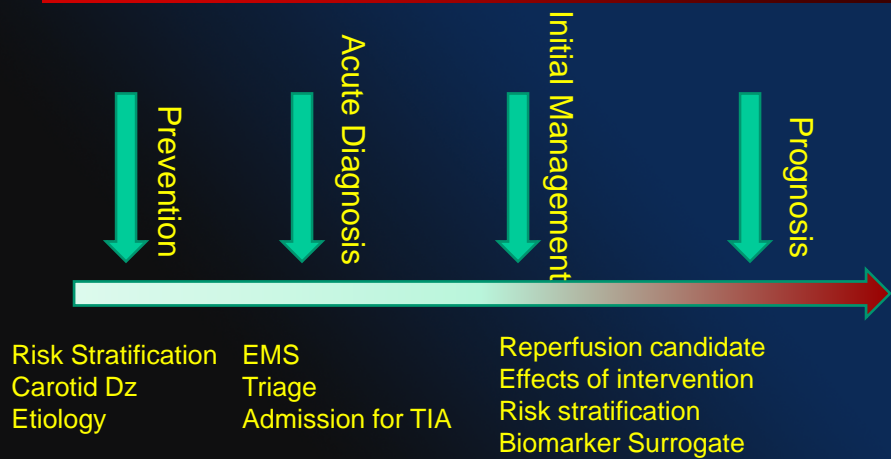


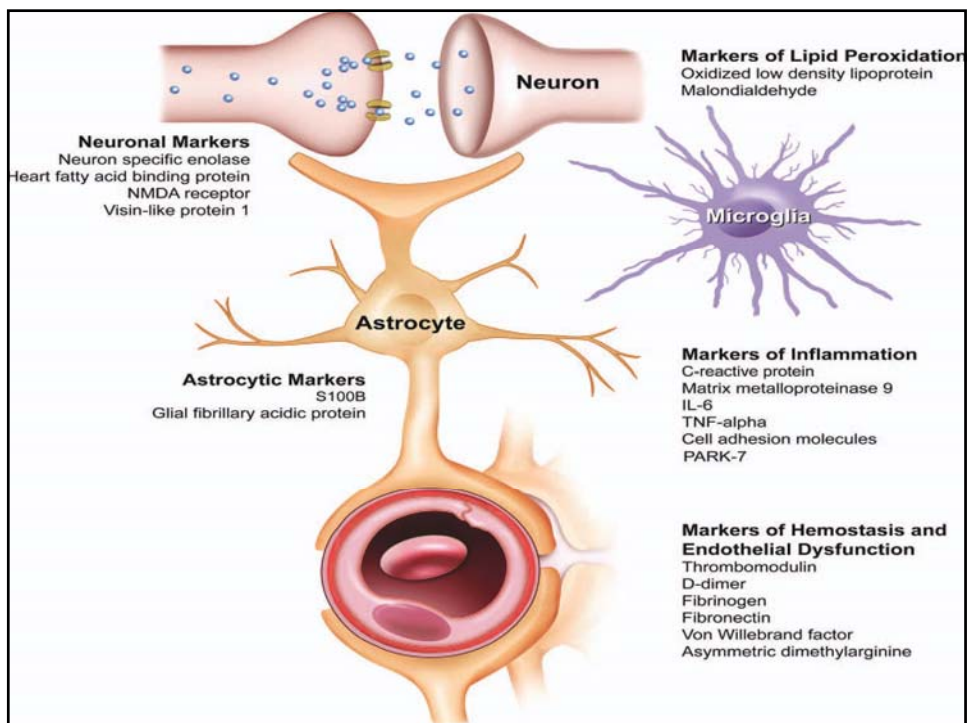
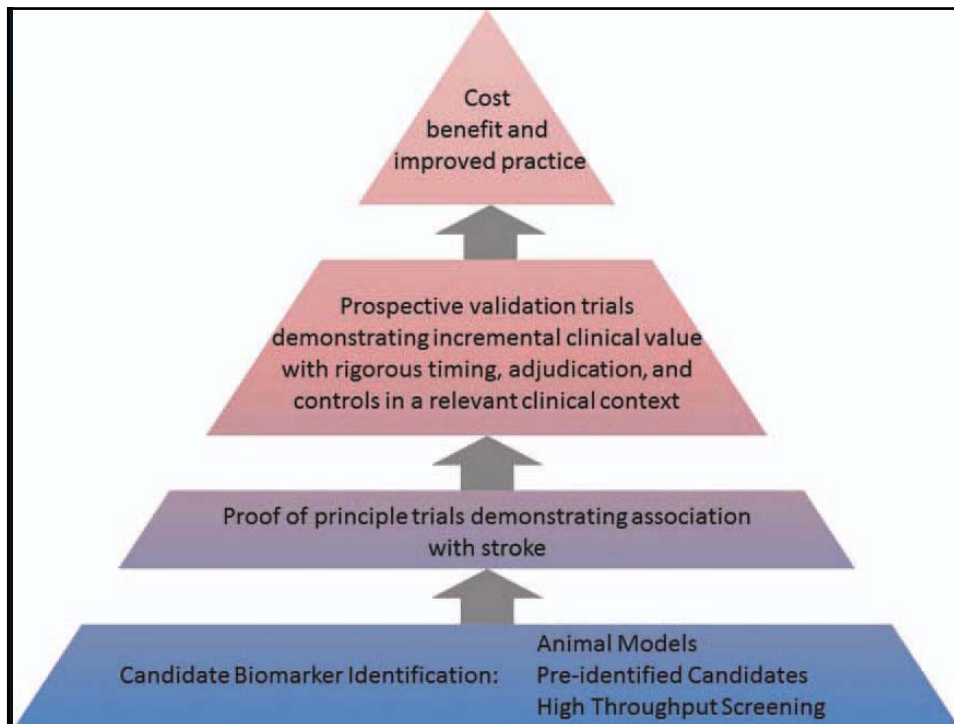
# Field Biomarkers for Stroke risk prediction



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# Biomarkers in the Spectrum of Care





## Biomarker Panel Hypothesis

The ideal biomarker characteristics (sensitivity to early ischemia, specificity, passage across BBB) may not be present in a single marker

An integrated panel of biomarkers targeting different components of the ischemic cascade would provide better diagnostic accuracy than any one marker alone

### Novel Diagnostic Test for Acute Stroke

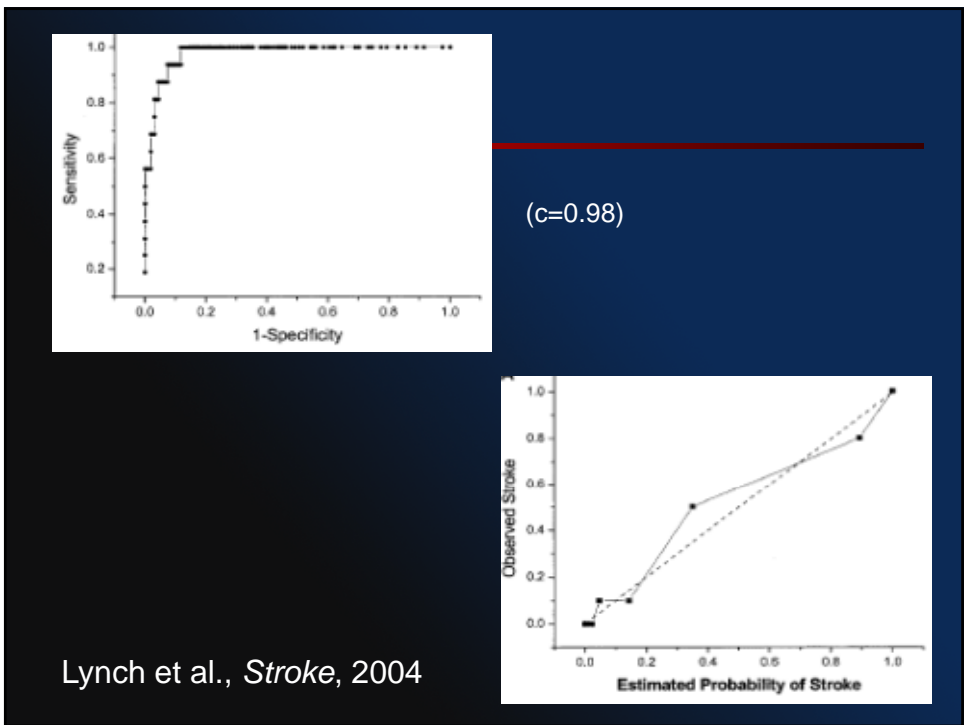
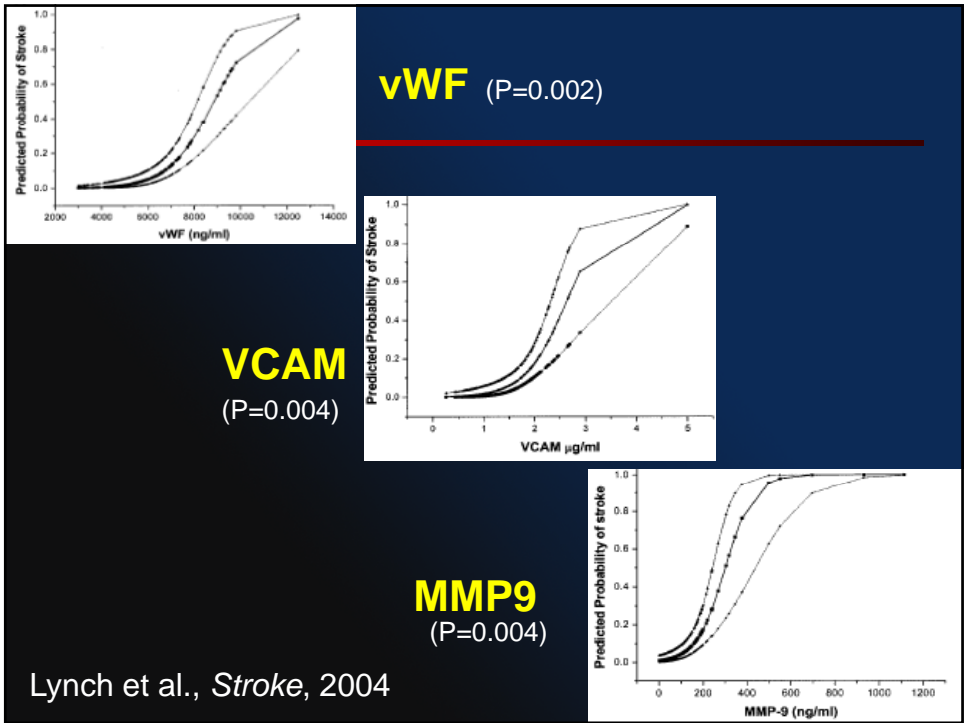
John R. Lynch, MD; Robert Blessing, MSN, ACNP; William D. White, MPH; Hilary P. Grocott, MD, FRCPC; Mark F. Newman, MD; Daniel T. Laskowitz, MD

TABLE 1. Patient Demographics for the Data Set in Which Blood Was Collected Acutely (Within 6 Hours of Symptom Onset) and Subacutely (Between 6 and 24 Hours After Symptom Onset)

	Acute			Subacute		
	Stroke (n=16)	No Stroke (n=165)	p	Stroke (n=38)	No Stroke (n=176)	p
Age	62±15	63.3±8	NS	63±5	62±9	NS
Female sex, %	62.5	32.3	0.026	57.9	32.0	0.005
History of myocardial infarction, %	30.8	1.2	<0.001	37.1	2.3	<0.001
Race, %			<0.001			
White	37.5	91.9		44.7	89.5	<0.001
Black	62.5	3.8		52.6	6.4	
Other	0	4.4		2.6	4.1	

Age is expressed as mean±SD. For the categorical characteristics, percents are given as proportion of patients with or without stroke who had the characteristics.

Lynch et al., *Stroke*, 2004



## Biomarker Rapid Assessment in Ischemic Injury (BRAIN) study

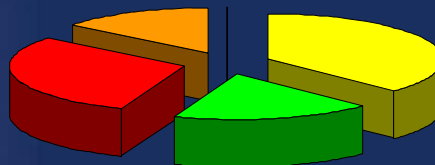
Alabama Neurological Institute	Birmingham, AL
Cleveland Clinic Foundation	Cleveland, OH
Denver Health	Denver, CO
Duke University Medical Center	Durham, NC
Hartford Hospital	Hartford, CT
Hennepin County Medical Center	Minneapolis, MN
Henry Ford Health Systems	Detroit, MI
Hospital of the University of Pennsylvania	Philadelphia, PA
Ingham Medical Center	Lansing, MI
Kentucky Neuroscience Research	Louisville, KY
OSF Saint Francis Medical Center	Peoria, IL
Sentara Norfolk General Hospital	Norfolk, VA
St. Luke's Health System	Kansas City, MO
UMASS, Worcester Medical Center	Worcester, MA
University of Cincinnati	Cincinnati, OH
University of California, Los Angeles	Los Angeles, CA
University of Colorado Health Science Center	Denver, CO

## Data Analysis

➤ Population:

Stroke Mimics	425
TIA	214
Ischemic Stroke	345
Intracranial Hemorrhage	162

TOTAL 1146

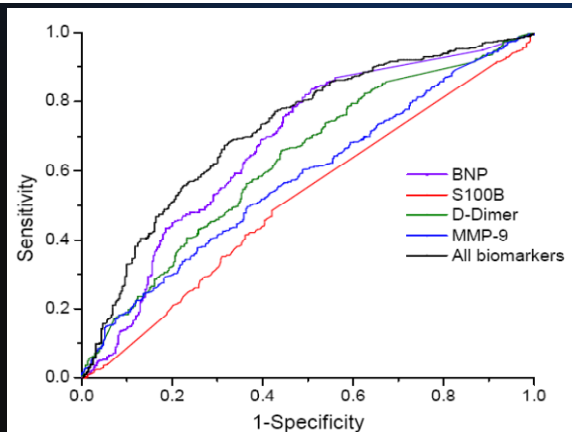


Laskowitz et al., *Stroke*, 2009

## Common mimics

Migraine	61
Post-ictal	39
Infectious/Systemic	35
Cardiovascular/Syncope	35
Functional/Psychiatric	29
Neuromuscular	24
Mass lesions (SDH)	22
Metabolic/Intoxication	20
Vertigo	17
Bell's palsy	7
Decompensation prior deficit	5

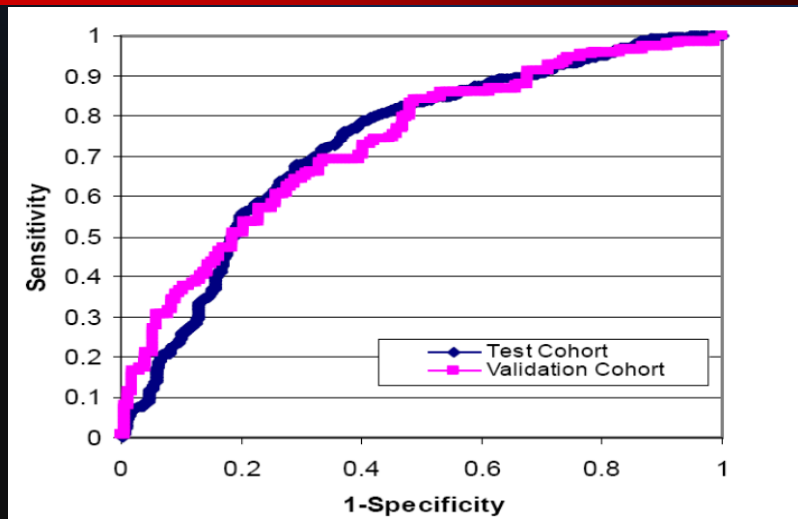
Latency from Symptom onset	Area under ROC (All Stroke)	Sensitivity (Stroke) (1st Quartile)	Specificity (Non-stroke) (4th Quartile)	Area under ROC (ICH)	Sensitivity(ICH) (1st Quartile)
0-3	0.85	100% (37/37)	96% (45/47)	0.81	100% (9/9)
3-6	0.67	91% (71/78)	81% (74/91)	0.68	75% (15/20)
6-12	0.74	89% (68/76)	90% (64/71)	0.81	90% (18/20)
12-24	0.74	87% (138/159)	88% (87/99)	0.76	91% (42/46)
>24	0.89	84% (64/76)	100% (13/13)	0.95	87% (48/55)
Total	0.73	89% (378/426)*	88% (283/321)**	0.79	88% (132/150)***



C=0.73

Laskowitz et al., *Stroke*, 2009

## Validation on a point of care platform



Laskowitz et al., *Stroke*, 2009

## Lessons Learned

- Importance of defining clinical context of biomarker approach
- Importance of site selection is greater obstacle than selecting the ideal biomarker

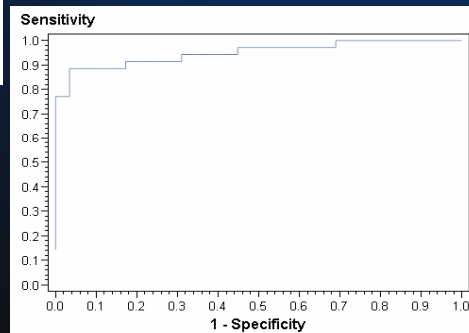


# Identifying stroke from mimic: Duke site

Population Group	Ischemic Stroke Patients (N=53)	Mimics (N=38)
Initial NIHSS:		
Average (SD)	10.5 (7.4)	2.9 (5.1)
NIHSS range	0-28	0-26
Age:		
Average (SD)	65 (16.3)	52 (19.2)
Sex:		
Females (%)	30 (57%)	24 (63%)
Males (%)	23 (43%)	14 (37%)
Race:		
Caucasian	35 (66%)	26 (68%)
African American	18 (34%)	12 (32%)
All Other	0 (0%)	0 (0%)

Discharge Diagnosis	Mimics (N=38)
Neuropathies	7 (18%)
Psychiatric Disorders	6 (16%)
Seizures	5 (13%)
Syncope	4 (11%)
Brain Tumors	3 (8%)
Headaches/Migraines	3 (8%)
Toxicities	2 (5%)
Endocrinopathies	2 (5%)
Cardiac Disorders	2 (5%)
Other (GI, ophthalmology)	4 (11%)

Marker	Model 1 (Unadjusted)			Model 2 (Adjusted for NIHSS)			Model 3 (Adjusted for age, gender, race, and NIHSS)		
	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
S-100B	6.0	1.1-32.6	0.04	8.0	0.7-90.1	0.09	13.2	0.8-237.7	0.07
CRP	11.4	2.0-65.3	<0.01	13.9	2.0-97.4	<0.01	15.4	1.35-174.7	0.03
D-dimer	2.0	0.7-5.5	0.17	0.8	0.2-3.6	0.82	0.9	0.2-4.5	0.89
MMP-9	13.3	2.4-74.3	<0.01	7.8	1.0-58.9	0.05	7.3	0.8-62.0	0.07
Overall likelihood ratio	P < 0.0001			P < 0.0001			P < 0.0001		
Goodness of fit test	P = 0.80			P = 0.93			P = 0.99		
R <sup>2</sup>	0.76			0.84			0.85		
C-index	0.96			0.98			0.98		





## Future Directions: Acute Diagnosis

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- Which TIA's merit admission?
- Identifying stroke etiology
- Differentiating ischemic vs. hemorrhage stroke?
- Who is a candidate for reperfusion therapy?
- **Use of biomarkers in pre-hospital setting**

## Thank You

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