Machine learning can predict neutropenic sepsis in chemotherapy patients

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The Christie NHS Foundation Trust, Manchester

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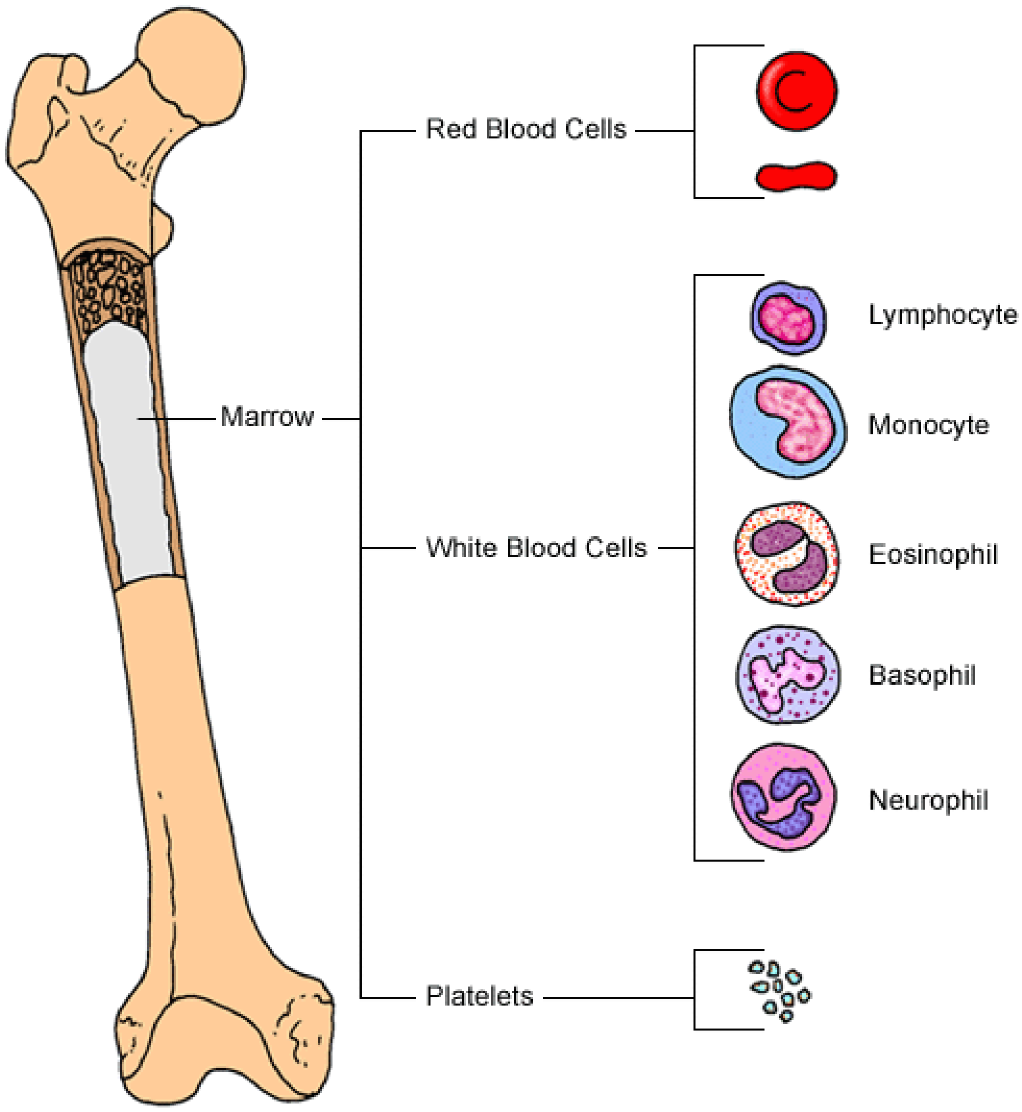
Background | Data | Models | Results

Febrile neutropenia and neutropenic sepsis



Other predictive models

Original Article

Predicting Individual Risk of Neutropenic Complications in Patients Receiving Cancer Chemotherapy

Gary H. Lyman, MD, MPH[1]; Nicole M. Kuderer, MD[1]; Jeffrey Crawford, MD[1]; Debra A. Wolff, MS, PCNP[1]; Eva Culakova, PhD, MS[1]; Marek S. Poniewierski, MD, MS[1]; and David C. Dale, MD[2]

BACKGROUND: A prospective cohort study was undertaken to develop and validate a risk model for neutropenic complications in cancer patients receiving chemotherapy. **METHODS:** The study population consisted of 3760 patients with common solid tumors or malignant lymphoma who were beginning a new chemotherapy regimen at 115 practice sites throughout the United States. A regression model for neutropenic complications was developed and then validated by using a random split-sample selection process. **RESULTS:** No significant differences in the derivation and validation populations were observed. The risk of neutropenic complications was greatest in cycle 1 with no significant difference in predicted risk between the 2 cohorts in univariate analysis. After adjustment for cancer type and age, major independent risk factors in multivariate analysis included: prior chemotherapy, abnormal hepatic and renal function, low white blood count, chemotherapy and planned delivery ≥85%. At a predicted risk cutpoint of 10%, model test performance included: sensitivity 90%, specificity 59%, and predictive value positive and negative of 34% and 96%, respectively. Further analysis confirmed model discrimination for risk of febrile neutropenia over multiple chemotherapy cycles. **CONCLUSIONS:** A risk model for neutropenic complications was developed and validated in a large prospective cohort of patients who were beginning cancer chemotherapy that may guide the effective and cost-effective use of available supportive care. *Cancer* 2011;117:1917–27. © *2010 American Cancer Society.*

KEYWORDS: neutropenia, febrile neutropenia, chemotherapy, risk model.

AUC 80%

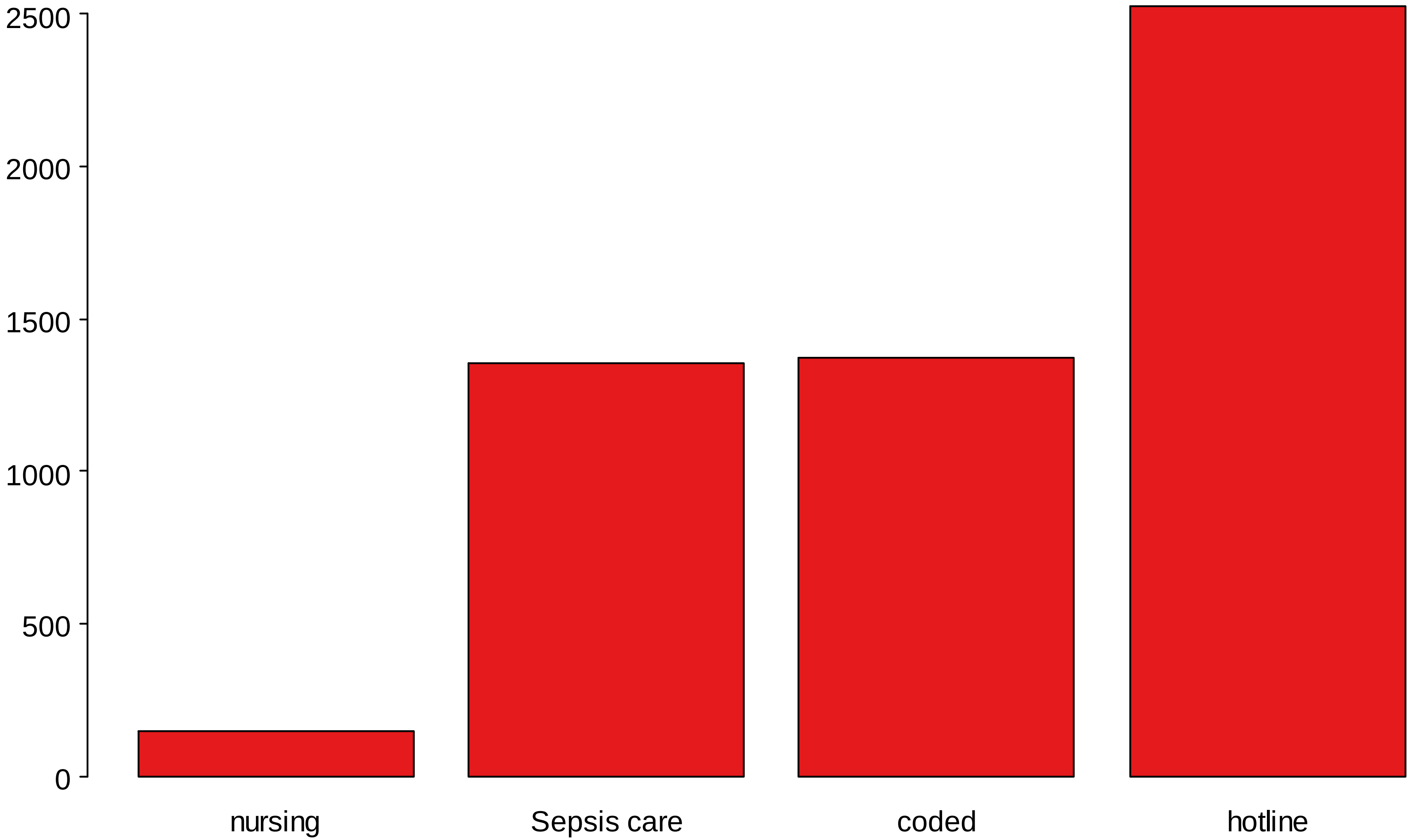
Study Design

Training Set
Dec 2014 – Dec 2015

Validation Set
Jan 2016 – April 2016

Training Set	Validation Set
9,000 patients	4,500 patients
70,000 cycles	15,000 cycles
2,500 events	500 events

Outcome data

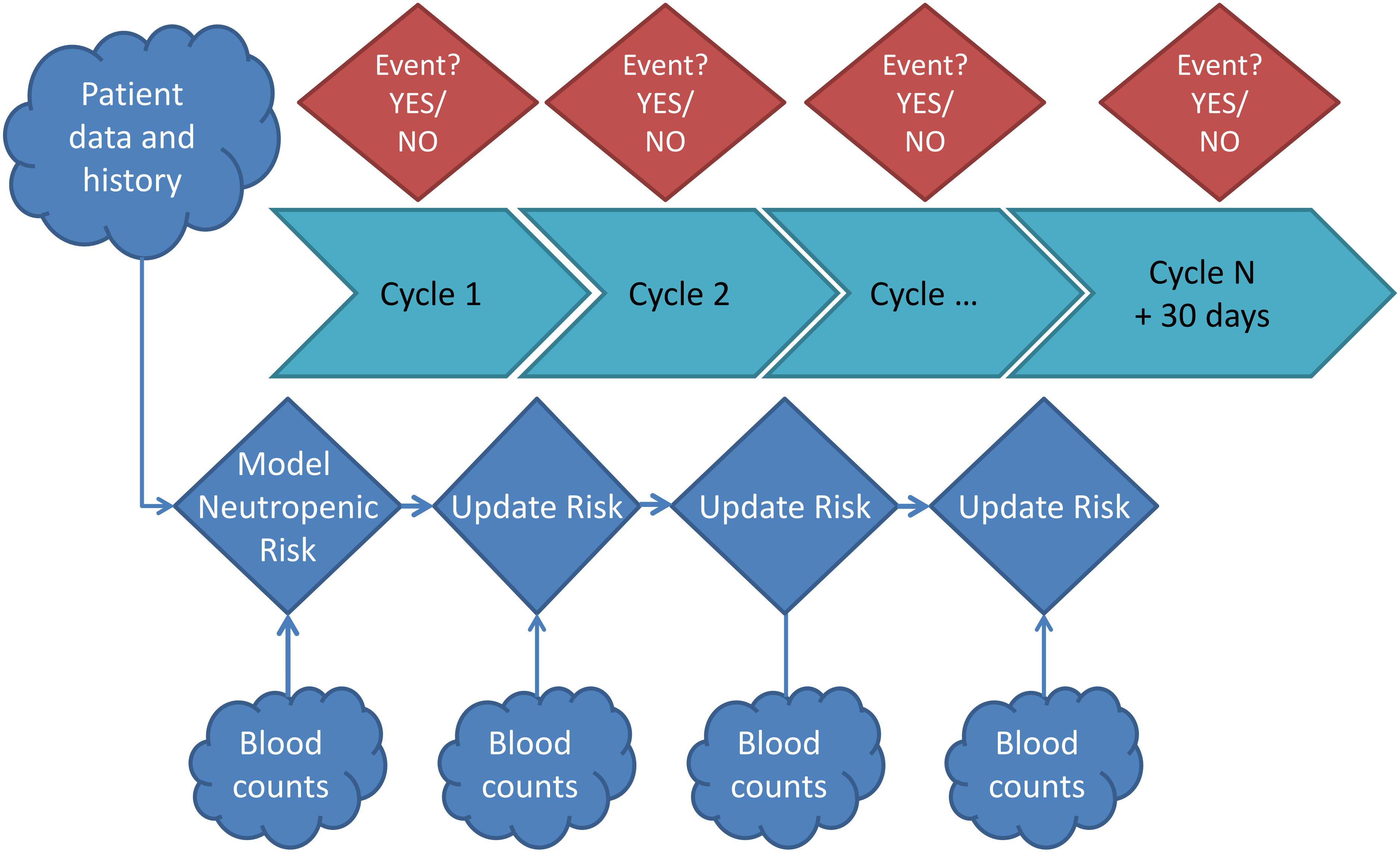


1,000+ binary predictors

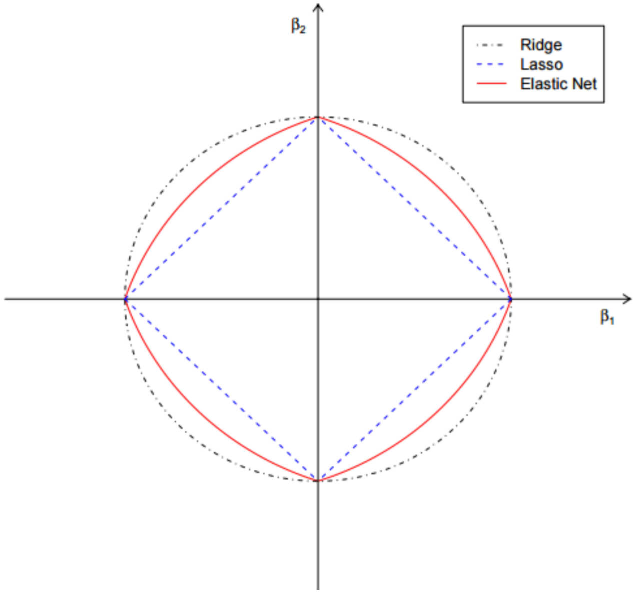
Previous events
Chemo regimen (350)
Primary disease site
Specialty
Consultant
Cycle number
Bloods
Comorbidities (20)
PS
Treatment intent
Concurrent radiotherapy
Stage
Age
Gender
Marital Status
Time since diagnosis
Time of year

Calcium
Albumin
Alkaline phosphatase
Aspartate aminotransferase
Phosphate
Potassium
Creatinine
Sodium
Bilirubin
Protein
Gamma-Glutamyl Transferase
Globulin
Basophils
Eosinophils
Haemoglobin
Hematocrit
Large Unstained Cells
Lymphocytes
Mean Corpuscular Haemoglobin
Monocytes
Neutrophils
Platelet count
Red blood cell distribution width
Red cell count
White cell count

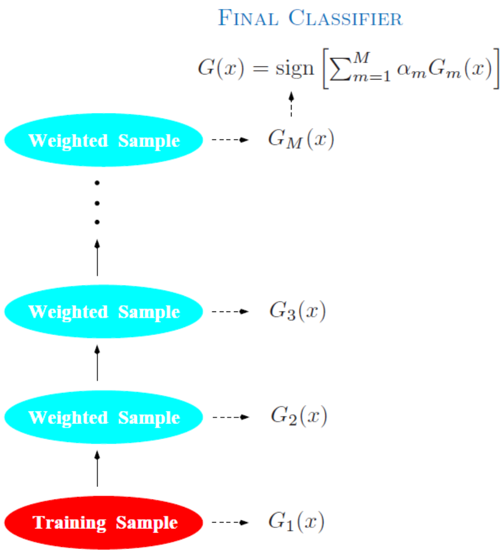
Data Model


Patient data and history
Event? YES/ NO
Event? YES/ NO
Event? YES/ NO
Event? YES/ NO
Cycle 1
Cycle 2
Cycle …
Cycle N + 30 days
Model Neutropenic Risk
Update Risk
Update Risk
Update Risk
Blood counts
Blood counts
Blood counts
Blood counts

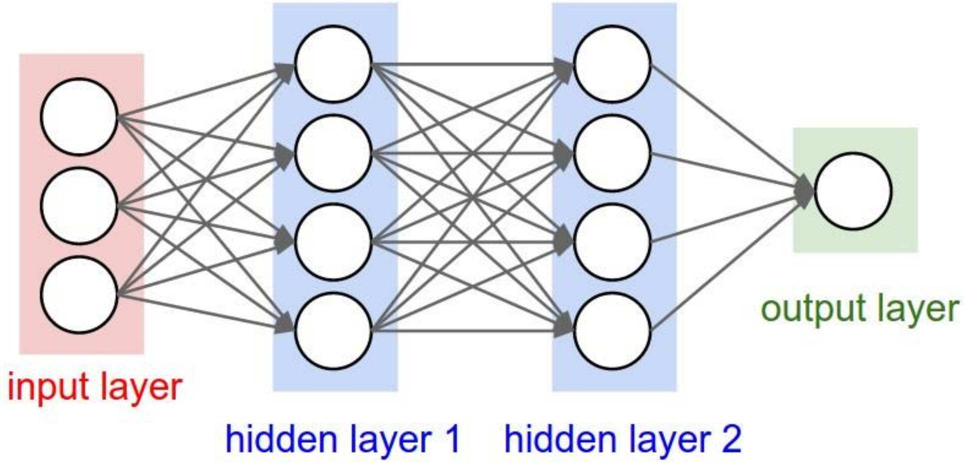
Elastic Net



Gradient Boosting



Deep Neural Networks



Validation

Training Set
Dec 2014 – Dec 2015

Validation Set
Jan 2016 – April 2016

Model	AUC (%)
Deep Learning	80
Elastic Net	82
Gradient Boosting	83
Ensemble	**84**

Validation – three groups

Training Set
Dec 2015 – Dec 2016

Validation Set
Jan 2016 – April 2016

	Neutropenic Event In Cycle			
Risk	True	False	Total	P (event)
Low	77	8,606	8,683	1%
Medium	295	5,901	6,196	5%
High	**129**	**106**	**235**	**55%**
Total	501	14,613	15,114	3%

	Sensitivity	Specificity
High only	26%	99.3%
High & Medium	85%	59%

Predictive application

BENJAMINSON, Arlen

Cycle start date: 2016-02-08

Risk | Risk Factors | Info

Neutropenic Risk: 74 %

30 Day Mortality Risk: 4 %

Show 10 entries

Search:

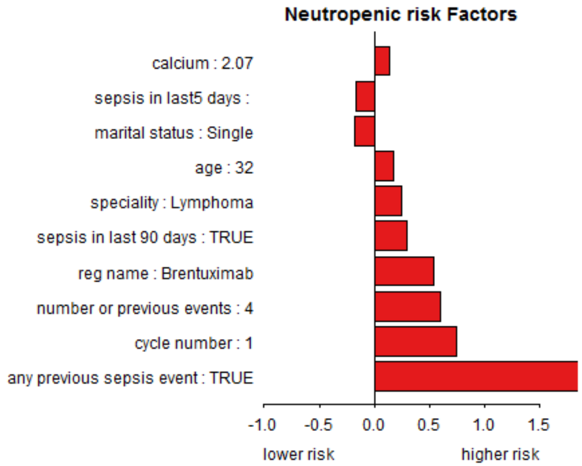
	row	Casenote	First Name	Surname	Consultant	Cycle Start	Regimen	Cycle	Speciality	Neutropenic risk (%)	Days to neutropenic event	30 Day Death Risk (%)	Days to Death	i
83160	201519165	xxxxxx	xxxxxx	xxxxxx	2016-02-08	Brentuximab	1	Lymphoma	74	0	4.5		83160	xx
83537	201600264	xxxxxx	xxxxxx	xxxxxx	2016-03-17	EC	1	Breast	64	1	0.6		83537	xx
20565	201109211	xxxxxx	xxxxxx	xxxxxx	2016-02-29	Trifluridine - Tipiracil	1	GI	63	14	7.5		20565	xx
77272	201513640	xxxxxx	xxxxxx	xxxxxx	2016-01-20	Docetaxel 100mg/m2 (21 day)	1	Breast	61	4	0.38		77272	xx
35917	201400365	xxxxxx	xxxxxx	xxxxxx	2016-02-18	Docetaxel 75mg/m2 (21 day)	1	Prostate	59	7	5.2		35917	xx
83224	201519227	xxxxxx	xxxxxx	xxxxxx	2016-03-18	Docetaxel 100mg/m2 (21 day)	1	Breast	59	4	0.56		83224	xx

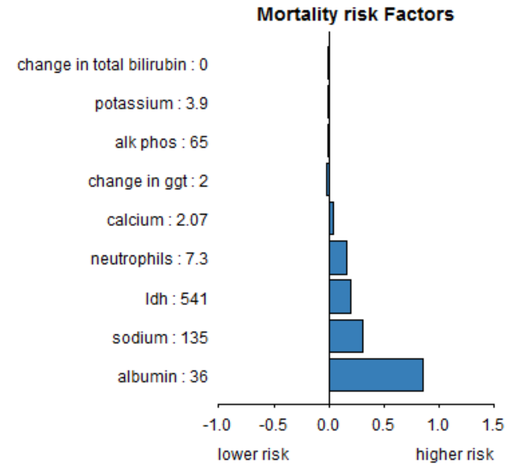
Predictive application

BENJAMINSON, Arlen

Cycle start date: 2016-02-08

Risk | Risk Factors | Info





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77272	201513640	xxxxxx	xxxxxx	xxxxxx	2016-01-20	Docetaxel 100mg/m2 (21 day)	1	Breast	61	4	0.38	77272	xx

Further work

1. Include HES outcome data
2. Plan implementation
3. Pilot feasibility study
4. Trial:
    - Cluster-randomised trial
    - Before-after prospective trial

Conclusions

Machine learning approach was successful

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Improves accuracy of patient risk assessment

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Used routinely collected data

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Focus on improving outcome data

Thank you

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