Risk-based Stratification of Sepsis Patients in the Emergency Ward

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Introduction and Purpose

Prediction of bacteraemia allows for cost-effective decisions on rapid diagnostics.

Methods

Prediction/Classification model

SepsisFinderLite is a partial model of the inflammatory response to sepsis. It uses a causal probabilistic network (CPN) to predict bacteraemia based on "infection variables" – laboratory variables including C-reactive protein, neutrophil fraction, platelet count and bilirubin. The model is a "lightweight" version of the SepsisFinder CPN which also included vital parameters [1]. Both CPNs were constructed manually and tuned via machine learning. The training dataset consisted of the infection variables, presence of bacteraemia, age and 30-day mortality recorded for 4707 patients with a community acquired infection at Beilinson Hospital, Petah Tikva, Israel. Patient data were acquired during studies/use of the TREAT decision support system in the period from 2002-2016 [2, unpublished data on file].

Setting and patients

Data were collected retrospectively for patients from whom blood cultures were drawn in the emergency ward at 7 hospitals in Emilia-Romagna, Italy from January 1 to June 30 2016, who also had other laboratory test data available. Episodes were excluded if they contained two or fewer infection variables, if infection variables were recorded more than fifteen minutes after blood samples were taken for culture, if the same patient had a previous infectious episode within the two weeks prior or if blood culture results were missing.

Analysis

The model was used to provide a probability of bacteraemia for each patient. Predictive power was assessed from the receiver-operating characteristic (ROC) curve.

Key Points

1. Model uses routine measurements, tolerant of missing data

2. Sub-group of ~20% of patients with ~50% bacteraemia rate

3. "Enrichment" can be used to improve cost-effectiveness of rapid diagnostic testing

Demographics/Descriptive Statistics

	N/%recorded	Median [IQR]/%
Patients	1035	
Cultures	1067	
Age	1035	71 [50-82]
30 day mortality	119/1011	11.8%
Infection variables		
Leukocytes	99.5%	12.2 [8.1-17.4]
Neutrophils	99.3%	9.6 [5.6-14.2]
Neutrophil fraction	99.3%	0.82 [0.71-0.89]
Platelets	99.5%	217 [156-308]
Albumin	1.2%	34 [32-38]
Lactate	20.1%	2.1 [1.3-3.4]
CRP	98.2%	91 [31-185]

Results

Patients

1064 patients (1106 episodes) were included. Following exclusion, the final dataset consisted of 1067 episodes for 1035 patients. 345 patients (32.3%) had positive blood cultures. After removal of potential contaminants, 248 patients (23.2%) had bacteraemia.

Predictive Performance - Bacteraemia

The area under the ROC curve for bacteraemia prediction was 0.74 (95% CI 0.70 – 0.78), indicating that the prediction was fair. When lactate measurements were included, the area under the ROC curve was 0.75 (95% CI 0.71 – 0.78) The predictions enabled the stratification of the patient group according to probability of bacteraemia.

Risk-based Stratification

Episodes were split into strata based on their predicted probability of bacteraemia:
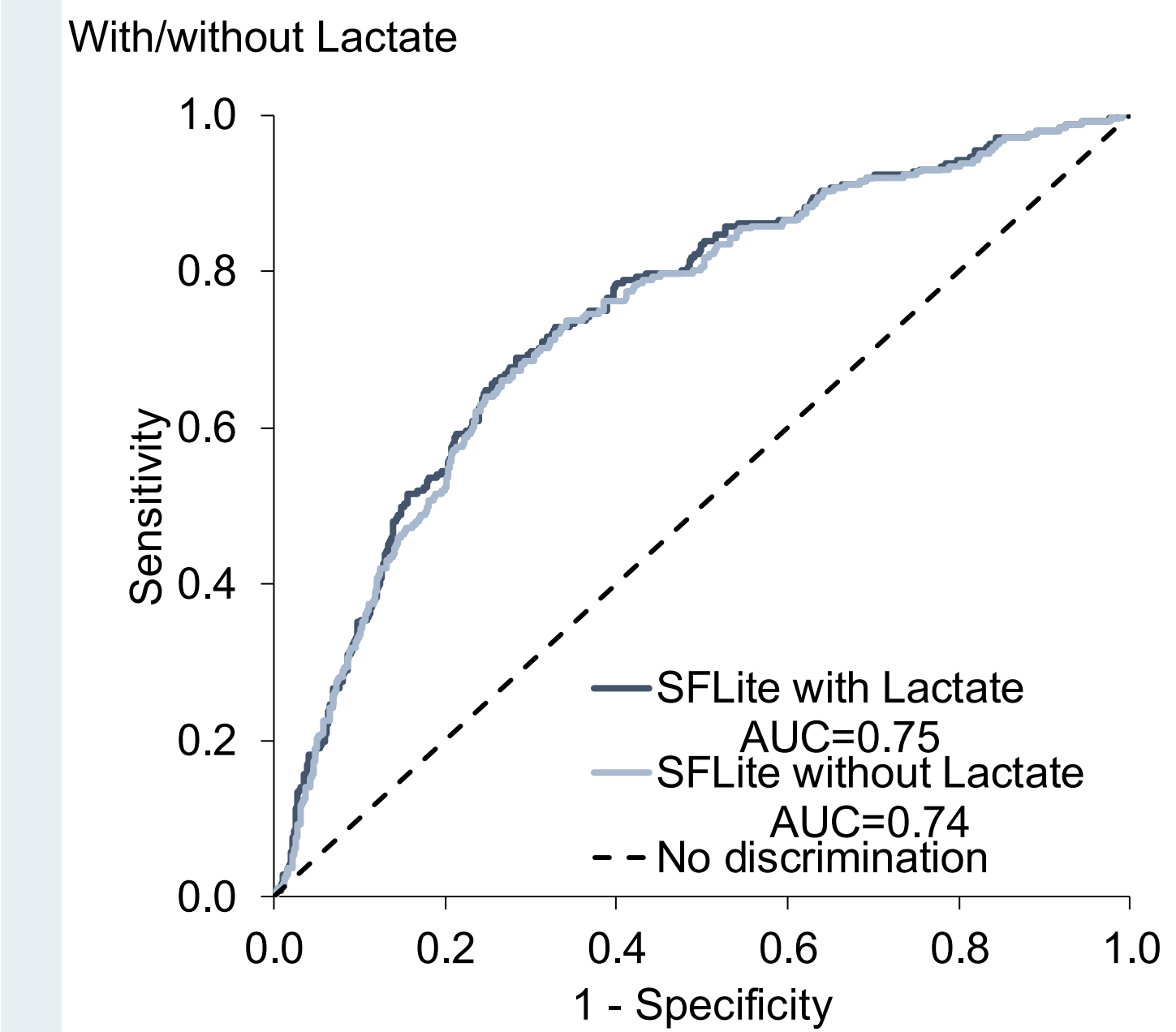
Risk stratum	Risk percentiles	Bacteraemia, n/N (%)	30-day mortality*
Low	0th - 30th	24/320 (7.5%)	12/301 (4.0%)
Medium	31st - 80th	116/533 (21.8%)	59/505 (11.7%)
High	81st - 100th	108/214 (50.5%)	57/205 (27.8%)

*30-day mortality calculated using each patient's first blood culture date

Survival Analysis

The same risk stratification was used for a survival analysis. Kaplan-Meier survival curves were constructed for each stratum as well as overall. There were significant differences between all three strata (p<0.001– log-rank).

ROC Curve: Bacteraemia Prediction
With/without Lactate

SFLite with Lactate AUC=0.75
SFLite without Lactate AUC=0.74
No discrimination

Conclusions

The model provided a valuable prediction of bacteraemia. The ability to make a continuous stratification of patients by risk allows for economic decisions to be made regarding the diagnostic workflow of the patient. This is particularly relevant in laboratories with several alternative technologies, with defined capacities, costs and benefits.

SepsisFinder
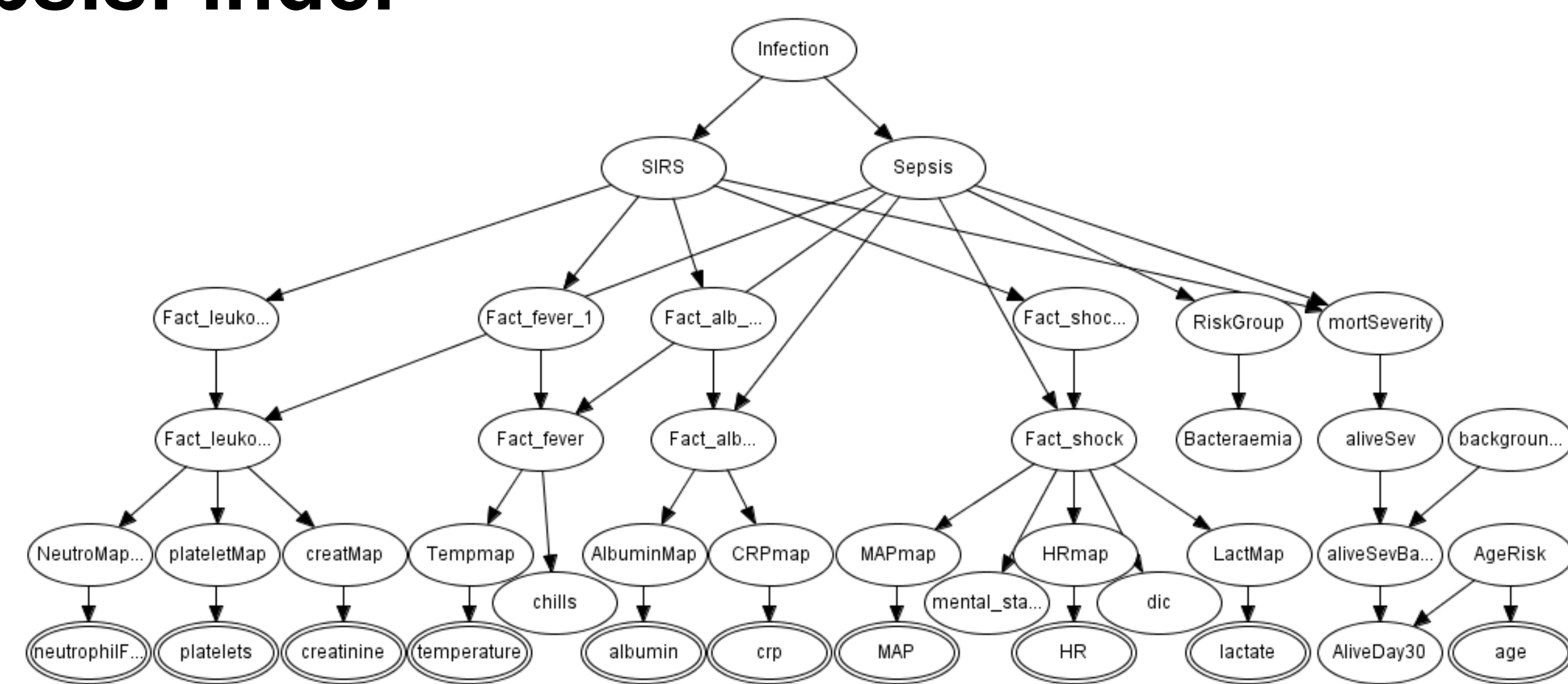
SepsisFinder Lite
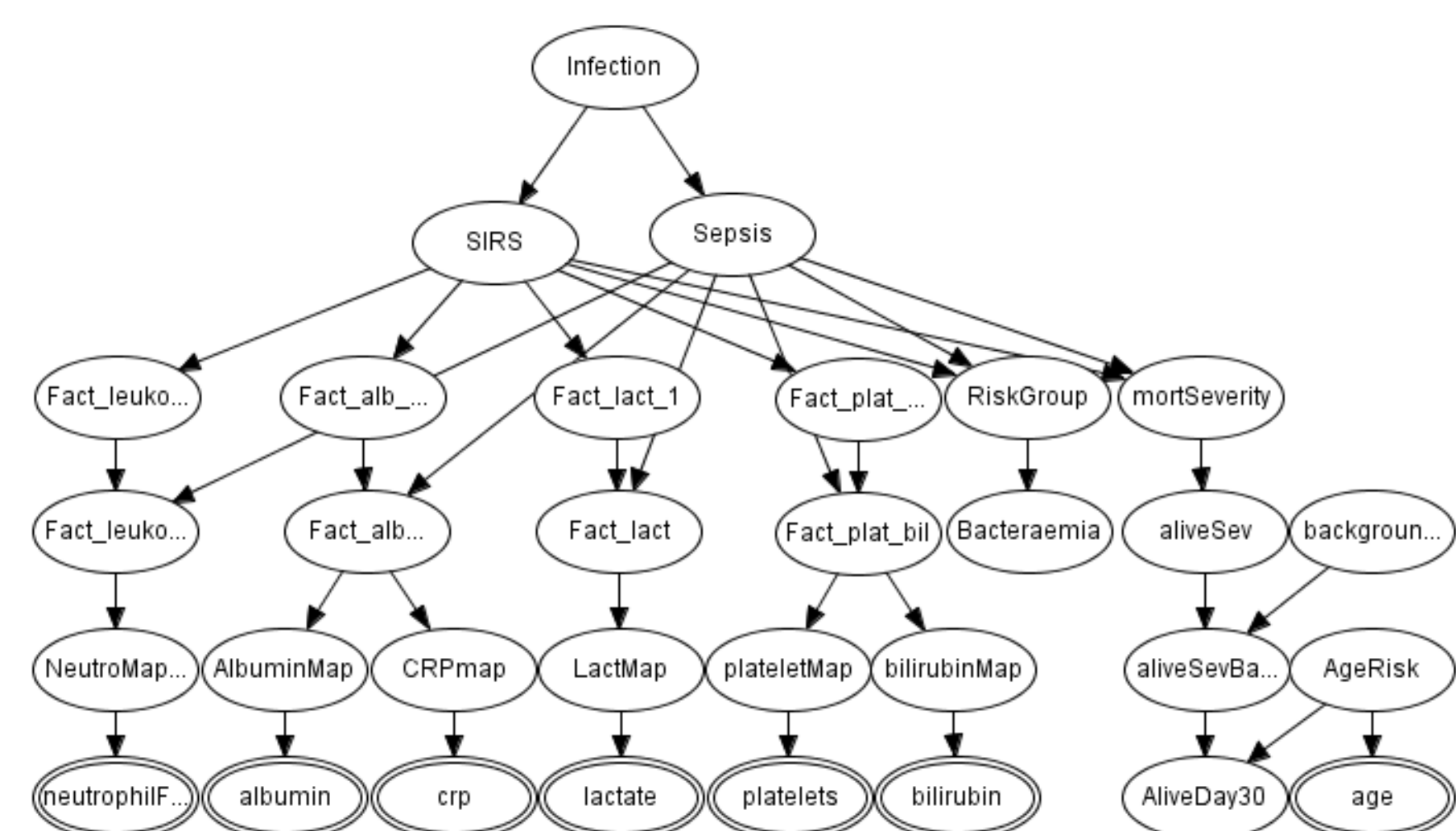
Transition to the laboratory

Many of the usual "infection variables" were not available, so we constructed the SepsisFinder Lite (SF-L) model. SF-L uses only data that is available in the laboratory information system. The model was trained using data from patients in the previous training set. Interestingly, SF-L performed as well as SepsisFinder in terms of area under the ROC curve for bacteraemia (below).

ROC Curve: Bacteraemia Prediction
Training dataset - SepsisFinder, SepsisFinder Lite

SF training data AUC=0.71
SFLite training data AUC=0.72
No discrimination
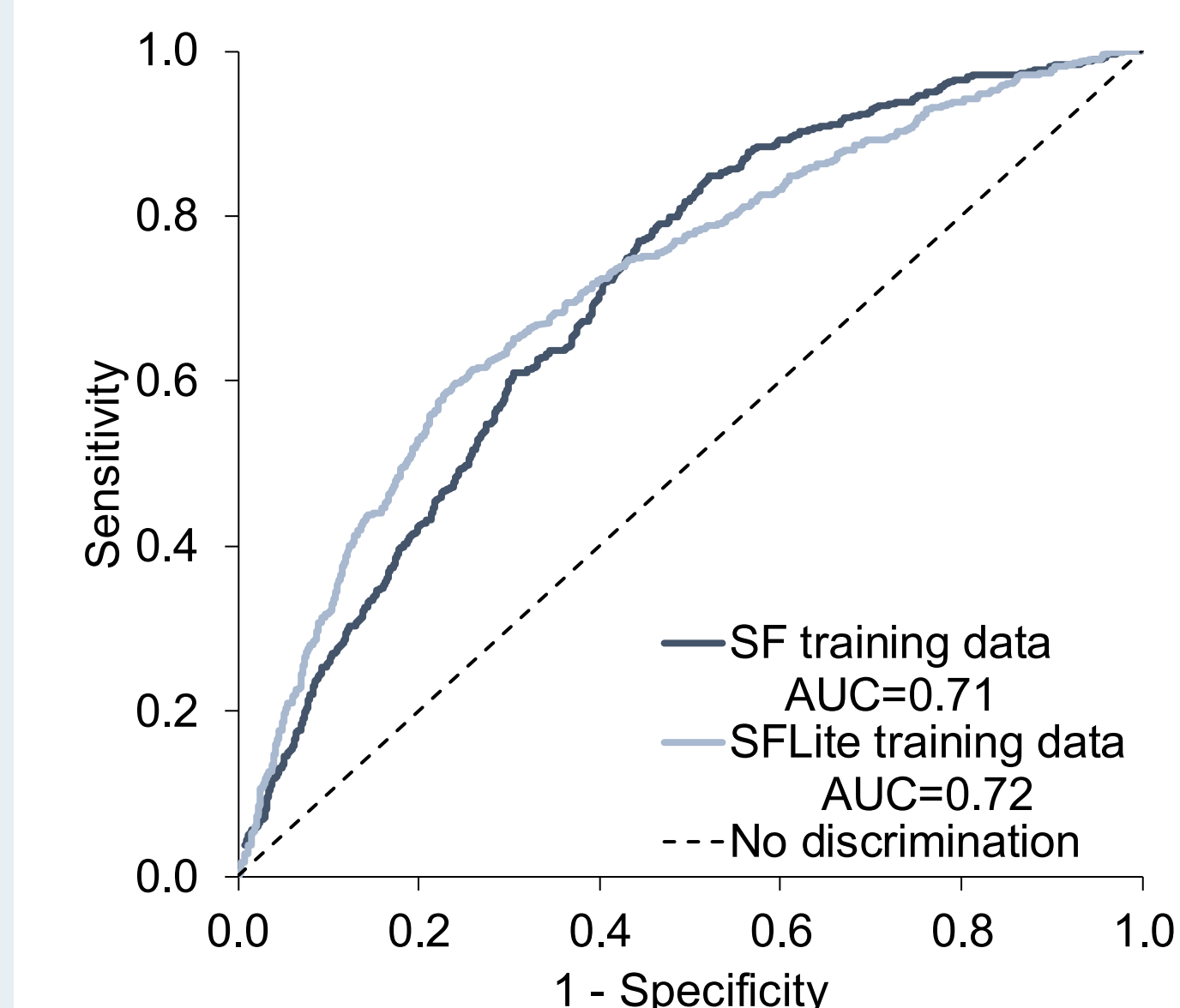
Blood Culture Isolates

	N (%)
BC+	345 (32.3%)
Bacteraemia*	248 (23.2%)
Isolates	434
Significant Isolates*	291
Gram negative	215
E. coli	130
Klebsiella spp.	22
Proteus spp.	19
Pseudomonas spp.	12
Haemophilus spp.	6
Bacteroides spp.	5
Other GN	21
Gram Positive	74
S. aureus	24
Enterococcus spp.	16
S. pneumoniae	15
Other Streptococci	10
Other GP	9
Isolates considered contaminants	143
Bacillus spp. (not *anthracis*)	
Corynebacterium spp.	
Coagulase negative Staphylococci	
Micrococcus spp.	
Proprionbacterium spp.	
Viridans Streptococci	

* Cultures were considered bacteraemic if any significant isolate was found. Significant isolates were bacterial species other than those considered contaminants

Kaplan-Meier Survival Curves

ALL Low Medium High
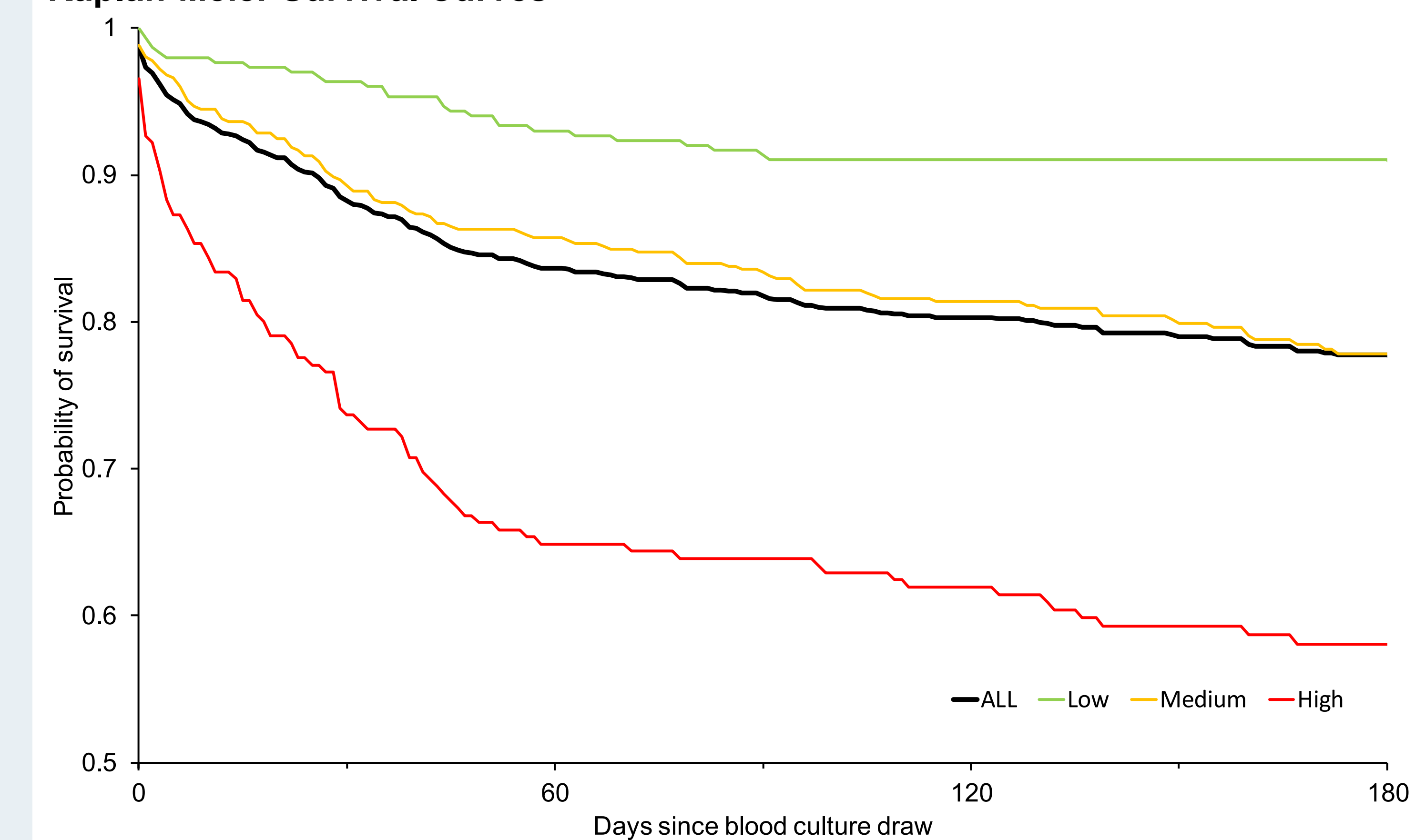
References

[1] Ward, L (2016) Gradation of the severity of Sepsis. PhD thesis. Aalborg Universitetsforlag.

[2] Paul, M et al. Improving empirical antibiotic treatment using TREAT, a computerized decision support system: cluster randomized trial, Journal of Antimicrobial Chemotherapy. 58 (2006) 1238-1245

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