Development and Validation of a Risk Prediction Model of linezolid-induced thrombocytopenia in Vietnamese patients

Saturday, March 9, 2024

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Checklist

Table 1: TRIPOD-Cluster checklist of items to include when reporting a study developing or validating a multivariable prediction model using clustered data

Section/topic	Item No	Description	Page No
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted	
Abstract	2	Provide a summary of research objectives, setting, participants, data source, sample size, predictors, outcome, statistical analysis, results, and conclusions*	
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the prediction model, including references to existing models, and the advantages of the study design*	
	3b	Specify the objectives, including whether the study describes the development or validation of the model*	
Methods			

Section/topic	Item No	Description	Page No
Participants and data	4a	Describe eligibility criteria for participants and datasets*	
	4b	Describe the origin of the data, and how the data were identified, requested, and collected	
Sample size	5	Explain how the sample size was arrived at*	
Outcomes and predictors	6a	Define the outcome that is predicted by the model, including how and when assessed*	
	6b	Define all predictors used in developing or validating the model, including how and when measured*	
Data preparation	7a	Describe how the data were prepared for analysis, including any cleaning, harmonisation, linkage, and quality checks	
	7b	Describe the method for assessing risk of bias and applicability in the individual clusters (eg, using PROBAST)	
	7c	For validation, identify any differences in definition and measurement from the development data (eg, setting, eligibility criteria, outcome, predictors)*	
	7d	Describe how missing data were handled*	
Data analysis	8a	Describe how predictors were handled in the analyses	
	8b	Specify the type of model, all model building procedures (eg, any predictor selection and penalisation), and method for validation*	
	8c	Describe how any heterogeneity across clusters (eg, studies or settings) in model parameter values was handled	
	8d	For validation, describe how the predictions were calculated	
	8e	Specify all measures used to assess model performance (eg, calibration, discrimination, and decision curve analysis) and, if relevant, to compare multiple models	
	8f	Describe how any heterogeneity across clusters (eg, studies or settings) in model performance was handled and quantified	
	8g	Describe any model updating (eg, recalibration) arising from the validation, either overall or for particular populations or settings*	
Sensitivity analysis	9	Describe any planned subgroup or sensitivity analysis—eg, assessing performance according to sources of bias, participant characteristics, setting	
Results			

Section/topic	Item No	Description	Page No
Participants and datasets	10a	Describe the number of clusters and participants from data identified through to data analysed; a flowchart might be helpful*	
	10b	Report the characteristics overall and where applicable for each data source or setting, including the key dates, predictors, treatments received, sample size, number of outcome events, follow-up time, and amount of missing data*	
	10c	For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors, and outcome)	
Risk of bias	11	Report the results of the risk-of-bias assessment in the individual clusters	
Model development and specification	12a	Report the results of any assessments of heterogeneity across clusters that led to subsequent actions during the model's development (eg, inclusion or exclusion of particular predictors or clusters)	
	12b	Present the final prediction model (ie, all regression coefficients, and model intercept or baseline estimate of the outcome at a given time point) and explain how to use it for predictions in new individuals*	
Model performance	13a	Report performance measures (with uncertainty intervals) for the prediction model, overall and for each cluster	
	13b	Report results of any heterogeneity across clusters in model performance	
Model updating	14	Report the results from any model updating (including the updated model equation and subsequent performance), overall and for each cluster*	
Sensitivity analysis	15	Report results from any subgroup or sensitivity analysis	
Discussion			
Interpretation	16a	Give an overall interpretation of the main results, including heterogeneity across clusters in model performance, in the context of the objectives and previous studies*	
	16b	For validation, discuss the results with reference to the model performance in the development data, and in any previous validations	
	16c	Discuss the strengths of the study and any limitations (eg, missing or incomplete data, non-representativeness, data harmonisation problems)	

Section/topic	Item No	Description	Page No
Implications	17	Discuss the potential use of the model and implications for future research, with specific view to generalisability and applicability of the model across different settings or (sub)populations	
Other information			
Supplementary information	18	Provide information about the availability of supplementary resources (eg, study protocol, analysis code, datasets)*	
Funding	19	Give the source of funding and the role of the funders for the present study	

Introduction

Background and objectives

Methods

Participants and data

Sample size

Outcomes and predictors

Data preparation

Data analysis

Sensitivity analysis

Results

Participants and datasets

Risk of bias

Model development and specification

Model performance

Model updating

Sensitivity analysis

Discussion

Interpretation

Implications

Other information

Supplementary information

Funding

Objectives

1. Investigating risk factors of linezolid-induced thrombocytopenia (LI-TP)

2. Developing and validating a logistics regression model to predict LI-TP in Vietnamese patients

Data cleaning

Source: Article Notebook

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Source: Article Notebook

Descriptive statistics

Source: Article Notebook

Characteristic	**Overall**, N = 817	**FALSE**, N = 553	**TRUE**, N = 264	**OR**	**95% CI**	**p-value**
patient__age	62 (50 - 73)	61 (47 - 72)	64 (54 - 74)	1.02	1.01, 1.03	**<0.001**
patient__sex	307 (38%)	207 (37%)	100 (38%)	1.02	0.75, 1.38	>0.9
LZD__dose__per__weight	21.8 (20.0 - 24.0)	21.8 (20.0 - 24.0)	21.8 (19.4 - 24.6)	0.99	0.96, 1.03	0.8

Characteristic	**Overall**, N = 817	**FALSE**, N = 553	**TRUE**, N = 264	**OR**	**95% CI**	**p-value**
baseline_CLCR	48 (21 - 83)	55 (26 - 88)	32 (15 - 64)	0.99	0.99, 0.99	**<0.001**
dept_ER	140 (17%)	95 (17%)	45 (17%)	0.99	0.67, 1.45	>0.9
dept_ICU	391 (48%)	241 (44%)	150 (57%)	1.70	1.27, 2.29	**<0.001**
baseline_HGB	102 (89 - 120)	105 (91 - 121)	98 (85 - 117)	0.99	0.98, 0.99	**<0.001**
baseline_WBC	12 (8 - 17)	12 (8 - 17)	12 (8 - 18)	1.01	0.99, 1.03	0.4
baseline_PLT	206 (142 - 288)	234 (167 - 309)	154 (103 - 211)	0.99	0.99, 0.99	**<0.001**
LZD_duration	9.0 (6.0 - 14.0)	9.0 (6.0 - 13.0)	10.0 (6.0 - 14.0)	1.03	1.01, 1.06	**0.018**
invasive_ETI	387 (47%)	231 (42%)	156 (59%)	2.01	1.50, 2.72	**<0.001**
invasive_CVC	424 (52%)	247 (45%)	177 (67%)	2.52	1.86, 3.43	**<0.001**
invasive_IHD	111 (14%)	64 (12%)	47 (18%)	1.65	1.10, 2.49	**0.016**
invasive_CRRT	148 (18%)	65 (12%)	83 (31%)	3.44	2.39, 4.98	**<0.001**
comorb_HTN	333 (41%)	218 (39%)	115 (44%)	1.19	0.88, 1.60	0.3
comorb_DM	222 (27%)	150 (27%)	72 (27%)	1.01	0.72, 1.40	>0.9
comorb_HF	226 (28%)	132 (24%)	94 (36%)	1.76	1.28, 2.42	**<0.001**
comorb_angina	32 (3.9%)	19 (3.4%)	13 (4.9%)	1.46	0.69, 2.97	0.3
comorb_cirr	48 (5.9%)	20 (3.6%)	28 (11%)	3.16	1.75, 5.80	**<0.001**
comorb_COPD	39 (4.8%)	25 (4.5%)	14 (5.3%)	1.18	0.59, 2.28	0.6
comorb_CVA	93 (11%)	64 (12%)	29 (11%)	0.94	0.58, 1.49	0.8
comorb_MI	20 (2.4%)	15 (2.7%)	5 (1.9%)	0.69	0.22, 1.81	0.5
comorb_K	67 (8.2%)	44 (8.0%)	23 (8.7%)	1.10	0.64, 1.85	0.7

Characteristic	Overall, N = 817	FALSE, N = 553	TRUE, N = 264	OR	95% CI	p-value
comorb_hematological	46 (5.6%)	27 (4.9%)	19 (7.2%)	1.51	0.81, 2.75	0.2
comorb_hema	61 (7.5%)	37 (6.7%)	24 (9.1%)	1.39	0.81, 2.37	0.2
infect_sepsis	134 (16%)	66 (12%)	68 (26%)	2.56	1.76, 3.74	**<0.001**
infect_CAP	118 (14%)	70 (13%)	48 (18%)	1.53	1.02, 2.28	**0.037**
infect_HAP	375 (46%)	255 (46%)	120 (45%)	0.97	0.73, 1.31	0.9
infect_SSTI	133 (16%)	100 (18%)	33 (13%)	0.65	0.42, 0.98	**0.044**
infect_CNS	68 (8.3%)	46 (8.3%)	22 (8.3%)	1.00	0.58, 1.68	>0.9
infect_IAI	50 (6.1%)	34 (6.1%)	16 (6.1%)	0.98	0.52, 1.79	>0.9
infect_UTI	53 (6.5%)	37 (6.7%)	16 (6.1%)	0.90	0.48, 1.62	0.7
infect_BJI	11 (1.3%)	10 (1.8%)	1 (0.4%)	0.21	0.01, 1.09	0.13
infect_septicemia	237 (29%)	148 (27%)	89 (34%)	1.39	1.01, 1.91	**0.041**
comed_aspirin	47 (5.8%)	30 (5.4%)	17 (6.4%)	1.20	0.64, 2.19	0.6
comed_diclofenac	27 (3.3%)	20 (3.6%)	7 (2.7%)	0.73	0.28, 1.66	0.5
comed_ibuprofen	26 (3.2%)	15 (2.7%)	11 (4.2%)	1.56	0.69, 3.42	0.3
comed_paracetamol	355 (43%)	244 (44%)	111 (42%)	0.92	0.68, 1.23	0.6
comed_penicillin	123 (15%)	78 (14%)	45 (17%)	1.25	0.83, 1.86	0.3
comed_cepha	207 (25%)	149 (27%)	58 (22%)	0.76	0.54, 1.08	0.13
comed_carbapenem	584 (71%)	382 (69%)	202 (77%)	1.46	1.05, 2.05	**0.028**
comed_cotrimoxazol	65 (8.0%)	37 (6.7%)	28 (11%)	1.65	0.98, 2.76	0.055
comed_vancomycin	68 (8.3%)	42 (7.6%)	26 (9.8%)	1.33	0.79, 2.21	0.3

Characteristic	Overall, N = 817	FALSE, N = 553	TRUE, N = 264	OR	95% CI	p-value
comed_levofloxacin	250 (31%)	161 (29%)	89 (34%)	1.24	0.90, 1.69	0.2
comed_teicoplanin	37 (4.5%)	23 (4.2%)	14 (5.3%)	1.29	0.64, 2.52	0.5
comed_ethambutol	8 (1.0%)	5 (0.9%)	3 (1.1%)	1.26	0.26, 5.17	0.8
comed_pyrazinamid	12 (1.5%)	6 (1.1%)	6 (2.3%)	2.12	0.66, 6.84	0.2
comed_rifampin	17 (2.1%)	10 (1.8%)	7 (2.7%)	1.48	0.53, 3.89	0.4
comed_heparin	207 (25%)	108 (20%)	99 (38%)	2.47	1.78, 3.43	**<0.001**
comed_clopidogrel	40 (4.9%)	30 (5.4%)	10 (3.8%)	0.69	0.31, 1.38	0.3
comed_enoxaparin	350 (43%)	233 (42%)	117 (44%)	1.09	0.81, 1.47	0.6
comed_dexamethason	105 (13%)	71 (13%)	34 (13%)	1.00	0.64, 1.54	>0.9
comed_amiodaron	36 (4.4%)	17 (3.1%)	19 (7.2%)	2.45	1.25, 4.83	**0.009**
comed_furosemid	436 (53%)	260 (47%)	176 (67%)	2.25	1.66, 3.07	**<0.001**
comed_haloperidol	52 (6.4%)	35 (6.3%)	17 (6.4%)	1.02	0.55, 1.83	>0.9
comed_valproic	32 (3.9%)	23 (4.2%)	9 (3.4%)	0.81	0.35, 1.73	0.6
comed_aceclofenac	0 (0%)	0 (0%)	0 (0%)			
comed_naproxen	0 (0%)	0 (0%)	0 (0%)			
comed_daptomycin	1 (0.1%)	0 (0%)	1 (0.4%)			
comed_cetirizin	6 (0.7%)	5 (0.9%)	1 (0.4%)			
comed_simvas	0 (0%)	0 (0%)	0 (0%)			
comed_bisoprolol	6 (0.7%)	4 (0.7%)	2 (0.8%)			
comed_diltiazem	0 (0%)	0 (0%)	0 (0%)			
comed_eptifibatid	0 (0%)	0 (0%)	0 (0%)			
comed_quinidin	0 (0%)	0 (0%)	0 (0%)			
comed_carbamazepin	8 (1.0%)	8 (1.4%)	0 (0%)			
comed_phenytoin	0 (0%)	0 (0%)	0 (0%)			
comed_mirtazapin	0 (0%)	0 (0%)	0 (0%)			
comed_quetiapin	4 (0.5%)	4 (0.7%)	0 (0%)			
comed_ondansetron	6 (0.7%)	4 (0.7%)	2 (0.8%)			

Characteristic	Overall, N = 817	FALSE, N = 553	TRUE, N = 264	OR	95% CI	p-value
comed_palonosetron	0 (0%)	0 (0%)	0 (0%)			
comed_oseltamivir	3 (0.4%)	1 (0.2%)	2 (0.8%)			
comed_quinin	0 (0%)	0 (0%)	0 (0%)			
comed_pembrolizumab	0 (0%)	0 (0%)	0 (0%)			
comed_trastuzumab	0 (0%)	0 (0%)	0 (0%)			
comed_atezolizumab	0 (0%)	0 (0%)	0 (0%)			
comed_durvalumab	0 (0%)	0 (0%)	0 (0%)			
comed_IVIG	0 (0%)	0 (0%)	0 (0%)			
comed_tacrolimus	1 (0.1%)	0 (0%)	1 (0.4%)			
comed_fluorouracil	0 (0%)	0 (0%)	0 (0%)			
comed_irinotecan	0 (0%)	0 (0%)	0 (0%)			
comed_leucovorin	0 (0%)	0 (0%)	0 (0%)			
comed_oxaliplatin	0 (0%)	0 (0%)	0 (0%)			

Source: Article Notebook

Source: Article Notebook

Characteristic	Overall, N = 817	BM1, N = 125	BM2, N = 77	ND1, N = 180	ND2, N = 116	TN1, N = 100	TN2, N = 219	p-value
patient_age	62 (50 - 73)	58 (43 - 69)	60 (45 - 72)	60 (45 - 68)	59 (46 - 68)	69 (60 - 78)	66 (58 - 78)	**<0.001**
patient_sex	307 (38%)	54 (43%)	27 (35%)	74 (41%)	28 (24%)	48 (48%)	76 (35%)	**0.004**
LZD_dose_per_weight	21.8 (20.0 - 24.0)	22.6 (20.0 - 25.5)	21.4 (19.0 - 24.0)	21.4 (19.4 - 24.0)	21.8 (20.0 - 24.0)	24.0 (20.0 - 24.6)	21.8 (19.7 - 24.0)	**0.027**
baseline_CLCR	46 (21 - 83)	50 (24 - 80)	40 (17 - 86)	70 (41 - 104)	60 (27 - 95)	29 (14 - 54)	35 (17 - 67)	**<0.001**
dept_ER	140 (17%)	7 (5.6%)	9 (12%)	67 (37%)	15 (13%)	16 (16%)	26 (12%)	**<0.001**
dept_ICU	391 (48%)	10 (8.0%)	23 (30%)	74 (41%)	42 (36%)	77 (77%)	165 (75%)	**<0.001**
baseline_HGB	109 (89 - 120)	105 (91 - 124)	99 (83 - 118)	105 (89 - 122)	100 (88 - 118)	99 (89 - 116)	104 (91 - 120)	0.2
baseline_WBC	12 (8 - 17)	11 (7 - 16)	11 (7 - 17)	12 (8 - 18)	11 (7 - 15)	12 (8 - 18)	13 (9 - 18)	**0.024**

Characteristic	Overall, N = 817	BM1, N = 125	BM2, N = 77	ND1, N = 180	ND2, N = 116	TN1, N = 100	TN2, N = 219	p-value
baseline_PLT	206 (142 - 288)	195 (139 - 247)	234 (160 - 318)	207 (129 - 292)	225 (127 - 310)	172 (122 - 245)	225 (161 - 299)	**<0.001**
LZD_duration	8.0 (6.0 - 14.0)	8.0 (6.0 - 13.0)	10.0 (6.0 - 14.0)	10.0 (6.0 - 14.0)	9.0 (6.0 - 12.0)	11.0 (6.0 - 15.0)	9.0 (6.0 - 12.0)	0.3
invasive_ETI	387 (47%)	63 (50%)	30 (39%)	112 (62%)	49 (42%)	48 (48%)	85 (39%)	**<0.001**
invasive_CVC	424 (52%)	75 (60%)	30 (39%)	100 (56%)	48 (41%)	50 (50%)	121 (55%)	**0.008**
invasive_IHD	111 (14%)	17 (14%)	16 (21%)	9 (5.0%)	0 (0%)	27 (27%)	42 (19%)	**<0.001**
invasive_CRRT	148 (18%)	17 (14%)	9 (12%)	53 (29%)	5 (4.3%)	20 (20%)	44 (20%)	**<0.001**
comorb_HTN	333 (41%)	42 (34%)	31 (40%)	49 (27%)	28 (24%)	59 (59%)	124 (57%)	**<0.001**
comorb_DM	222 (27%)	28 (22%)	24 (31%)	28 (16%)	27 (23%)	31 (31%)	84 (38%)	**<0.001**
comorb_HF	226 (28%)	55 (44%)	11 (14%)	15 (8.3%)	7 (6.0%)	70 (70%)	68 (31%)	**<0.001**
comorb_angina	32 (3.9%)	0 (0%)	0 (0%)	1 (0.6%)	0 (0%)	13 (13%)	18 (8.2%)	**<0.001**
comorb_cirr	48 (5.9%)	6 (4.8%)	1 (1.3%)	10 (5.6%)	5 (4.3%)	12 (12%)	14 (6.4%)	0.080
comorb_COPD	39 (4.8%)	3 (2.4%)	0 (0%)	2 (1.1%)	2 (1.7%)	9 (9.0%)	23 (11%)	**<0.001**
comorb_CVA	93 (11%)	19 (15%)	11 (14%)	6 (3.3%)	4 (3.4%)	16 (16%)	37 (17%)	**<0.001**
comorb_MI	20 (2.4%)	10 (8.0%)	3 (3.9%)	2 (1.1%)	0 (0%)	1 (1.0%)	4 (1.8%)	**0.002**
comorb_K	67 (8.2%)	5 (4.0%)	5 (6.5%)	8 (4.4%)	6 (5.2%)	11 (11%)	32 (15%)	**<0.001**
comorb_hematological	46 (5.6%)	9 (7.2%)	12 (16%)	10 (5.6%)	5 (4.3%)	8 (8.0%)	2 (0.9%)	**<0.001**
comorb_hema	61 (7.5%)	13 (10%)	17 (22%)	14 (7.8%)	2 (1.7%)	13 (13%)	2 (0.9%)	**<0.001**
infect_sepsis	134 (16%)	10 (8.0%)	14 (18%)	16 (8.9%)	15 (13%)	44 (44%)	35 (16%)	**<0.001**

Characteristic	Overall, N = 817	BM1, N = 125	BM2, N = 77	ND1, N = 180	ND2, N = 116	TN1, N = 100	TN2, N = 219	p-value
infect_CAP	118 (14%)	7 (5.6%)	6 (7.8%)	11 (6.1%)	1 (0.9%)	26 (26%)	67 (31%)	**<0.001**
infect_HAP	375 (46%)	38 (30%)	33 (43%)	93 (52%)	59 (51%)	52 (52%)	100 (46%)	**0.004**
infect_SSTI	133 (16%)	33 (26%)	34 (44%)	1 (0.6%)	4 (3.4%)	23 (23%)	38 (17%)	**<0.001**
infect_CNS	68 (8.3%)	0 (0%)	5 (6.5%)	24 (13%)	20 (17%)	4 (4.0%)	15 (6.8%)	**<0.001**
infect_IAI	50 (6.1%)	8 (6.4%)	8 (10%)	1 (0.6%)	2 (1.7%)	12 (12%)	19 (8.7%)	**<0.001**
infect_UTI	53 (6.5%)	6 (4.8%)	8 (10%)	10 (5.6%)	5 (4.3%)	4 (4.0%)	20 (9.1%)	0.3
infect_BJI	11 (1.3%)	3 (2.4%)	0 (0%)	0 (0%)	2 (1.7%)	1 (1.0%)	5 (2.3%)	0.2
infect_septicemia	237 (29%)	35 (28%)	24 (31%)	57 (32%)	60 (52%)	7 (7.0%)	54 (25%)	**<0.001**
comed_aspirin	47 (5.8%)	8 (6.4%)	9 (12%)	3 (1.7%)	0 (0%)	5 (5.0%)	22 (10%)	**<0.001**
comed_diclofenac	27 (3.3%)	24 (19%)	0 (0%)	0 (0%)	1 (0.9%)	0 (0%)	2 (0.9%)	**<0.001**
comed_ibuprofen	26 (3.2%)	0 (0%)	0 (0%)	0 (0%)	2 (1.7%)	0 (0%)	24 (11%)	**<0.001**
comed_paracetamol	355 (43%)	66 (53%)	0 (0%)	90 (50%)	69 (59%)	47 (47%)	83 (38%)	**<0.001**
comed_penicillin	123 (15%)	0 (0%)	5 (6.5%)	34 (19%)	19 (16%)	17 (17%)	48 (22%)	**<0.001**
comed_cepha	207 (25%)	12 (9.6%)	10 (13%)	35 (19%)	33 (28%)	11 (11%)	106 (48%)	**<0.001**
comed_carbapenem	584 (71%)	52 (42%)	46 (60%)	154 (86%)	78 (67%)	80 (80%)	174 (79%)	**<0.001**
comed_cotrimoxazol	65 (8.0%)	0 (0%)	5 (6.5%)	18 (10%)	14 (12%)	9 (9.0%)	19 (8.7%)	**0.010**
comed_vancomycin	68 (8.3%)	8 (6.4%)	3 (3.9%)	11 (6.1%)	22 (19%)	3 (3.0%)	21 (9.6%)	**<0.001**
comed_levofloxacin	259 (31%)	27 (22%)	6 (7.8%)	24 (13%)	20 (17%)	34 (34%)	139 (63%)	**<0.001**
comed_teicoplanin	37 (4.5%)	0 (0%)	0 (0%)	7 (3.9%)	2 (1.7%)	0 (0%)	28 (13%)	**<0.001**

Characteristic	Overall, N = 817	BM1, N = 125	BM2, N = 77	ND1, N = 180	ND2, N = 116	TN1, N = 100	TN2, N = 219	p-value
comed_ethambutol	8 (1.0%)	0 (0%)	0 (0%)	2 (1.1%)	6 (5.2%)	0 (0%)	0 (0%)	**<0.001**
comed_pyrazinamid	12 (1.5%)	0 (0%)	0 (0%)	5 (2.8%)	7 (6.0%)	0 (0%)	0 (0%)	**<0.001**
comed_rifampin	17 (2.1%)	0 (0%)	0 (0%)	7 (3.9%)	9 (7.8%)	1 (1.0%)	0 (0%)	**<0.001**
comed_heparin	207 (25%)	12 (9.6%)	2 (2.6%)	74 (41%)	24 (21%)	33 (33%)	62 (28%)	**<0.001**
comed_clopidogrel	40 (4.9%)	7 (5.6%)	4 (5.2%)	1 (0.6%)	0 (0%)	8 (8.0%)	20 (9.1%)	**<0.001**
comed_enoxaparin	350 (43%)	33 (26%)	13 (17%)	117 (65%)	44 (38%)	40 (40%)	103 (47%)	**<0.001**
comed_dexamethason	105 (13%)	0 (0%)	0 (0%)	74 (41%)	20 (17%)	2 (2.0%)	9 (4.1%)	**<0.001**
comed_amiodaron	36 (4.4%)	8 (6.4%)	0 (0%)	14 (7.8%)	5 (4.3%)	4 (4.0%)	5 (2.3%)	**0.026**
comed_furosemid	436 (53%)	72 (58%)	15 (19%)	81 (45%)	49 (42%)	71 (71%)	148 (68%)	**<0.001**
comed_haloperidol	52 (6.4%)	3 (2.4%)	4 (5.2%)	20 (11%)	4 (3.4%)	5 (5.0%)	16 (7.3%)	**0.034**
comed_valproat	32 (3.9%)	0 (0%)	1 (1.3%)	10 (5.6%)	5 (4.3%)	3 (3.0%)	13 (5.9%)	**0.024**
comed_aceclofenac	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_naproxen	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_daptomycin	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	1 (0.9%)	0 (0%)	0 (0%)	0.4
comed_cetirizin	6 (0.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	6 (2.7%)	**0.016**
comed_simvas	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_bisoprolol	6 (0.7%)	4 (3.2%)	0 (0%)	1 (0.6%)	1 (0.9%)	0 (0%)	0 (0%)	**0.031**
comed_diltiazem	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_eptifibatid	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_quinidin	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_carbamazepin	8 (1.0%)	0 (0%)	0 (0%)	7 (3.9%)	0 (0%)	0 (0%)	1 (0.5%)	**0.005**
comed_phenytoin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_mirtazapin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

Characteristic	Overall, N = 817	BM1, N = 125	BM2, N = 77	ND1, N = 180	ND2, N = 116	TN1, N = 100	TN2, N = 219	p-value
comed_quetiapin	4 (0.5%)	1 (0.8%)	1 (1.3%)	0 (0%)	0 (0%)	0 (0%)	2 (0.9%)	0.5
comed_ondansetron	6 (0.7%)	2 (1.6%)	1 (1.3%)	0 (0%)	3 (2.6%)	0 (0%)	0 (0%)	**0.020**
comed_palonosetron	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_oseltamivir	3 (0.4%)	1 (0.8%)	1 (1.3%)	1 (0.6%)	0 (0%)	0 (0%)	0 (0%)	0.4
comed_quinin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_pembrolizumab	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_trastuzumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_atezolizumab	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_durvalumab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_IVIG	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_tacrolimus	1 (0.1%)	1 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.5
comed_fluorouracil	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_irinotecan	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_leucovorin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_oxaliplatin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
flag_ADR_TRID	264 (32%)	34 (27%)	22 (29%)	59 (33%)	35 (30%)	38 (38%)	76 (35%)	0.5
ADR_CTCAE_max								**<0.001**
1	85 (32%)	11 (32%)	9 (41%)	17 (29%)	7 (20%)	7 (18%)	34 (45%)	
2	78 (30%)	10 (29%)	6 (27%)	12 (20%)	6 (17%)	17 (45%)	27 (36%)	
3	49 (19%)	4 (12%)	3 (14%)	17 (29%)	7 (20%)	6 (16%)	12 (16%)	
4	52 (20%)	9 (26%)	4 (18%)	13 (22%)	15 (43%)	8 (21%)	3 (3.9%)	
ADR_onset_first	4.0 (2.0 - 10.0)	2.0 (1.0 - 9.8)	3.5 (2.0 - 7.8)	4.0 (2.0 - 9.0)	6.0 (2.5 - 11.0)	4.0 (2.0 - 9.0)	6.0 (2.0 - 11.0)	0.15
ADR_PLT_ratio	0.36 (0.22 - 0.52)	0.55 (0.26 - 0.64)	0.39 (0.21 - 0.58)	0.37 (0.26 - 0.50)	0.30 (0.16 - 0.45)	0.36 (0.20 - 0.48)	0.35 (0.25 - 0.50)	0.077

Source: Article Notebook

Model Performance

performance_type	C_index	calibration_intercept	calibration_slope
Apparent	0.7805907	0.0000000	1.0000000
Bootstrap	0.7460291	-0.0133039	0.8155761
K-fold	0.7508108	-0.0206981	0.9113817

Source: Article Notebook