

# **Discussion**

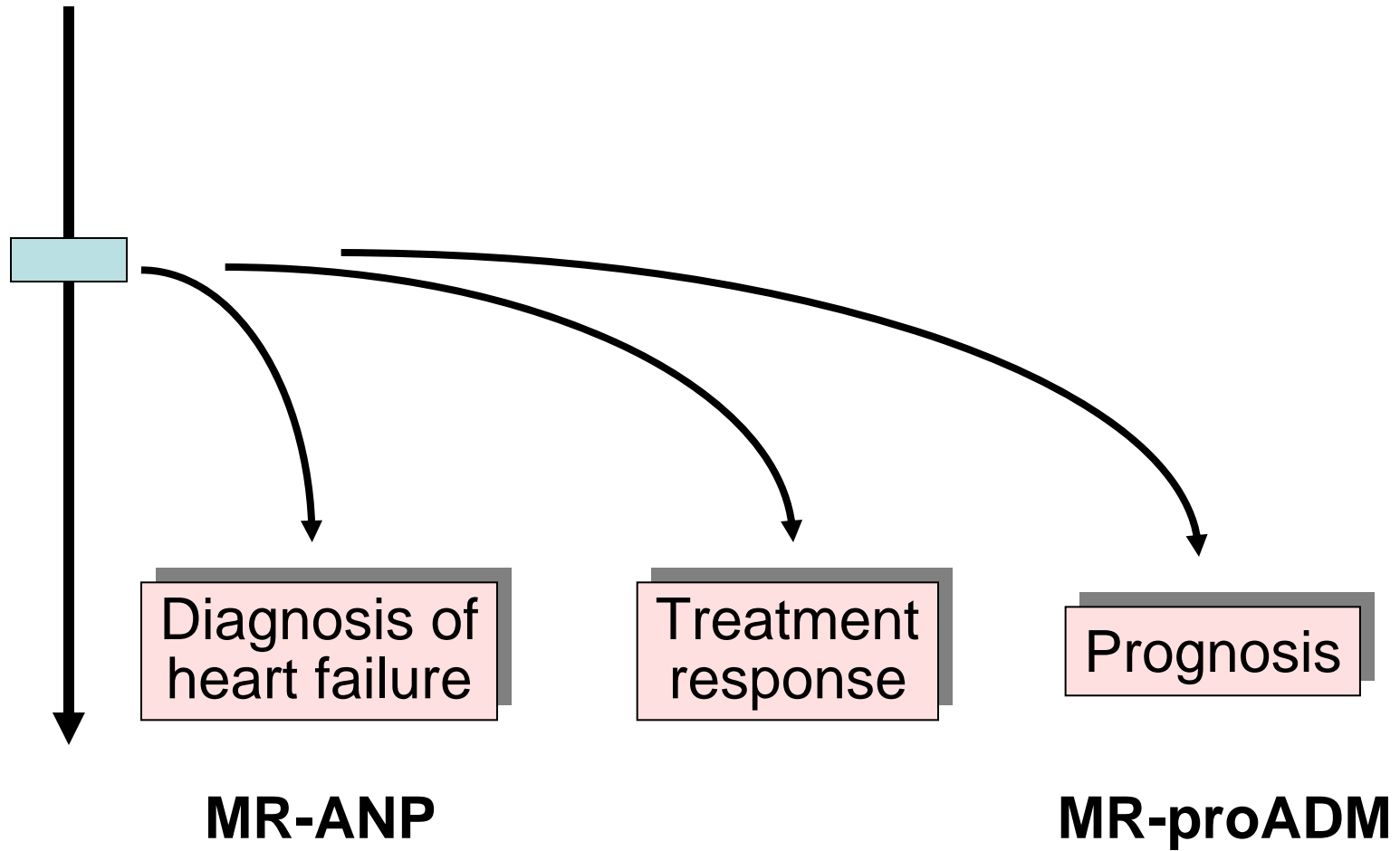
## **Results of the BACH Trial**

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Conflicts of interest in relation to topic: None

Measurement of serum biomarkers at time of presentation of the patient to the hospital with acute dyspnea



# How Clinicians Should Evaluate the Results of Trials of Biomarkers

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## **1. Do we really need a new biomarker?**

How well do clinicians currently perform without the new biomarker?

## **2. How does the new biomarker perform?**

How often does the new biomarker miss the right answer and how often does it provide the wrong answer in a setting of uncertainty?

## **3. Should we care about the results?**

Does the information provided by the biomarker alter the management of the patient?

# Do We Really Need a New Biomarker?

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Acute onset of dyspnea		Acute onset of dyspnea
38 years old		78 years old
No underlying medical illnesses		Hypertension, COPD and CHF
Ejection fraction 0.62		Ejection fraction 0.24
Creatinine 0.6 mg/dl		Creatinine 2.1 mg/dl

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Low level of biomarker	Low level of biomarker	High level of biomarker

# Do We Really Need a New Biomarker?

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38 years old	78 years old	78 years old
No underlying conditions	Hypertension, COPD and CHF	Hypertension, COPD and CHF
<b>Is MR-pro-ADM a useful biomarker?</b>	Ejection fraction 0.24	Ejection fraction 0.24
Ejection fraction 0.62	Creatinine 2.1 mg/dl	Creatinine 2.1 mg/dl
Creatinine 0.6 mg/dl	Low level of biomarker	High level of biomarker
Low level of biomarker		

# Statistical Approaches Used to Evaluate the Utility of Biomarkers

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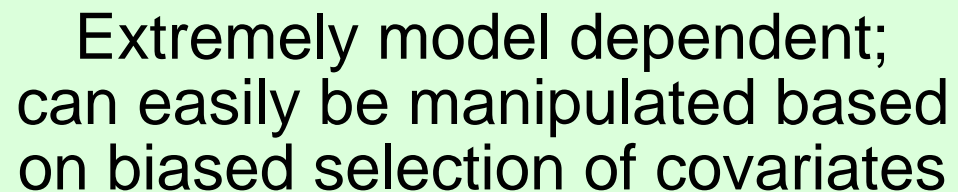
- Placing the new biomarker high on a hierarchy of P values
- Placing the new biomarker high on a hierarchy of Chi<sup>2</sup> statistics
- Placing the new biomarker high on a hierarchy of hazard ratios
- Discrimination: calculation of the area under the ROC curve (c statistic)
- Calibration: Hosmer-Lemeshow statistic
- Clinical reclassification

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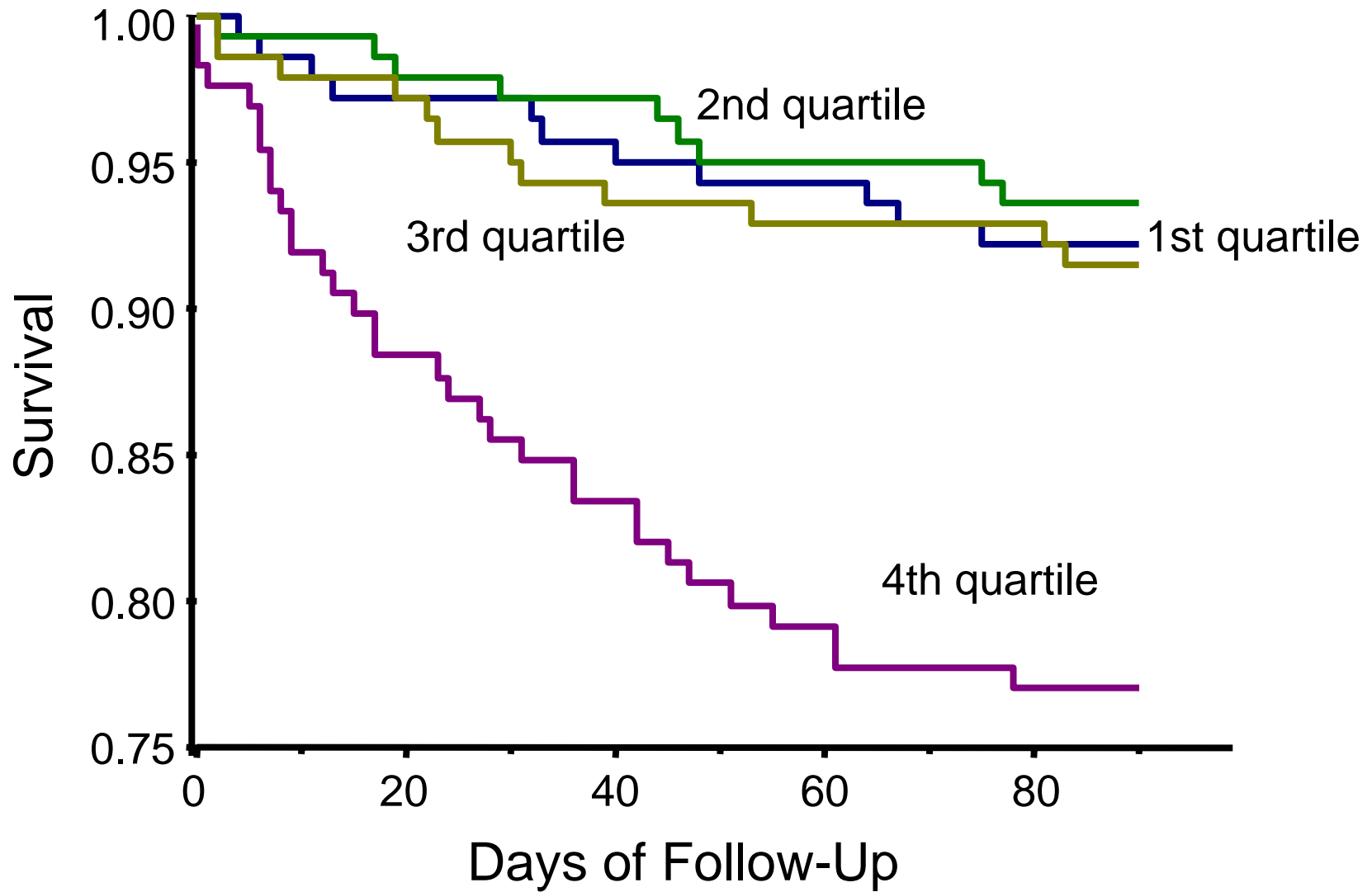
- Discrimination: calculation of the area under the ROC curve
- Calibration: comparison of predicted vs. observed probabilities
- Clinical reclassification



Extremely model dependent;  
can easily be manipulated based  
on biased selection of covariates

# Prognostic Value of MR-pro-ADM

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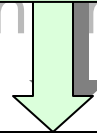
# Statistical Approaches Used to Evaluate the Utility of Biomarkers

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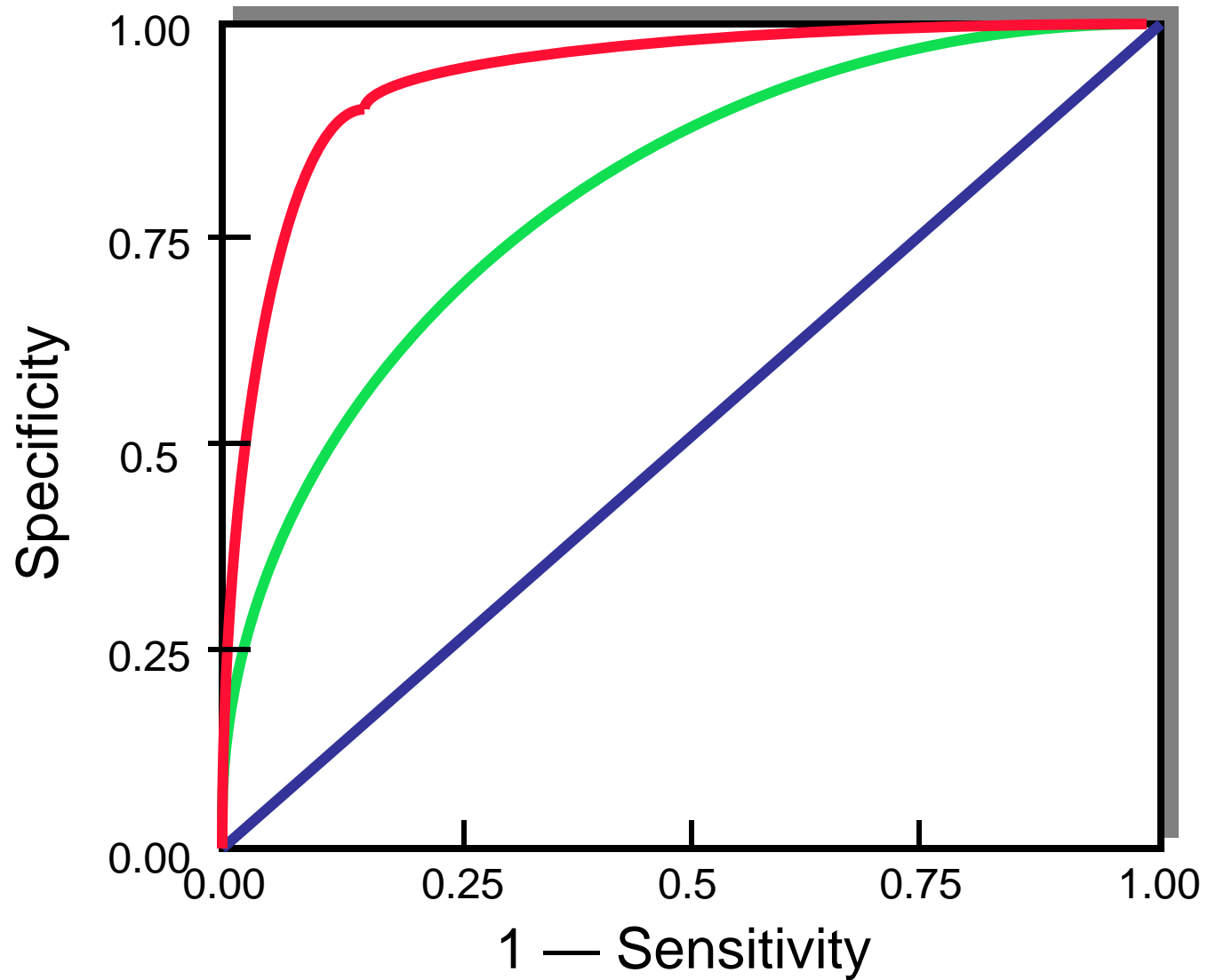
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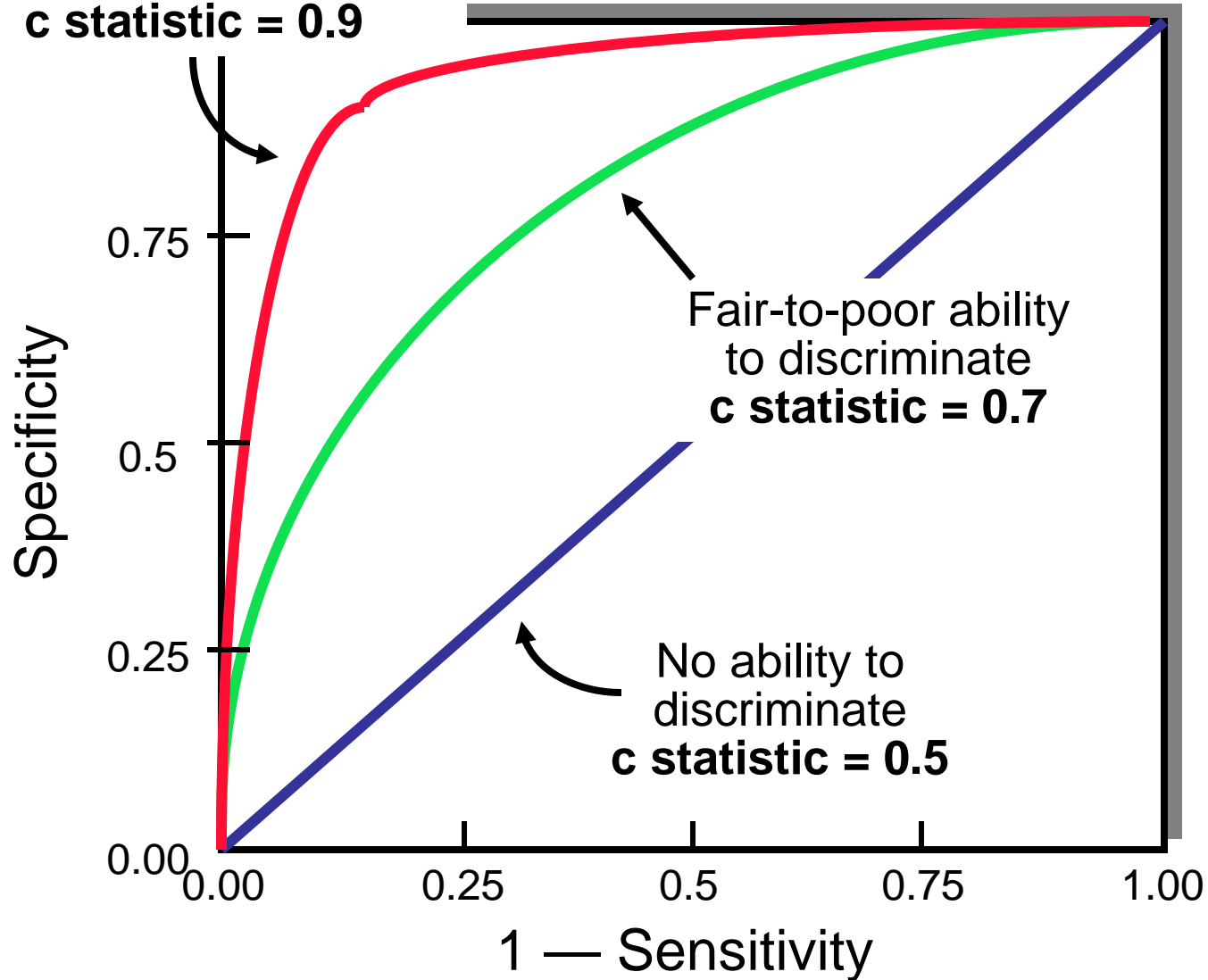
# Area Under the Receiver Operator Curve

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# Area Under the Receiver Operator Curve

Good-to-excellent ability  
to discriminate  
**c statistic = 0.9**




# Biomarkers Evaluated in the BACH Trial Had Relatively Poor Discriminant Ability

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Ability to discriminate	AUC (c statistic)
Excellent	0.9
Good	0.8
Fair	0.7
Poor	0.6
None	0.5

Would have been even worse if analyses had focused on areas of clinical uncertainty

MR-pro-ADM [0.67]



BNP [0.60]



# Statistical Approaches Used to Evaluate the Utility of Biomarkers

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- Placing the new biomarker high on a hierarchy of P values
- Placing the new biomarker high on a hierarchy of Chi<sup>2</sup> statistics
- Placing the new biomarker high on a hierarchy of AUC statistics
- Discrimination: Area under the ROC curve (C statistic)
- Calibration: Hosmer-Lemeshow statistic

How often does the new biomarker provide information that changes patient management?

- Clinical reclassification

# What Would Be the Clinical Value of Using MR-pro-ADM to Assess Prognosis?

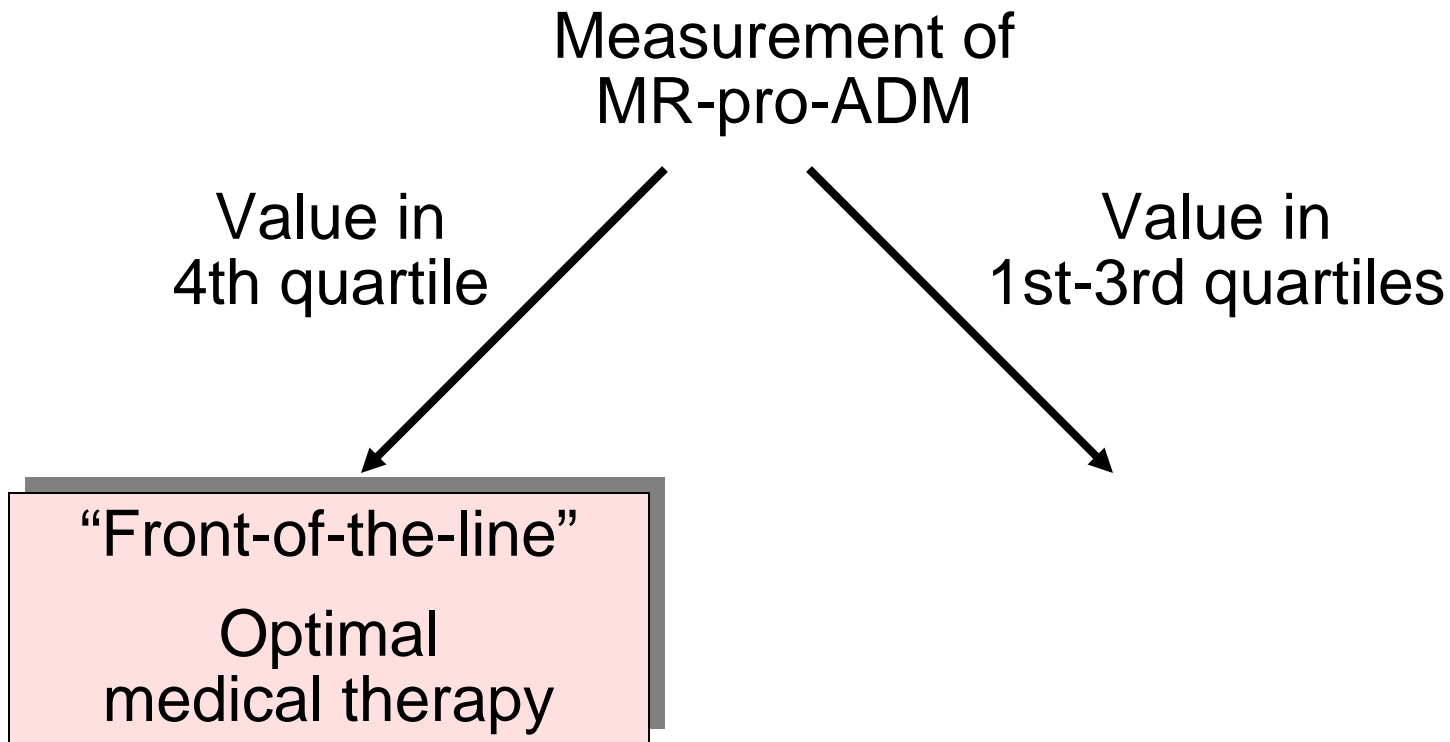
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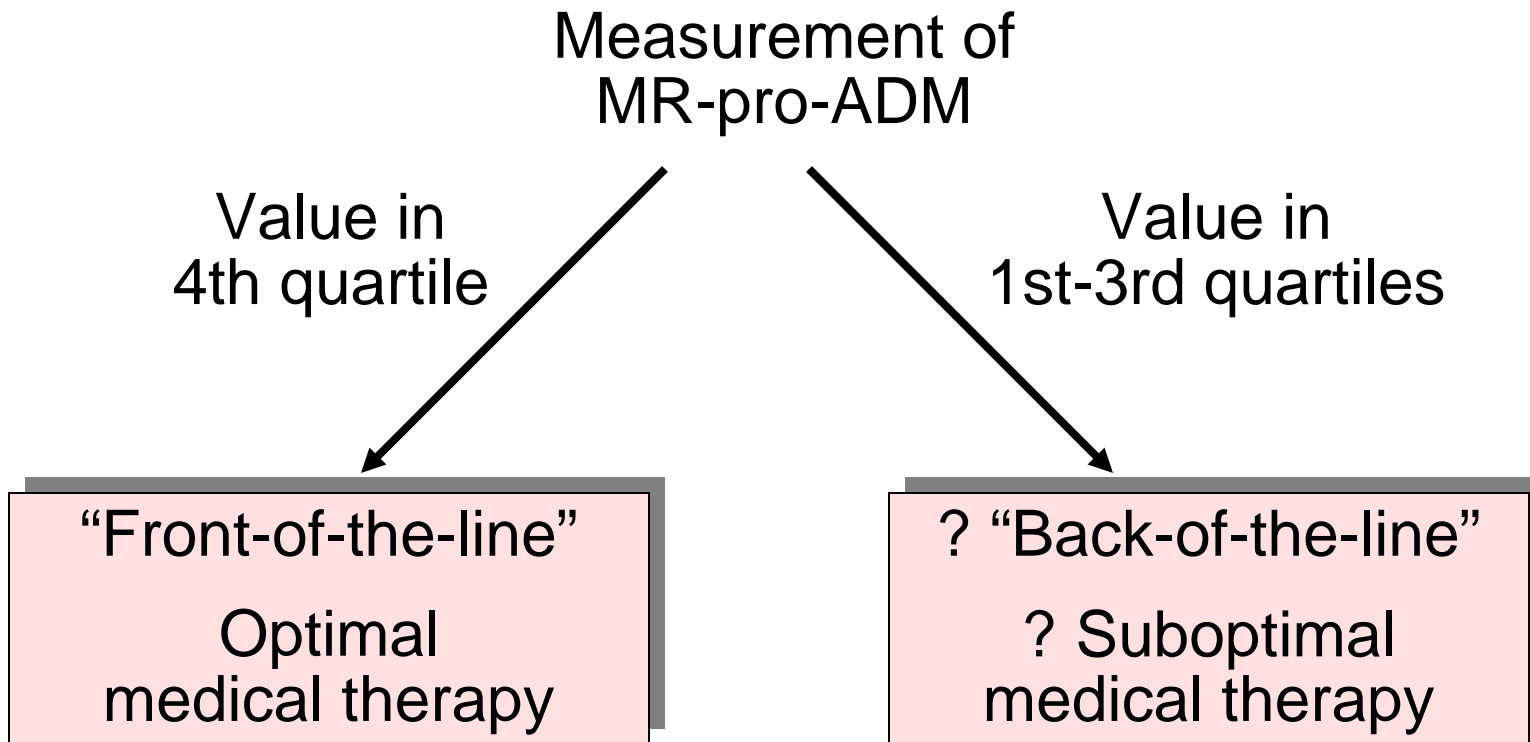
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# What Would Be the Clinical Value of Using MR-pro-ADM to Assess Prognosis?

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**Every** elderly patient with associated medical conditions who presents with acute heart failure is at high risk of death during the following 90 days.



# The Fact Is That . . .

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- Every elderly patient with underlying medical conditions who presents with acute heart failure is at high risk of death during the following 90 days.
- Every patient who presents with acute heart failure should receive optimal therapy.
- The treatment of the very high risk patient with acute heart failure does not differ from the treatment of the high risk patient with acute heart failure.
- There is no treatment that can be offered to the very high risk patient with acute heart failure that should not also be offered for all other patients with acute heart failure (who are all at high risk).

# Conclusions

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- Like BNP and NT-pro-BNP, the measurement of MR-pro-ADM has prognostic significance in some patients presenting with acute dyspnea.
- However, like BNP and NT-pro-BNP, the measurement of MR-pro-ADM has poor ability to reliably discriminate survivors from nonsurvivors.
- The measurement of MR-pro-ADM is not likely to influence clinical decision-making or change the management of patients with acute heart failure.