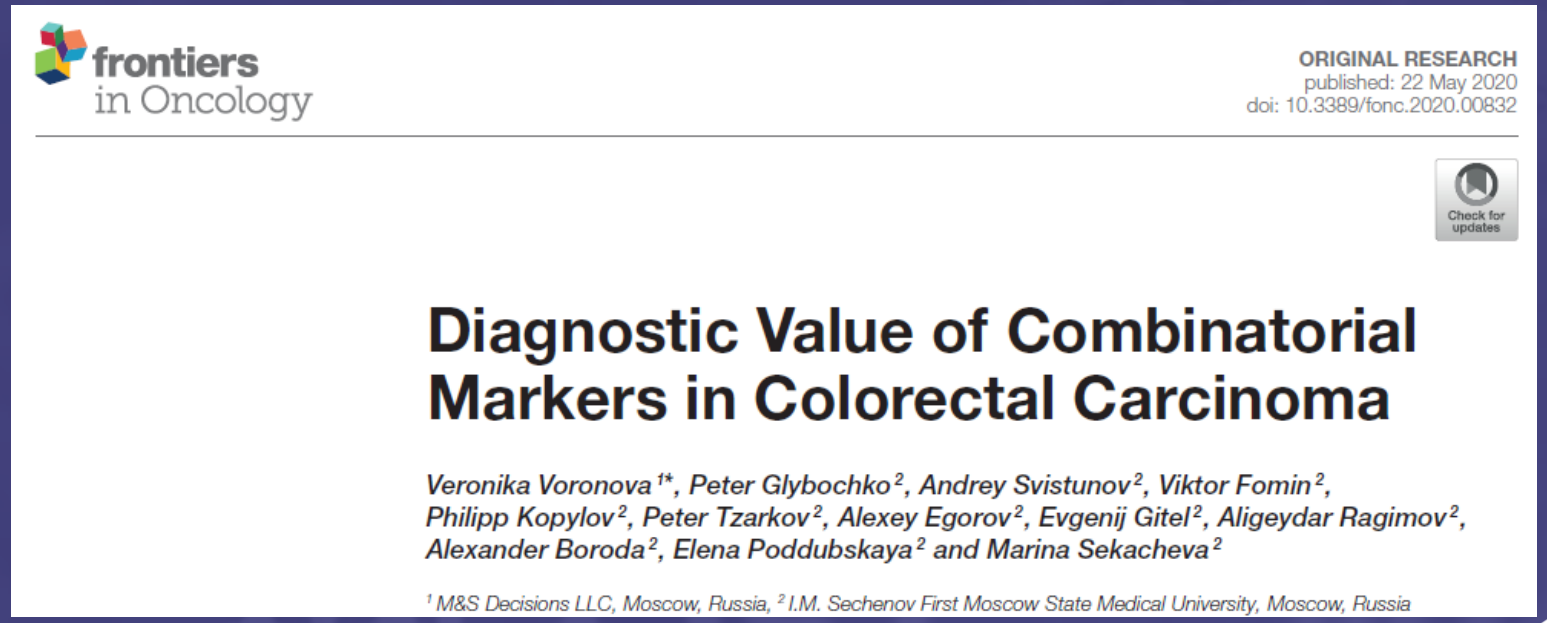
Modeling & Simulation Decisions

Diagnostic value of combinatorial markers in colorectal carcinoma



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Diagnostic Value of Combinatorial Markers in Colorectal Carcinoma

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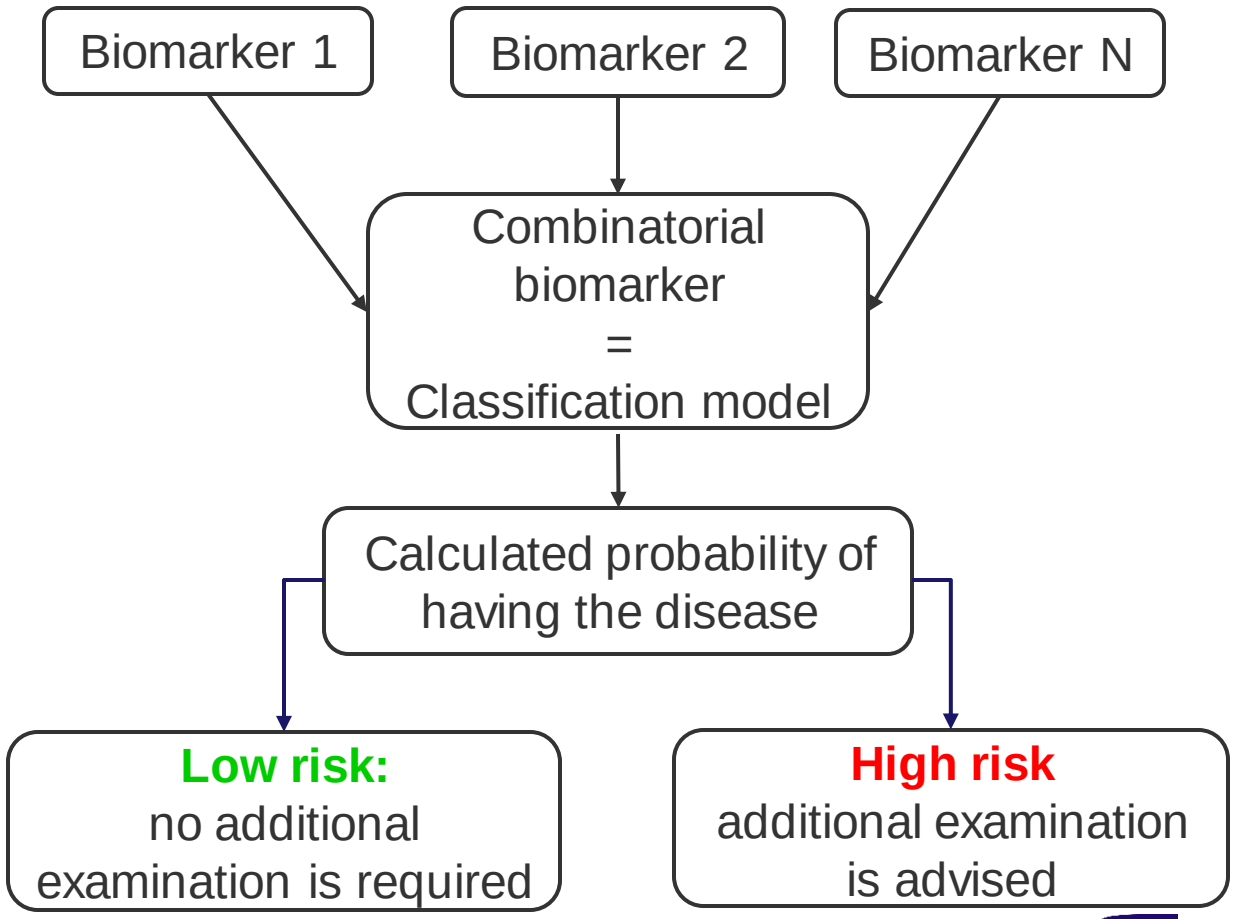
Visual abstract + annotation

- Diagnostic performance of 20 blood-based cancer-related 20 biomarkers was evaluated using the data from 203 healthy subjects and 102 patients with colon cancer.
- Cancer patients were characterized by multiple abnormalities in biomarker levels; diagnostic performance, evaluated *via* ROC analysis, varied across considered biomarkers (0.52<ROC AUC<0.90)
- Combinatorial biomarkers, exploiting several classification algorithms to predict patient status based on levels of multiple biomarkers and patient's characteristics, were developed
- Combinatorial biomarkers demonstrated higher diagnostic performance over single-protein biomarkers



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Decisions

Compact work review

Compact work review: Objectives

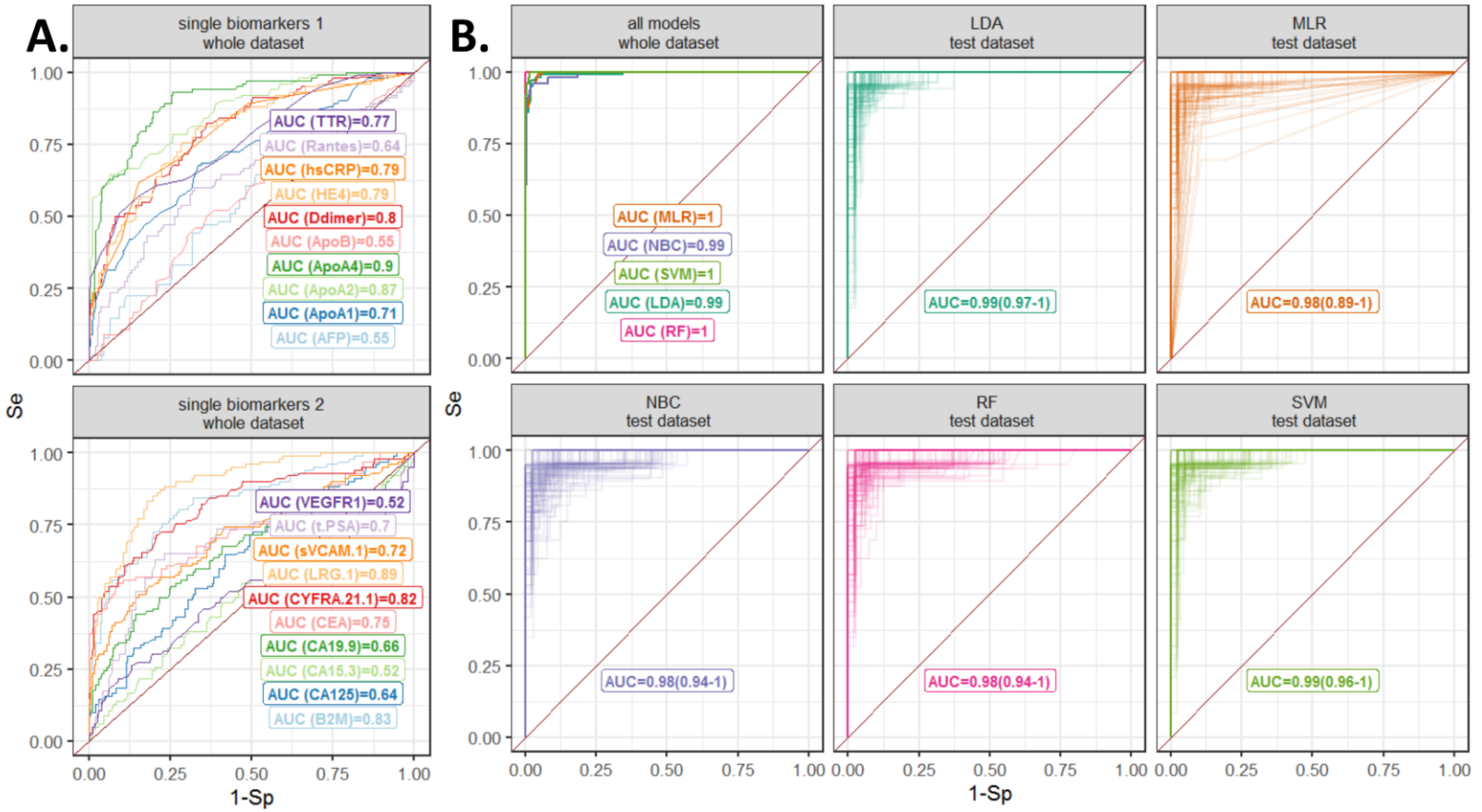
The study is aimed to test the performance of 20 single-protein blood–based tests and combinatorial biomarkers, exploiting several classification algorithms and joint information on protein levels and patients characteristics, in detection of colon cancer.

Abb.	Algorithm
NBC	Naïve Bayes classifier
LDA	Linear discriminant analysis
MLR	Multiple logistic regression
RF	Random forest
SVM	Support vector machine

Abb.	Marker	Group
ApoA1	Apolipoprotein A1	Metabolism
ApoA2	Apolipoprotein A2	Metabolism
ApoA4	Apolipoprotein A4	Metabolism
ApoB	Apolipoprotein B	Metabolism
AFP	Alphafetoprotein	Oncofetal protein
B2M	Beta 2 microglobulin	Acute phase protein
CA125	Cancer antigen 125	Oncofetal protein
CA15-3	Cancer antigen 15-3	Oncofetal protein
CA19-9	Carbohydrate antigen 19-9	Oncofetal protein
CEA	Carcinoembryonic antigen	Oncofetal protein
CYFRA.21.1	Cytokeratin 19-fragments	Oncoprotein
Ddimer	Ddimer	Acute phase protein
HE4	Human epididymis protein 4	Fibrin degradation product
hsCRP	Human-specific C-reactive protein	Acute phase protein
LRG.1	Leucine-rich alpha-2-glycoprotein 1	Acute phase protein
Rantes	Regulated on activation, normal T cell expressed and secreted	Acute phase protein
sVCAM.1	Soluble vascular cell adhesion molecule 1	Adhesion
TTR	Transthyretin	Acute phase protein
t-PSA	Total prostate-specific antigen	Oncofetal protein
VEGFR1	Vascular endothelial growth factor receptor	Vascularization

Diagnostic performance of single biomarker-based tests and combinatorial biomarkers

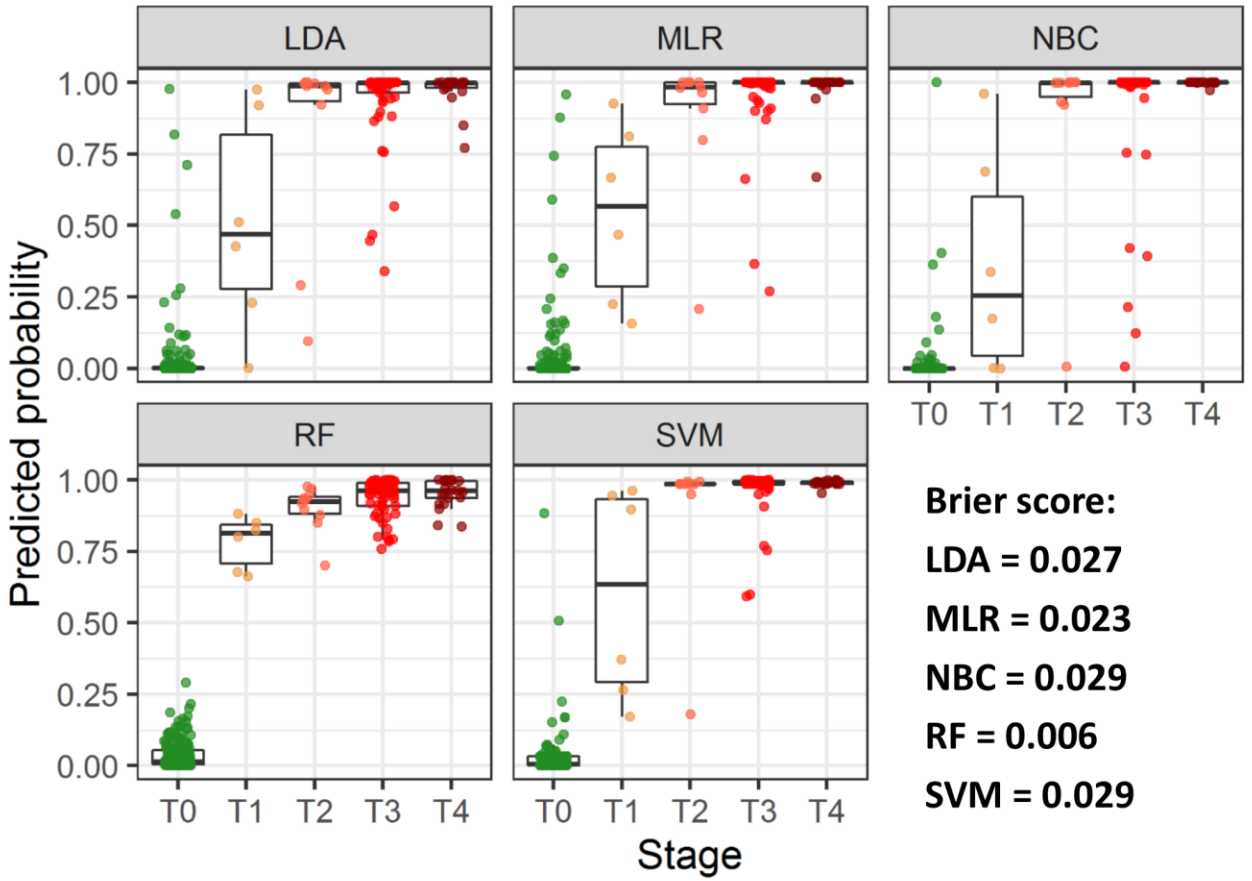
- The highest diagnostic performance was observed for ApoA4, followed by LRG-1 and ApoA2
- AFP, ApoB, CA 15-3 and VEGFR-1 demonstrated low diagnostic performance (ROC AUC<0.6) and were excluded from further analysis
- Combinatorial biomarkers, considering measurements of 15 significant proteins + age + gender demonstrated superiority over single-protein biomarkers
- 5-fold cross-validation did not indicate overfitting problem and confirmed high predictive power for developed combinatorial biomarkers



*ROC curves for **A.** Single biomarkers; **B.** Combinatorial biomarkers. Different models are shown by color. Numbers denote AUROC values; 90% confidence 397 intervals for validation are shown in brackets.*

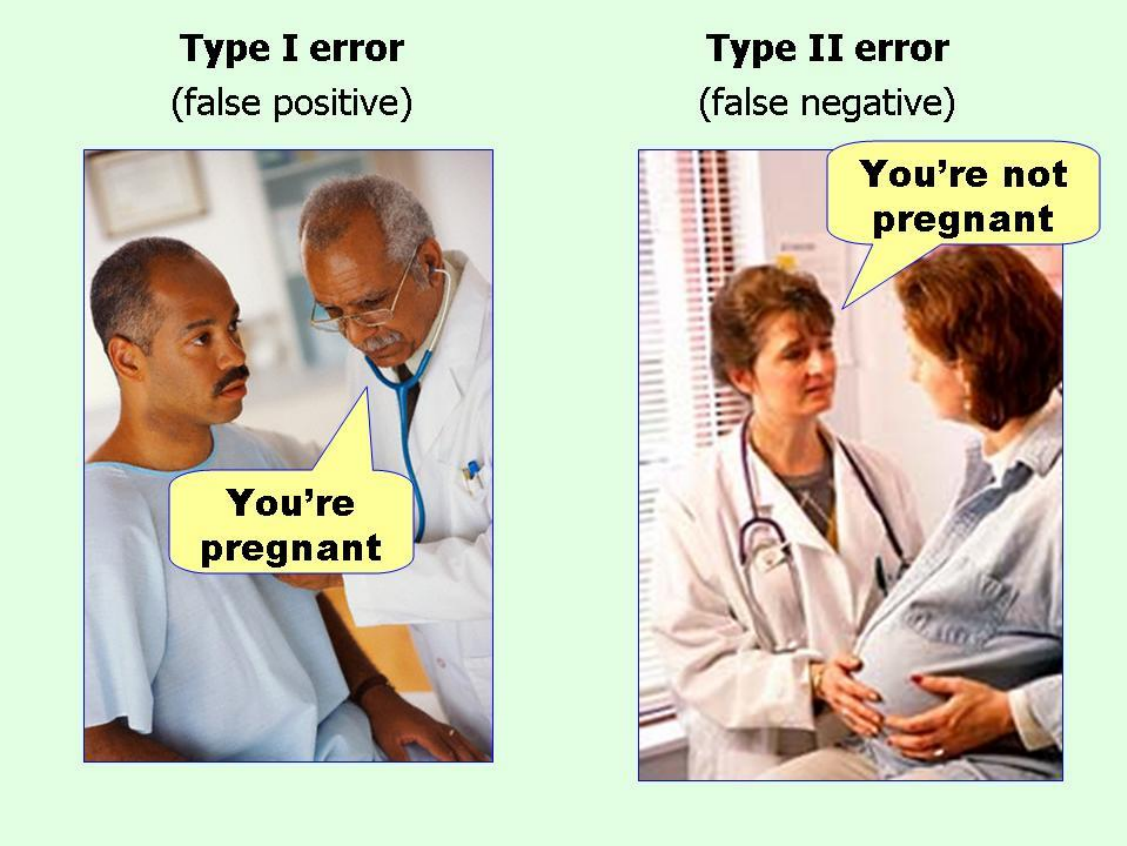
Model utility for early cancer detection

- Model-predicted probabilities of having the disease were calculated for healthy subjects and cancer patients with different disease stages, enrolled into the study
- To evaluate the accuracy of probabilistic classification model predictions a Brier score was calculated (lower Brier score value = better accuracy)
- RF algorithm demonstrated the highest accuracy and showed diagnostic potential for early cancer detection



Predicted probability of having cancer across patient populations. Different cancer stages are shown by color

Conclusions



1. Multi-protein combinatorial biomarkers represent a perspective strategy for early cancer detection

2. Further prospective trials are required to confirm utility of the developed diagnostic tool