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

Sunday, March 10, 2024

Write abstract here, note the indentation

Checklist

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

	Iten	1	Page
Section/top	olic	Description	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	n		
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			

	Iten	1	Page
Section/top	o M o	Description	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 prepara- tion	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	
ū	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		,	

	Item	1	Pag
Section/top	o f fq	Description	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 per- formance	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 Discussion	15	Report results from any subgroup or sensitivity analysis	
Interpretatio	n16a	Give an overall interpretation of the main results, including heterogeneity across clusters in model performance, in the context	
	16b	of the objectives and previous studies* 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)	

Iten	1	$\overline{\text{Pag}}$				
Section/topNo	Description					
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						
informa-						
tion						
Supplementary 8	Provide information about the availability of supplementary					
informa- tion	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 6 **Funding Objectives**

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

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

Data cleaning

Source: Article Notebook

Rows: 817 Columns: 58 <dbl> 90, 80, 79, 71, 72, 61, 60, 64, 92, 75, 86, 93, 6~ \$ patient_age <lgl> TRUE, TRUE, FALSE, FALSE, TRUE, FALSE, FALSE, TRU~ \$ patient_sex <dbl> 25.00000, 30.00000, 30.00000, 13.33333, 17.14286,~ \$ LZD_dose_per_weight <dbl> 27.22860, 63.15805, 29.93031, 50.89929, 10.87932,~ \$ baseline_CLCR <lgl> TRUE, FALSE, FALSE, FALSE, FALSE, FALSE, T~ \$ dept_ER <lgl> FALSE, TRUE, TRUE, TRUE, TRUE, TRUE, TRUE, FALSE,~ \$ dept_ICU \$ baseline_HGB <dbl> 96, 101, 86, 94, 86, 99, 98, 119, 60, 118, 99, 10~ \$ baseline_WBC <dbl> 6.75, 11.91, 14.05, 14.61, 7.92, 21.79, 13.27, 6.~ <dbl> 244, 180, 259, 179, 236, 113, 196, 154, 147, 101,~ \$ baseline_PLT <dbl> 6, 8, 15, 3, 7, 8, 22, 4, 3, 16, 14, 7, 13, 20, 6~ \$ LZD duration \$ invasive ETI <lgl> FALSE, FALSE, FALSE, TRUE, TRUE, FALSE, TRUE, FAL~ <lg1> FALSE, FALSE, TRUE, FALSE, TRUE, FALSE, TRUE, FALSE \$ invasive CVC \$ invasive_IHD <lgl> FALSE, FALSE, FALSE, FALSE, TRUE, FALSE, FALSE, F~ <lgl> FALSE, FALSE, FALSE, TRUE, FALSE, FALSE, FALSE, F~ \$ invasive_CRRT \$ comorb_HTN <lgl> TRUE, TRUE, TRUE, TRUE, TRUE, FALSE, FALSE, TRUE,~ <lg1> TRUE, FALSE, FALSE, FALSE, TRUE, TRUE, FALSE, FAL~ \$ comorb_DM <lgl> FALSE, TRUE, TRUE, TRUE, TRUE, FALSE, FALSE, TRUE~ \$ comorb_HF \$ comorb_angina <lg>| FALSE, TRUE, TRUE, FALSE, FALSE, FALSE, FALSE, FA~ <lgl> FALSE, FALSE, FALSE, FALSE, FALSE, TRUE, FALSE, F~ \$ comorb_cirr \$ comorb_COPD <lgl> FALSE, FALSE, FALSE, TRUE, FALSE, FALSE, FALSE, F~ <lgl> FALSE, FALSE, FALSE, FALSE, FALSE, FALSE, ~ \$ comorb_CVA \$ comorb_MI <lgl> FALSE, FALSE, FALSE, FALSE, FALSE, FALSE, ~ \$ comorb_K <lg>| < lg| > FALSE, FALSE, FALSE, FALSE, FALSE, TRUE, F~ \$ comorb_hematological <lgl> FALSE, FALSE, FALSE, FALSE, FALSE, FALSE, FALSE, ~ <lg>| < lg| > FALSE, FALSE, FALSE, TRUE, FALSE, FALSE, FALSE, F~ \$ comorb hema <lgl> FALSE, FALSE, FALSE, FALSE, TRUE, TRUE, TR~ \$ infect_sepsis \$ infect CAP <lgl> FALSE, FALSE, TRUE, FALSE, FALSE, FALSE, FALSE, F~ \$ infect HAP <lgl> TRUE, FALSE, FALSE, TRUE, TRUE, FALSE, FALSE, TRU~ <lgl> FALSE, FALSE, FALSE, FALSE, TRUE, FALSE, FALSE, T~ \$ infect_SSTI \$ infect_CNS <lgl> FALSE, FALSE, FALSE, FALSE, FALSE, TRUE, FALSE, F~ <lgl> FALSE, TRUE, FALSE, FALSE, FALSE, TRUE, TRUE, FAL~ \$ infect_IAI <lg>| < lg| > FALSE, FALSE, FALSE, FALSE, FALSE, FALSE, ~ \$ infect_UTI \$ infect_BJI <lg1> FALSE, FALSE, FALSE, FALSE, FALSE, FALSE, ~

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Source: Article Notebook

Descriptive statistics

	Overall, N =	FALSE, N	TRUE, N		95%	
Characteristic	817	= 553	= 264	\mathbf{OR}	\mathbf{CI}	p-value
patient_age	62 (50 - 73)	61 (47 - 72)	64 (54 - 74)	1.02	1.01,	< 0.001
					1.03	
$patient_sex$	307~(38%)	207 (37%)	100 (38%)	1.02	0.75,	> 0.9
					1.38	
LZD_dose_per		21.8 (20.0 -	21.8 (19.4 -	0.99	0.96,	0.8
	24.0)	24.0)	24.6)		1.03	

	Overall, $N =$	FALSE, N	TRUE, N		95%	
Characteristic	817	= 553	= 264	\mathbf{OR}	\mathbf{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
$\operatorname{dept}_{-}\operatorname{ICU}$	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
${\bf comorb_HTN}$	333 (41%)	218 (39%)	115 (44%)	1.19	0.88, 1.60	0.3
${\bf comorb_DM}$	$222\ (27\%)$	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
${\bf comorb_MI}$	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	1.81 0.64, 1.85	0.7

	Overall, N =	FALSE, N	TRUE, N		95%	
Characteristic	817	= 553	= 264	\mathbf{OR}	\mathbf{CI}	p-value
comorb_hemat	ologic(1.6%)	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,	0.2
infect_sepsis	134 (16%)	66 (12%)	68 (26%)	2.56	2.37 1.76,	< 0.001
$infect_CAP$	118 (14%)	70 (13%)	48 (18%)	1.53	3.74 1.02,	0.037
infect_HAP	375 (46%)	255 (46%)	120 (45%)	0.97	2.28 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	0.98 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_septicen	nia 237 (29%)	148 (27%)	89 (34%)	1.39	1.09 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_diclofer	$\mathbf{ac}\ 27\ (3.3\%)$	$20 \ (3.6\%)$	7~(2.7%)	0.73	0.28, 1.66	0.5
comed_ibuprof	Gen 26 (3.2%)	15~(2.7%)	$11\ (4.2\%)$	1.56	0.69, 3.42	0.3
comed_paracet	am 31 5 (43%)	244 (44%)	111 (42%)	0.92	0.68, 1.23	0.6
comed_penicill	in 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_carbape	e ne 564 (71%)	382 (69%)	202~(77%)	1.46	1.05, 2.05	0.028
$comed_cotrimo$	\mathbf{pxa} \mathbf{z}	37 (6.7%)	28 (11%)	1.65	0.98, 2.76	0.055
comed_vancom	nyci68 (8.3%)	42 (7.6%)	26 (9.8%)	1.33	0.79, 2.21	0.3

	Overall, N =	FALSE, N	TRUE, N		95%	
Characteristic	817	=553	= 264	\mathbf{OR}	\mathbf{CI}	p-value
comed_levoflox	ка сі2 б0 (31%)	161 (29%)	89 (34%)	1.24	0.90, 1.69	0.2
comed_teicopla	anin 7 (4.5%)	$23 \ (4.2\%)$	14 (5.3%)	1.29	$0.64, \\ 2.52$	0.5
comed_ethamb	outo8 (1.0%)	5 (0.9%)	3 (1.1%)	1.26	$0.26, \\ 5.17$	0.8
comed_pyrazin	namid (1.5%)	6 (1.1%)	6~(2.3%)	2.12	$0.66, \\ 6.84$	0.2
comed_rifampi	in 17 (2.1%)	10 (1.8%)	7(2.7%)	1.48	$0.53, \\ 3.89$	0.4
comed_heparin	n 207 (25%)	108 (20%)	99 (38%)	2.47	$1.78, \\ 3.43$	< 0.001
comed_clopido	grel 10 (4.9%)	30 (5.4%)	10 (3.8%)	0.69	$0.31, \\ 1.38$	0.3
comed_enoxap	ari ß 50 (43%)	233 (42%)	117 (44%)	1.09	$0.81, \\ 1.47$	0.6
comed_dexame	etha s5 n(13%)	71 (13%)	34 (13%)	1.00	$0.64, \\ 1.54$	>0.9
comed_amioda	aron36 (4.4%)	17 (3.1%)	19 (7.2%)	2.45	$1.25, \\ 4.83$	0.009
comed_furosen	nid 436 (53%)	260 (47%)	176 (67%)	2.25	$1.66, \\ 3.07$	< 0.001
comed_haloper	,	35 (6.3%)	17 (6.4%)	1.02	$0.55, \\ 1.83$	>0.9
comed_valproi	c 32 (3.9%)	$23 \ (4.2\%)$	9 (3.4%)	0.81	$0.35, \\ 1.73$	0.6
comed_aceclofe	` /	0 (0%)	0 (0%)			
comed_naprox	(/	0 (0%)	0 (0%)			
comed_daptom	- '	0 (0%)	1 (0.4%)			
comed_cetirizi	` /	5 (0.9%)	1(0.4%)			
comed_simvas	0 (0%)	0 (0%)	0 (0%)			
comed_bisopro	, ,	4 (0.7%)	2(0.8%)			
comed_diltiaze	` /	0 (0%)	0 (0%)			
comed_eptifiba	` '	0 (0%)	0 (0%)			
comed_quinidi	` '	0(0%)	0 (0%)			
comed_carbam	- \ /	8 (1.4%)	0 (0%)			
comed_phenyt	` '	0 (0%)	0 (0%)			
comed_mirtaza	- \ /	0 (0%)	0 (0%)			
comed_quetiap comed_ondans		4 (0.7%) 4 (0.7%)	$0 (0\%) \\ 2 (0.8\%)$			
comed_ondans	en on (0.1/0)	4 (0.7/0)	2 (0.8/0)			

_	Overall, N =	FALSE, N	TRUE, N		95%	
Characteristic	817	=553	= 264	\mathbf{OR}	\mathbf{CI}	p-value
comed_palonos	setroù (0%)	0 (0%)	0 (0%)			
$comed_oseltam$	nivir $3~(0.4\%)$	1~(0.2%)	2~(0.8%)			
$comed_quinin$	0 (0%)	0 (0%)	0 (0%)			
comed_pembro	olizum (16%)	0 (0%)	0 (0%)			
comed_trastuz	umab (0%)	0 (0%)	0 (0%)			
comed_atezoliz	$\mathbf{umab}(0\%)$	0 (0%)	0 (0%)			
$comed_durvalu$	$\mathbf{mab}0 \ (0\%)$	0 (0%)	0 (0%)			
$comed_IVIG$	0 (0%)	0 (0%)	0 (0%)			
comed_tacrolin	$\mathbf{nus} \ 1 \ (0.1\%)$	0 (0%)	1~(0.4%)			
comed_fluorou	racil0 (0%)	0 (0%)	0 (0%)			
comed_irinoted	can 0 (0%)	0 (0%)	0 (0%)			
comed_leucovo	rin 0 (0%)	0 (0%)	0 (0%)			
$comed_oxalipla$	atin 0 (0%)	0 (0%)	0 (0%)			

Source: Article Notebook

	BM1,		ND1,	ND2,	TN1,	TN2,	
Overall,	N =	$\mathbf{BM2},$	N =	N =	N =	N =	p -
CharacterisMc= 817	125	N = 77	180	116	100	219	value
patient_age62 (50 -	58 (43 -	60 (45 -	60 (45 -	59 (46 -	69 (60 -	66 (58 -	<0.001
73)	69)	72)	68)	68)	78)	78)	
patient_sex 307	54	27	74	28	48	76	0.004
(38%)	(43%)	(35%)	(41%)	(24%)	(48%)	(35%)	
LZD_dose_pær_8_w	eigh 2 2.6	21.4	21.4	21.8	24.0	21.8	0.027
(20.0 -	(20.0 -	(19.0 -	(19.4 -	(20.0 -	(20.0 -	(19.7 -	
24.0)	25.5)	24.0)	24.0)	24.0)	24.6)	24.0)	
baseline_CllCll -	50 (24 -	40 (17 -	70 (41 -	60 (27 -	29 (14 -	35 (17 -	< 0.001
83)	80)	86)	104)	95)	54)	67)	
$dept_ER$ 140	7	9 (12%)	67	15	16	26	< 0.001
(17%)	(5.6%)		(37%)	(13%)	(16%)	(12%)	
dept_ICU 391	10	23	74	42	77	165	< 0.001
(48%)	(8.0%)	(30%)	(41%)	(36%)	(77%)	(75%)	
baseline_H@B(89 -	105 (91	99 (83 -	105 (89	100 (88	99 (89 -	104 (91	0.2
120)	- 124)	118)	- 122)	- 118)	116)	- 120)	
$baseline_WBC(8 -$	11 (7 -	11 (7 -	12 (8 -	11 (7 -	12 (8 -	13 (9 -	0.024
17)	16)	17)	18)	15)	18)	18)	

	BM1,		ND1,	ND2,	TN 1,	TN2 ,	
${\bf Overall},$	N =	BM2,	N =	N =	N =	N =	p -
CharacterisMe= 817	125	N = 77	180	116	100	219	value
baseline_ PLO 6 (142	195	234	207	225	172	225	<0.00
- 288)	(139 -	(160 -	(129 -	(127 -	(122 -	(161 -	
,	247)	318)	292)	310)	245)	299)	
LZD_dura@0(6.0 -	8.0 (6.0	10.0	10.0	9.0(6.0)	11.0	9.0(6.0)	0.3
14.0)	- 13.0)	(6.0 -	(6.0 -	- 12.0)	(6.0 -	- 12.0)	
,	,	14.0)	14.0)	,	15.0)	,	
invasive_ETI387	63	30	$112^{'}$	49	48	85	< 0.00
(47%)	(50%)	(39%)	(62%)	(42%)	(48%)	(39%)	
$invasive_CV @24$	75	30	100	48	50	121	0.008
(52%)	(60%)	(39%)	(56%)	(41%)	(50%)	(55%)	
invasive IHD111	17	16	9	0(0%)	27	42	< 0.00
- (14%)	(14%)	(21%)	(5.0%)	()	(27%)	(19%)	
invasive_CRR48	17	9(12%)	53	5	20	44	< 0.00
— (18%)	(14%)	()	(29%)	(4.3%)	(20%)	(20%)	
comorb_HTN33	42	31	49	28	59	124	< 0.00
- (41%)	(34%)	(40%)	(27%)	(24%)	(59%)	(57%)	
$comorb_DM$ 222	28	24	28	27	31	84	< 0.00
- (27%)	(22%)	(31%)	(16%)	(23%)	(31%)	(38%)	•
comorb_HF 226	55	11	15	7	70	68	< 0.00
(28%)	(44%)	(14%)	(8.3%)	(6.0%)	(70%)	(31%)	•
comorb_angina	0 (0%)	0 (0%)	1	0 (0%)	13	18	< 0.00
(3.9%)	- (-, -)	- (-, -)	(0.6%)	- (-, -)	(13%)	(8.2%)	•
comorb_cirr 48	6	1	10	5	12	14	0.080
(5.9%)	(4.8%)	(1.3%)	(5.6%)	(4.3%)	(12%)	(6.4%)	
comorb COP39	3	0 (0%)	2	2	9	23	< 0.00
(4.8%)	(2.4%)	0 (0,0)	(1.1%)	(1.7%)	(9.0%)	(11%)	(0.00
comorb_C V3 (11%)	19	11	6	4	16	37	< 0.00
<u> </u>	(15%)	(14%)	(3.3%)	(3.4%)	(16%)	(17%)	•
comorb_MI 20	10	3	2	0 (0%)	1	4	0.002
(2.4%)	(8.0%)	(3.9%)	(1.1%)	- (-, -)	(1.0%)	(1.8%)	
comorb_K 67	5	5	8	6	11	32	< 0.00
(8.2%)	(4.0%)	(6.5%)	(4.4%)	(5.2%)	(11%)	(15%)	,,,,,
comorb_hemalfologi	, ,	12	10	5	8	2	< 0.00
(5.6%)	(7.2%)	(16%)	(5.6%)	(4.3%)	(8.0%)	(0.9%)	(3.00
comorb_hema61	13	17	14	2	13	$\frac{(0.570)}{2}$	< 0.00
(7.5%)	(10%)	(22%)	(7.8%)	(1.7%)	(13%)	(0.9%)	(3.00
infect_sepsis 134	10	14	16	15	44	35	< 0.00
(16%)	(8.0%)	(18%)	(8.9%)	(13%)	(44%)	(16%)	\3.00 .

	$\mathbf{BM1},$		ND1,	$\mathbf{ND2},$	TN1,	$\mathbf{TN2},$	
${\bf Overall},$	N =	$\mathbf{BM2},$	N =	N =	N =	N =	p-
Characterishic= 817	125	N = 77	180	116	100	219	value
infect_CAP 118	7	6	11	1	26	67	<0.00
(14%)	(5.6%)	(7.8%)	(6.1%)	(0.9%)	(26%)	(31%)	
infect_HAP 375	38	33	93	59	52	100	0.004
(46%)	(30%)	(43%)	(52%)	(51%)	(52%)	(46%)	
infect_SSTI 133	33	34	1	4	23	38	< 0.00
(16%)	(26%)	(44%)	(0.6%)	(3.4%)	(23%)	(17%)	
infect_CNS 68	0 (0%)	5	24	20	4	15	< 0.00
(8.3%)		(6.5%)	(13%)	(17%)	(4.0%)	(6.8%)	
infect_IAI 50	8	8 (10%)	1	2	12	19	< 0.00
(6.1%)	(6.4%)		(0.6%)	(1.7%)	(12%)	(8.7%)	
$infect_UTI$ 53	6	8 (10%)	10	5	4	20	0.3
(6.5%)	(4.8%)		(5.6%)	(4.3%)	(4.0%)	(9.1%)	
infect_BJI 11	3	0 (0%)	0 (0%)	2	1	5	0.2
(1.3%)	(2.4%)			(1.7%)	(1.0%)	(2.3%)	
infect_septicemia	35	24	57	60	7	54	< 0.00
(29%)	(28%)	(31%)	(32%)	(52%)	(7.0%)	(25%)	
comed_aspirin47	8	9 (12%)	3	0 (0%)	5	22	< 0.00
(5.8%)	(6.4%)		(1.7%)		(5.0%)	(10%)	
comed_diclofe27ac	24	0 (0%)	0 (0%)	1	0 (0%)	2	< 0.00
(3.3%)	(19%)		, ,	(0.9%)	, ,	(0.9%)	
comed_ibupr@fen	0 (0%)	0 (0%)	0 (0%)	2	0 (0%)	24	< 0.00
(3.2%)	, ,		, ,	(1.7%)	, ,	(11%)	
comed_paracetamol	66	0 (0%)	90	69	47	83	< 0.00
(43%)	(53%)		(50%)	(59%)	(47%)	(38%)	
comed_penicil2in	0 (0%)	5	34	19	17	48	< 0.00
(15%)	, ,	(6.5%)	(19%)	(16%)	(17%)	(22%)	
comed_cepha207	12	10	35	33	11	106	< 0.00
(25%)	(9.6%)	(13%)	(19%)	(28%)	(11%)	(48%)	
comed_carbapenem	52	46	154	78	80	174	< 0.00
(71%)	(42%)	(60%)	(86%)	(67%)	(80%)	(79%)	
${f comed_cotrin} {f 65} {f xazol}$	0 (0%)	5	18	14	9	19	0.010
(8.0%)	, ,	(6.5%)	(10%)	(12%)	(9.0%)	(8.7%)	
comed_vancofæycin	8	3	11	22	3	21	< 0.00
- (8.3%)	(6.4%)	(3.9%)	(6.1%)	(19%)	(3.0%)	(9.6%)	
comed_levofl@xacin	27	6	24	20	34	139	< 0.00
(31%)	(22%)	(7.8%)	(13%)	(17%)	(34%)	(63%)	
comed_teicoplanin	0(0%)	0 (0%)	7	$\stackrel{\cdot}{2}$	0(0%)	28	< 0.00
(4.5%)			(3.9%)	(1.7%)		(13%)	

	BM1 ,		ND1,	ND2,	TN1,	TN2 ,	
${\bf Overall},$	N =	$\mathbf{BM2},$	N =	N =	N =	N =	p-
CharacterisNic= 817	125	N = 77	180	116	100	219	value
comed_ethandbuttol	0 (0%)	0 (0%)	2	6	0 (0%)	0 (0%)	<0.00
, ,		, ,	(1.1%)	(5.2%)	, ,	, ,	
comed_pyrazihamid	l 0 (0%)	0 (0%)	5	7	0(0%)	0(0%)	< 0.00
(1.5%)		, ,	(2.8%)	(6.0%)	, ,	, ,	
comed_rifamplin	0 (0%)	0 (0%)	7	9	1	0 (0%)	< 0.00
(2.1%)			(3.9%)	(7.8%)	(1.0%)		
comed_hepar207	12	2	74	24	33	62	< 0.00
(25%)	(9.6%)	(2.6%)	(41%)	(21%)	(33%)	(28%)	
comed_clopid	7	4	1	0 (0%)	8	20	< 0.00
(4.9%)	(5.6%)	(5.2%)	(0.6%)		(8.0%)	(9.1%)	
comed_enoxaparin	33	13	117	44	40	103	< 0.001
(43%)	(26%)	(17%)	(65%)	(38%)	(40%)	(47%)	
comed_dexanhethas	on (0%)	0 (0%)	74	20	2	9	< 0.001
(13%)	` ,	, ,	(41%)	(17%)	(2.0%)	(4.1%)	
comed_amiod36ron	8	0 (0%)	14	5	4	5	0.026
(4.4%)	(6.4%)	, ,	(7.8%)	(4.3%)	(4.0%)	(2.3%)	
comed_furosemid	72	15	81	49	71	148	< 0.00
- (53%)	(58%)	(19%)	(45%)	(42%)	(71%)	(68%)	
comed_halopeddol	3	4	20	4	5	16	0.034
- (6.4%)	(2.4%)	(5.2%)	(11%)	(3.4%)	(5.0%)	(7.3%)	
comed_valproi2	0 (0%)	1	10	5	$\stackrel{\cdot}{3}$	13	0.024
- (3.9%)	, ,	(1.3%)	(5.6%)	(4.3%)	(3.0%)	(5.9%)	
comed_acedo(femac	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_naproven	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_dapitomiyen	` ,	0 (0%)	0 (0%)	1	0 (0%)	0 (0%)	0.4
_ 1 (0)	()	()	()	(0.9%)	()	()	
comed_cetirizin%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	6	0.016
_	()	, ,	()	()	()	(2.7%)	
comed_simva(s0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_bis6p(to761)	4	0 (0%)	1	1	0 (0%)	0 (0%)	0.031
_ 1(''')	(3.2%)	(/	(0.6%)	(0.9%)	(/	(' ' ')	
comed_diltiaz(01%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_eptifibatid	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_quinid(0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_carbaimazep	` /	0 (0%)	7	0 (0%)	0 (0%)	1	0.005
	(0/0)	• (0,0)	(3.9%)	· (0,0)	· (0,0)	(0.5%)	2.300
comed_pheny(tolin)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_mirtazatin	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
	0 (0/0)	0 (0/0)	0 (0/0)	0 (0/0)	0 (0/0)	0 (0/0)	

	BM1,		ND1,	ND2,	TN 1,	TN2 ,	
${\bf Overall},$	N =	$\mathbf{BM2},$	N =	N =	N =	N =	p-
Characterishic= 817	125	N = 77	180	116	100	219	value
comed_queti@pi%)	1	1	0 (0%)	0 (0%)	0 (0%)	2	0.5
	(0.8%)	(1.3%)	, ,	, ,	, ,	(0.9%)	
comed_ondansetro	$\mathbf{n} 2$	1	0(0%)	3	0(0%)	0(0%)	0.020
_	(1.6%)	(1.3%)	, ,	(2.6%)	, ,	` ,	
comed_palon(set)ro	$\mathbf{n} \ \hat{0} \ (0\%)$	0(0%)	0(0%)	0 (0%)	0(0%)	0(0%)	
comed_oseltanii/ii)r	1	1	1	0 (0%)	0 (0%)	0 (0%)	0.4
	(0.8%)	(1.3%)	(0.6%)	, ,	, ,	` ,	
\mathbf{comed} _quinin(0%)	0 (0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	
comed_pembronzu	ma0b (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_trastuzióna	` /	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_atez@li@mna	, ,	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_durva(um)ak	` /	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
$\operatorname{\mathbf{comed}}_{-}\operatorname{\mathbf{IVIG}}(0\%)$	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_tacito(linh)(ts)	1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.5
_ ('')	(0.8%)	(/	(/	()	()	(/	
comed_fluofo@%cil	,	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
comed_irin@t@an	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%)	
comed_oxal0p(12%i)n	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
flag_ADR_T264_ID	` ′	$\frac{3}{22}$	59	35	38	76	0.5
(32%)	(27%)	(29%)	(33%)	(30%)	(38%)	(35%)	0.0
ADR_CTCAE_ma	` ,	(-, -,	(, -)	(, -)	(, -)	(, -)	< 0.00
1 85 (32%)	11	9 (41%)	17	7 (20%)	7 (18%)	34	•
()	(32%)	(/	(29%)	(/	(/	(45%)	
2 78 (30%)	10	6 (27%)	12	6 (17%)	17	27	
(,-)	(29%)	- (- , •)	(20%)	- (-, •)	(45%)	(36%)	
3 49 (19%)	4 (12%)	3 (14%)	17	7 (20%)	6 (16%)	12	
- (- , v)	(, , ,	- (, , ,	(29%)	(1, 0)	- (-, •)	(16%)	
4 52 (20%)	9 (26%)	4 (18%)	13	15	8 (21%)	3	
- (-, -,	- (-, 0)	(-, •)	(22%)	(43%)	- (, , ,	(3.9%)	
ADR_onset.0f(2st -	2.0 (1.0	3.5 (2.0	4.0 (2.0	6.0 (2.5)	4.0 (2.0	6.0 (2.0	0.15
10.0)	- 9.8)	- 7.8)	- 9.0)	- 11.0)	- 9.0)	- 11.0)	00
ADR_PLT_fla360	0.55	0.39	0.37	0.30	0.36	0.35	0.077
(0.22 -	(0.26 -	(0.21 -	(0.26 -	(0.16 -	(0.20 -	(0.25 -	0.011
(0.52)	0.64)	(0.21)	(0.20)	(0.10)	0.48)	(0.29)	
	0.04)	0.00)	0.00)	0.40)	0.40)	0.00)	

Model Performance

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