	48/6188 (0.8)	15/2596 (0.6)
Area under the ROC curve†	0.89	0.84	0.79	0.77	0.77	0.77	0.75	0.81	0.82	0.80

\*The derivation of the risk groups is shown in Figure 1.

†None of the differences between the derivation set and the validation set were significant, except that for the entire 72-hour period, the event rate among the high-risk patients differed significantly between the two sets (P=0.04). ROC denotes receiver-operating-characteristic.



# Flow chart



- Easy and simple to understand and use
- If not constructed from a regression tree, the author must make it by hand the rationale of the tree.
- As the number of nodes and branches increases, precision of the estimates decreases.

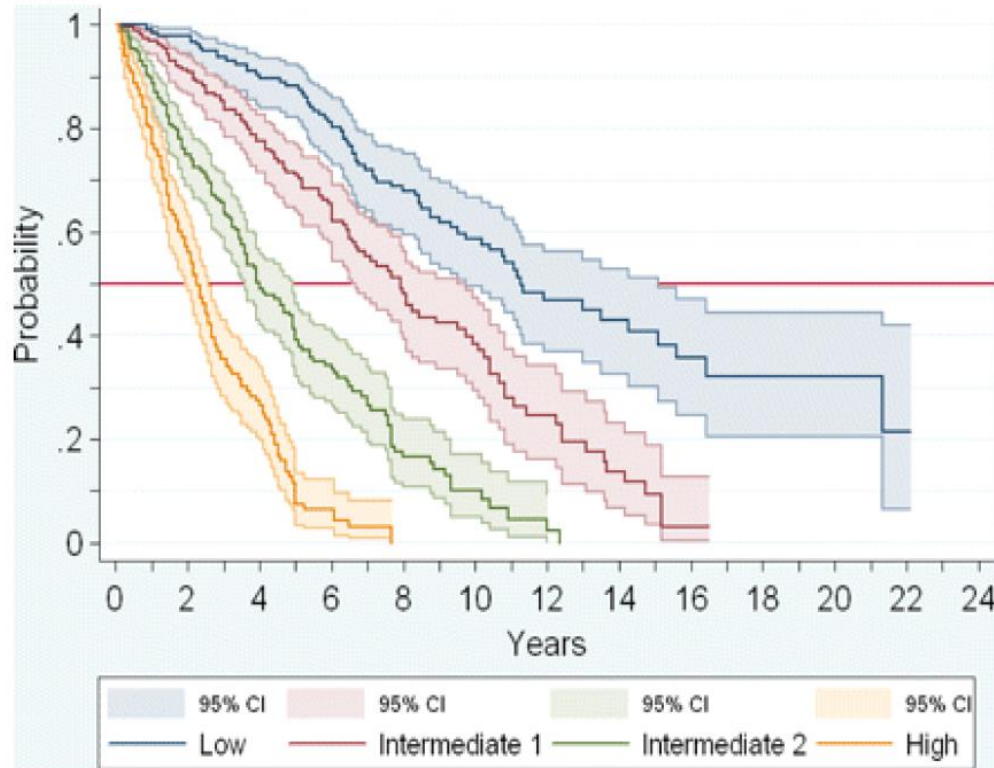
Figure 1. Prospectively Validated Multivariate Algorithm for the Prediction of a Patient's Risk of Acute Myocardial Infarction on the Basis of Emergency Room Data.

On the basis of the algorithm, patients can be assigned to 1 of 14 subgroups, each of which has been classified as having a low ( $\leq 7$  percent) or a high ( $> 7$  percent) risk of acute myocardial infarction. The values shown for each subgroup are the number of patients with acute myocardial infarction, divided by the total number of patients in a subgroup of 6149 patients enrolled in the Chest Pain Study, with the corresponding percentages.<sup>2</sup> "Pain worse than usual angina" denotes worse in frequency, severity, or duration, or failure to respond to usual measures.

The New England Journal of Medicine



# Survival by risk groups



Actuarial survival curves of the 4 risk groups of patients according to the new PMF prognostic system

<http://bloodjournal.hematologylibrary.org/content/113/13/2895/F2.expansion.html>

- Easy and simple to understand and use
- Cutoffs for survival usually estimated on the risk rather than decision analytical considerations.



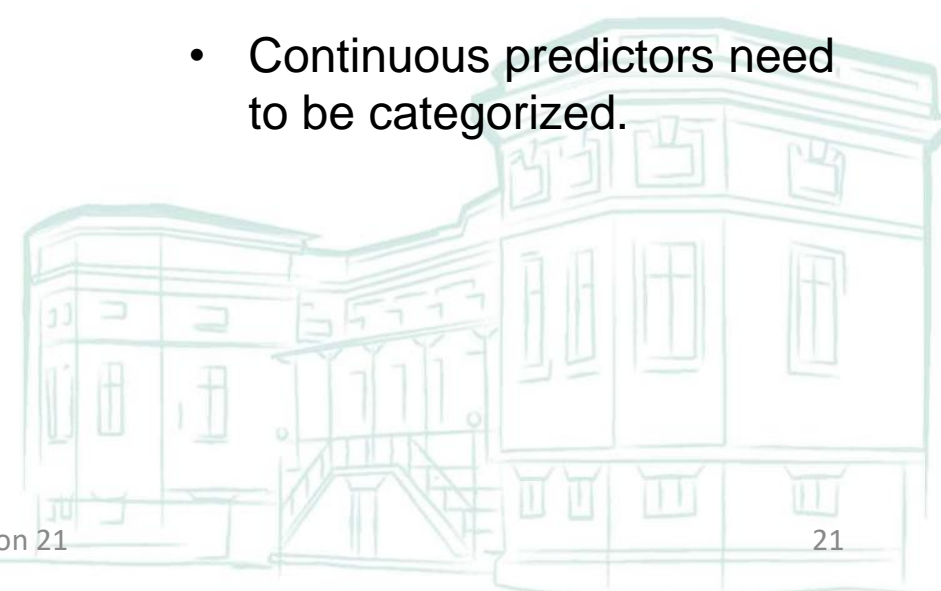
# Survival table

Table 6. Estimated Event-free Survival According to Base-Line Hemodynamic Variables, with Stratification According to the Reduction in the Peak Aortic-Valve Gradient.\*

DECREASE IN pAVG	BEFORE VALVULOPLASTY		EVENT-FREE SURVIVAL (%)			
	PCWP	AOSP	AT 6 MO	AT 12 MO	AT 18 MO	AT 24 MO
%	mm Hg					
≥55	<18	≥140	87	79	69	59
		110-139	83	72	58	48
		<110	76	61	46	34
	18-25	≥140	83	73	60	49
		110-139	78	64	49	37
		<110	69	52	35	24
	>25	≥140	79	66	51	40
		110-139	72	56	39	28
		<110	62	43	26	15
40-54	<18	≥140	85	76	64	54
		110-139	80	68	54	42
		<110	73	57	40	28
	18-25	≥140	81	69	55	34
		110-139	75	60	44	32
		<110	65	47	30	19
	>25	≥140	76	62	46	34
		110-139	68	51	34	23
		<110	57	37	21	11
<40	<18	≥140	79	66	51	39
		110-139	72	56	39	27
		<110	62	42	25	15
	18-25	≥140	73	57	41	29
		110-139	64	46	29	18
		<110	52	32	16	8
	>25	≥140	66	48	31	20
		110-139	56	36	20	11
		<110	43	23	9	4

\*pAVG denotes peak aortic-valve gradient, PCWP mean pulmonary-capillary wedge pressure, and AOSP aortic systolic pressure.

- Easy and simple to understand and use
- As the number of predictors increases tables become very large as each combination of predictors needs to be expressed.
- Continuous predictors need to be categorized.





# Concluding

- The format should consider the intended audience preference
- Show predictions in relation to a single continuous predictor and one or two categorical predictors may be considered
- Electronic patient records and computer/mobile devices availability during health care may enable the direct and easy access to prediction tools from detailed and rather complex prediction models.



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# fim

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