SUPPLEMENTARY TABLES AND FIGURES

Automatic Extraction of Comprehensive Drug Safety Information from Adverse Drug Event Narratives in the Korea Adverse Event Reporting System using Natural Language Processing Techniques

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Supplementary Fig. 1. Examples of token tagging for NER

Word-level phrase	삼중음성*triple-negative*	유방암*breast cancer*	진단*diagnosis*	이후에*after*
Entity type	ADE	ADE	None	None
WordPiece tokens	[_삼] [중] [음] [성]	[_유] [방] [암]	[_진단]	[_이후] [에]
Tagging result	<B-ADE> <X> <X> <X>	<I-ADE> <X> <X>	<O>	<O> <X>

Supplementary Table 1. Inter-annotator agreements on entity annotation

Annotators	IAA (%)	Number of documents annotated by two annotators
Agreements between the main reviewer and an annotator, annotator ID		
1	97.55	134
2	94.98	108
3	94.91	102
4	97.68	148
5*	95.87	16
Weighted average, without annotator 5	**96.48**	**492**
Weighted average	**96.46**	**508**
Agreements between two annotators, annotator IDs		
(1, 2)	83.95	37
(1, 3)	86.01	35
(1, 4)	90.74	36
(1, 5)	83.41	4
(2, 3)	82.43	38
(2, 4)	85.27	38
(2, 5)	75.26	4
(3, 4)	89.29	35
(3, 5)	72.84	4
(4, 5)	92.63	4
Weighted average, without annotator 5	**86.21**	**219**
Weighted average	**85.86**	**235**

Abbreviation: IAA, inter-annotator agreement

* Annotator 5 dropped out after the first week

Supplementary Table 2. Entity labels in annotated ADE narratives and total ICSRs

Entity labels types	Annotated ADE narratives, Train (N = 3,408)	Annotated ADE narratives, Validation (N = 315)	Total ICSRs* (N=1,199,498)
'occurred' label			
'occurred'	30,386 (60.1)	2,905 (58.5)	NA
'not occurred'	20,168 (39.9)	2,061 (41.5)	NA
Total	50,554 (100.0)	4,966 (100.0)	NA
'concerned' label			
'concerned'	13,088 (83.5)	1,221 (77)	NA
'not concerned'	2,580 (16.5)	365 (23.0)	NA
Total	15,668 (100.0)	1,586 (100.0)	NA
'WHO-UMC assessment' label			
'certain'	186 (4.6)	15 (4.2)	58,044 (2.6)
'probable'	844 (20.9)	82 (22.8)	476,393 (21.7)
'possible'	1,839 (45.6)	187 (52.1)	1,151,751 (52.4)
'unlikely'	831 (20.6)	51 (14.2)	362,490 (16.5)
'unclassified'	143 (3.5)	5 (1.4)	30,825 (1.4)
'unassessable'	188 (4.7)	19 (5.3)	116,835 (5.3)
Total	4,031 (100.0)	359 (100.0)	2,196,338 (100.0)
'ADE seriousness' label			
'death'	70 (13.4)	12 (28.6)	10,562 (7.7)
'life threatening'	17 (3.3)	3 (7.1)	4,621 (3.4)
'caused hospitalization'	151 (28.9)	9 (21.4)	66,838 (48.7)
'disabling'	2 (0.4)	0 (0.0)	1,023 (0.7)
'medically important, but unclassified'	130 (24.9)	8 (19.0)	54,202 (39.5) †
'medically not important'	152 (29.1)	10 (23.8)	
Total	522 (100.0)	42 (100.0)	137,246 (100.0)
'ADE at the last observation' label			
'recovered'	987 (55.3)	102 (57)	NA
'recovering'	522 (29.2)	54 (30.2)	NA
'not recovered'	271 (15.2)	21 (11.7)	NA
'recovered with sequel'	6 (0.3)	2 (1.1)	NA
Total	1,786 (100.0)	179 (100.0)	NA
'action take with drug' label			
'Stop dosing'	1,341 (68.5)	126 (71.2)	NA
'Decrease dose'	126 (6.4)	14 (7.9)	NA
'Increase dose'	51 (2.6)	1 (0.6)	NA
'Maintain dosing and dose'	380 (19.4)	30 (16.9)	NA
'Unknown'	60 (3.1)	6 (3.4)	NA
Total	1,958 (100.0)	177 (100.0)	NA
Total entity labels	**74,519**	**7,309**	**2,333,584**

The total number (column %) is displayed.

Abbreviations: ADE, adverse event; N, number; ICSR, individual case safety report; WHO-UMC, World Health Organization-Uppsala Monitoring Centre

* NA, not applicable because the label information had not been structured in KIDS-KD

†'Medically important, but unclassified' and 'Medically not important' had been labeled as 'others' in KIDS-KD.

Supplementary Table 3. Entity relations in annotated ADE narratives

Relation between two entities	Annotated ADE narratives		
	Total	Train	Validation
(ADE, WHO-UMC assessment)	7,711 (17.1)	7,030 (17.1)	681 (16.6)
(Drug product, WHO-UMC assessment)	3,947 (8.8)	3,604 (8.8)	343 (8.4)
(ADE, Date)*	3,204 (7.1)	2,879 (7.0)	325 (7.9)
(ADE at the last observation, ADE)	3,043 (6.7)	2,746 (6.7)	297 (7.2)
(ADE, ADE)	2,330 (5.2)	2,150 (5.2)	180 (4.4)
(Drug product, Dose)*	2,366 (5.2)	2,135 (5.2)	231 (5.6)
(Drug product, Date)*	2,211 (4.9)	2,000 (4.9)	211 (5.1)
(Test name, Test result)*	1,877 (4.2)	1,712 (4.2)	165 (4.0)
(Drug product, RoA or formulation)*	1,544 (3.4)	1,432 (3.5)	112 (2.7)
(Drug product, Action taken with drug)	1,473 (3.3)	1,361 (3.3)	112 (2.7)
(Date, Test name)*	1,386 (3.1)	1,273 (3.1)	113 (2.8)
(Drug compound, Date)*	1,425 (3.2)	1,255 (3.1)	170 (4.1)
(Drug compound, WHO-UMC assessment)*	1,366 (3.0)	1,236 (3.0)	130 (3.2)
(Drug compound, Drug product)	1,129 (2.5)	1,030 (2.5)	99 (2.4)
(Drug compound, Dose)*	1,030 (2.3)	928 (2.3)	102 (2.5)
(Disease, Drug product)*	849 (1.9)	773 (1.9)	76 (1.9)
(ADE seriousness, ADE)	725 (1.6)	666 (1.6)	59 (1.4)
(Disease, Date)	665 (1.5)	579 (1.4)	86 (2.1)
(ADE, Period)*	587 (1.3)	537 (1.3)	50 (1.2)
(Drug compound, RoA or formulation)*	591 (1.3)	535 (1.3)	56 (1.4)
(Date, Hospitalization event)	575 (1.3)	533 (1.3)	42 (1.0)
(Drug product, Dosing interval)*	576 (1.3)	521 (1.3)	55 (1.3)
(Disease, Drug compound)*	564 (1.3)	500 (1.2)	64 (1.6)
(Drug compound, Action taken with drug)	520 (1.2)	468 (1.1)	52 (1.3)
(ADE at the last observation, Date)	482 (1.1)	442 (1.1)	40 (1.0)
(Date, Non-drug treatment)	466 (1.0)	424 (1.0)	42 (1.0)
(Date, Action taken with drug)	449 (1.0)	406 (1.0)	43 (1.0)
(Drug group, Date)	277 (0.6)	248 (0.6)	29 (0.7)
(Disease, Disease)	265 (0.6)	241 (0.6)	24 (0.6)
(Drug product, Period)	189 (0.4)	173 (0.4)	16 (0.4)

(Date, Period)	175 (0.4)	167 (0.4)	8 (0.2)
(Drug compound, Dosing interval)*	161 (0.4)	144 (0.4)	17 (0.4)
(Drug group, Action taken with drug)	133 (0.3)	123 (0.3)	10 (0.2)
(Drug group, WHO-UMC assessment)	126 (0.3)	111 (0.3)	15 (0.4)
(Disease, Period)	111 (0.2)	107 (0.3)	4 (0.1)
(ADE at the last observation, Period)	82 (0.2)	77 (0.2)	5 (0.1)
(ADE seriousness, Date)	85 (0.2)	76 (0.2)	9 (0.2)
(Drug group, RoA or formulation)	79 (0.2)	71 (0.2)	8 (0.2)
(Drug compound, Period)	78 (0.2)	69 (0.2)	9 (0.2)
(Disease, Drug group)	52 (0.1)	48 (0.1)	4 (0.1)
(Drug group, Period)	38 (0.1)	35 (0.1)	3 (0.1)
(Drug group, Dose)	30 (0.1)	30 (0.1)	0 (0.0)
(Period, Action taken with drug)	31 (0.1)	28 (0.1)	3 (0.1)
(Period, Test name)	29 (0.1)	28 (0.1)	1 (0.0)
(Disease, WHO-UMC assessment)	22 (0.0)	22 (0.1)	0 (0.0)
(Period, Non-drug treatment)	22 (0.0)	20 (0.0)	2 (0.0)
(Period, Hospitalization event)	15 (0.0)	13 (0.0)	2 (0.0)
(Drug group, Dosing interval)	12 (0.0)	12 (0.0)	0 (0.0)
(ADE seriousness, Period)	4 (0.0)	3 (0.0)	1 (0.0)
Total	**45,107 (100.0)**	**41,001 (100.0)**	**4,106 (100.0)**

The total number (column %) is displayed.
Abbreviations: ADE, adverse event; N, number; WHO-UMC, World Health Organization-Uppsala Monitoring Centre; RoA, route of administration;
* We used an annotation data of only selected 15 relations for developing baseline models among total 49 annotated relations.

Supplementary Table 4. Entity recognition for 19 word entities by the KAERS-BERT model

True entity types	Predicted entity type (%)																		
	none	ADE	Dis.	ADE seriousness	ADE at last obs.	Drug comp.	Drug prod.	Drug group	Dose	Dos. inter.	RoA or form.	Date	Per.	Ptnt. sex	Ptnt. age	Hosp. event	Test name	Test result	NDT	Action t/w drug
ADE	5.85	91.99	0.89	0.07	0.12	0.07	0.10	0.24	0.00	0.05	0.10	0.00	0.00	0.00	0.00	0.00	0.29	0.10	0.07	0.07
Disease	4.40	10.26	80.77	0.00	0.00	0.18	0.18	1.10	0.00	0.00	0.00	0.00	0.18	0.00	0.00	0.18	0.37	0.55	1.83	0.00
ADE seriousness	31.91	3.19	0.00	61.70	1.06	0.00	1.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.06	0.00	0.00	0.00	0.00
ADE at last obs.	22.95	4.26	0.00	0.00	68.20	0.00	0.33	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.33	0.33	2.95
Drug compound	4.57	0.55	1.28	0.00	0.00	78.79	1.83	10.24	0.55	0.00	0.55	0.00	0.00	0.00	0.00	0.00	0.55	0.00	1.10	0.00
Drug product	7.34	0.70	0.35	0.00	0.00	0.35	84.27	0.70	0.00	0.00	2.80	0.00	0.00	0.00	0.00	0.00	0.70	0.00	2.80	0.00
Drug group	4.07	0.85	0.09	0.00	0.09	4.64	0.28	86.74	0.19	0.00	2.84	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.00	0.00
Dose	3.23	0.00	0.00	0.00	0.00	0.00	0.00	0.60	92.14	2.82	0.00	0.60	0.20	0.00	0.00	0.00	0.20	0.00	0.20	0.00
Dosing interval	9.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	11.57	76.03	1.65	1.65	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RoA or formulation	8.33	1.00	0.00	0.00	0.00	0.00	2.00	2.67	0.33	0.67	84.33	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.33	0.00
Date	13.27	0.00	0.00	0.00	0.00	0.00	0.00	0.00	6.64	1.42	0.00	65.88	11.85	0.00	0.47	0.00	0.00	0.47	0.00	0.00
Period	1.69	0.17	0.00	0.00	0.08	0.08	0.00	0.17	0.34	0.08	0.00	1.01	95.53	0.00	0.00	0.08	0.08	0.59	0.00	0.08
Patient sex	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	100.00	0.00	0.00	0.00	0.00	0.00	0.00
Patient age	2.44	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	7.32	0.00	0.00	90.24	0.00	0.00	0.00	0.00	0.00
Hospitalization event	10.64	0.00	0.00	2.13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	87.23	0.00	0.00	0.00	0.00
Test name	9.59	2.40	2.05	0.00	0.00	1.37	0.68	0.34	0.00	0.00	0.68	0.00	0.34	0.00	0.00	0.00	76.37	4.45	1.71	0.00
Test result	20.00	2.17	1.74	0.00	2.61	0.00	0.00	0.43	1.74	0.00	0.00	0.87	1.30	1.30	0.00	0.00	3.48	63.04	1.30	0.00
Non-drug treatment	14.29	0.53	10.58	0.00	0.00	6.35	5.29	1.06	0.00	0.00	1.06	0.00	0.53	0.00	0.00	0.00	1.06	1.59	57.67	0.00
ction t/w drug	21.64	0.37	0.00	0.00	0.37	0.00	0.00	0.00	0.37	0.00	0.00	0.75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	76.49

Abbreviations: ADE, adverse drug event; Dis., disease; ADE at last obs., ADE at last observation; Drug comp., drug compound; Drug prod., drug product; Dos. inter., Dosing interval; RoA, route of administration; Per., period; Ptnt., patient; Hosp., hospitalization; NDT, non-drug treatment; Action t/w drug, action taken with drug

Supplementary Table 5. NER performance metrics of the KAERS-BERT model for entities labeled as '*occurred*' and '*not occurred*'

Performance metrics	ADE	Disease	Drug compound	Drug product	Drug group
Precision					
'occurred'	97.38	82.02	90.46	91.75	92.41
'not occurred'	93.69	86.31	87.75	92.48	90.40
Difference†	3.69	-4.29	2.70	-0.73	2.02
Recall					
'occurred'	90.69	79.46	69.90	89.48	88.06
'not occurred'	88.31	75.90	80.18	86.00	80.73
Difference†	2.38	3.56	-10.28	3.48	7.33
F1-score					
'occurred'	93.80	80.43	78.60	90.19	89.98
'not occurred'	90.92	80.77	83.67	88.83	85.27
Difference†	2.88	-0.34	-5.08	1.36	4.71

Abbreviations: NER, named entity recognition; KAERS-BERT, Korea Adverse Event Reporting System-bidirectional encoder representations from transformers; ADE, adverse event

†The difference is performance score on entities labeled as 'occurred'