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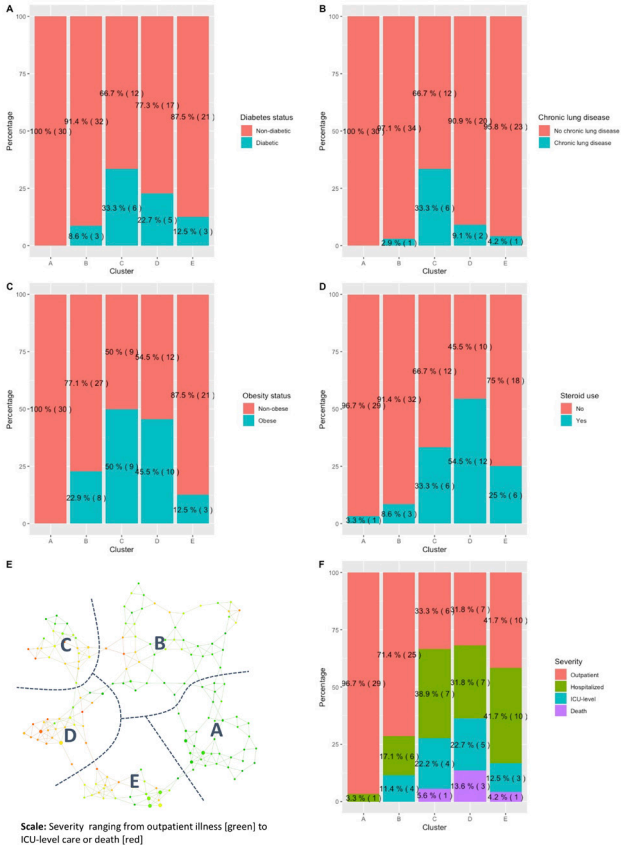
EPICC COVID-19 Cohort Study Group

Session: P-20. COVID-19 Pathogenesis

Background. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections peak during an inflammatory 'middle' phase and lead to severe illness predominately among those with certain comorbid noncommunicable diseases (NCDs). We used network machine learning to identify inflammation biomarker patterns associated with COVID-19 among those with NCDs.

Methods. SARS-CoV-2 RT-PCR positive subjects who had specimens available within 15-28 days post-symptom onset were selected from the DoD/USU EPICC COVID-19 cohort study. Plasma levels of 15 inflammation protein biomarkers were measured using a broad dynamic range immunoassay on samples collected from individuals with COVID-19 at 8 military hospitals across the United States. A network machine learning algorithm, topological data analysis (TDA), was performed using results from the 'hyperinflammatory' middle phase. Backward selection stepwise logistic regression was used to identify analytes associated with each cluster. NCDs with a significant association (0.05 significance level) across clusters using Fisher's exact test were further evaluated comparing the NCD frequency in each cluster against all other clusters using a Kruskal-Wallis test. A sensitivity analysis excluding mild disease was also performed.

Results. The analysis population (n=129, 33.3% female, median 41.3 years of age) included 77 ambulatory, 31 inpatient, 16 ICU-level, and 5 fatal cases. TDA identified 5 unique clusters (Figure 1). Stepwise regression with a Bonferroni-corrected cutoff adjusted for severity identified representative analytes for each cluster (Table 1). The frequency of diabetes (p=0.01), obesity (p< 0.001), and chronic pulmonary disease (p< 0.001) differed among clusters. When restricting to hospitalized patients, obesity (8 of 11), chronic pulmonary disease (6 of 11), and diabetes (6 of 11) were more prevalent in cluster C than all other clusters.



Cluster differences in comorbid diseases and severity by cluster. 1A: bar plot of diabetes prevalence; 1B: bar plot of chronic lung disease ; 1C: bar plot of obesity prevalence; 1D: prevalence of steroid treatment ; 1E: Topologic data analysis network with clusters labeled; 1F: Bar plot of ordinal levels of severity.

Table 1. Multivariable logistic regression models for clusters and immune biomarkers. Models were fitted comparing each cluster against all other clusters.

Cluster	Covariates in unadjusted model*	OR** (95% CI)	AIC	Covariates in severity-adjusted*** model	OR (95% CI)	AIC
A			82.9			95.2
	VEGFA	0.02 (0.003, 0.2)		CRP	0.2 (0.08, 0.5)	
	RAGE	650.1 (9.6, 44016.7)		Severity	0.03 (0.003, 0.3)	
	IL6	0.02 (0.002, 0.1)				
B			92.3			91.2
	Ferritin	0.02 (0.004, 0.10)		Ferritin	0.03 (0.006, 0.1)	
	ICAM1	519.6 (37.6, 7176.3)		ICAM1	1676.1 (68.9, 40760.0)	
				Severity	0.4 (0.2, 1.2)	
C			74.5			76.4
	IL5	0.08 (0.02, 0.4)		IL5	0.08 (0.02, 0.4)	
	IL1RA	53.7 (8.9, 324.3)		IL1RA	59.2 (8.3, 422.6)	
				Severity	0.9 (0.5, 1.9)	
D			111.0			108.6
	VEGFA	8.8 (2.5, 31.7)		Severity	2.3 (1.4, 3.8)	
E			83.7			82.1
	Ferritin	111.1 (12.5, 986.9)		Ferritin	75.9 (6.9, 837.9)	
	ICAM1	0.0008 (0.00002, 0.03)		ICAM1	0.0006 (0.00001, 0.02)	
	RAGE	203.8 (6.1, 6785.0)		RAGE	242.6 (6.9, 8588.6)	
				Severity	1.4 (0.5, 3.4)	

AIC: Akaike information criterion, CRP: c-reactive protein.

*IL6ra and LCN2 removed due to collinearity with ICAM1

**Estimates are in $\log_{10}$ pg/ml scale.

***Severity on an ordinal scale with outpatient-level= 0, inpatient-level=1, ICU-level care =2, death =3

Conclusion. Machine learning clustering methods are promising analytical tools for identifying inflammation marker patterns associated with baseline risk factors and severe illness due to COVID-19. These approaches may offer new insights for COVID19 prognosis, therapy, and prevention.

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439. Corowa-kun: Impact of a COVID-19 Vaccine Information Chatbot on Vaccine Hesitancy, Japan 2021

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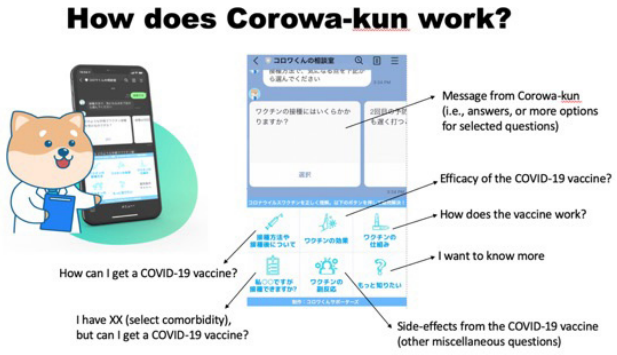
Session: P-21. COVID-19 Research

Background. Japan has one of the highest vaccine hesitancy rates in the world. According to a previous study, less than 30% of people strongly agreed that vaccines were safe, important, or effective. We created a COVID-19 vaccine information chatbot in a popular messenger app in Japan to answer COVID-19 vaccine frequently asked questions (FAQs) via text messages. We assessed the impact of chatbot text messages on COVID-19 vaccine hesitancy by conducting a cross-sectional survey among chatbot users.

Methods. LINE is the most popular messenger app in Japan; about 86 million people in Japan (roughly two-thirds of the population) use this messenger app. Corowa-kun, a free chatbot, was created in LINE on February 6, 2021. Corowa-kun provides instant, automated answers to frequently asked COVID-19 vaccine questions. A cross-sectional survey assessing COVID-19 vaccine hesitancy was conducted via Corowa-kun during April 5 to 12, 2021. We included persons ages 16 years old and older who had not received a COVID-19 vaccine. The survey was written in Japanese and consisted of 21 questions.

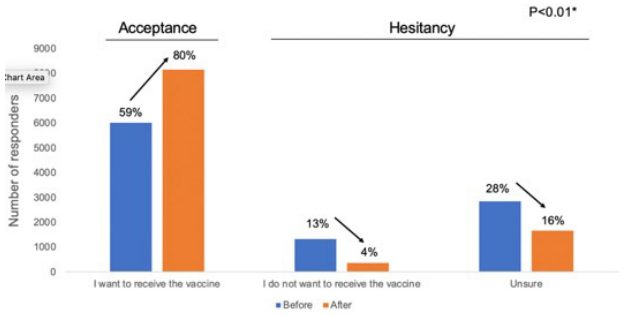
Corowa-kun's Consultation Room



Corowa-kun is the mascot of an online chatbot. This chatbot in LINE is used to answer COVID-19 vaccine frequently asked questions (FAQs) via text messages. As of May 10th, 70 FAQs are available.

Results. A total of 59,676 persons used Corowa-kun during February to April 2021. The most commonly accessed message categories were: "I have (select comorbidity), can I get a COVID-19 vaccine?" (23%); followed by questions on adverse reactions (22%) and how the vaccine works (20%). 10,192 users (17%) participated in the survey. Median age was 55 years (range 16 to 97), and most were female (74%). Intention to receive a COVID-19 vaccine increased from 59% to 80% after using Corowa-kun ($p < 0.01$). Overall, 20% remained hesitant: 16% (1,675) were unsure, and 4% (364) did not intend to be vaccinated. Factors associated with vaccine hesitancy were: age 16 to 34 (odds ratio [OR] = 3.7, 95% confidential interval [CI]: 3.0–4.6, compared to age ≥65), female sex (OR = 2.4, Cl: 2.1–2.8), and history of another vaccine side-effect (OR = 2.5, Cl: 2.2–2.9). Being a physician (OR = 0.2, Cl: 0.1-0.4) and having received a flu vaccine the prior season (OR = 0.4, Cl: 0.3-0.4) were protective.

COVID-19 vaccine acceptance increased and hesitancy decreased after using Corowa-kun, Japan, 2021 (n=10,192)



*There was a statistically significant difference in responses between before and after using Corowa-kun ($p < 0.01$, Chi-square test).

AQ13

Univariable logistic regression models of factors associated with COVID-19 vaccine hesitancy, Japan, 2021 (n=10,192)

	Vaccine hesitancy N=2,039		Vaccine acceptance N=8,153		Odds ratio
Age					
16-34	229	11.2%	569	7.0%	3.7 (3.0-4.6)
35-49	648	31.8%	2046	25.1%	2.9 (2.5-3.5)
50-64	953	46.7%	3609	44.3%	2.4 (2.1-2.9)
≥65	209	10.3%	1929	23.7%	Ref
Sex					
Male	278	13.63%	2278	27.9%	Ref
Female	1727	84.7%	5816	71.3%	2.4 (2.1-2.8)
Other	3	0.2%	14	0.2%	NA
No answer	31	1.5%	45	0.6%	5.6 (3.5-9.1)
Educational attainment					
Elementary or junior high school	57	2.8%	151	1.9%	1.4 (1.0-1.9)
High school	660	32.4%	2008	24.6%	1.2 (1.1-1.3)
College or professional school	730	35.8%	2635	32.3%	Ref
Undergraduate school	536	26.3%	2966	36.4%	0.7 (0.6-0.7)
Postgraduate school	56	2.8%	393	4.8%	0.5 (0.4-0.7)
Employment status					
Full-time	724	35.5%	3142	38.5%	Ref
Part-time	631	31.0%	2097	25.7%	1.3 (1.2-1.5)
Student	27	1.3%	73	0.9%	1.6 (1.0-2.5)
Retied	59	2.9%	681	8.4%	0.4 (0.3-0.5)
Homemaker	437	21.4%	1555	19.1%	1.2 (1.1-1.4)
Unemployed due to COVID-19	37	1.8%	91	1.1%	1.8 (1.2-2.6)
Unemployed irrelevant to COVID-19	124	6.1%	514	6.3%	1.0 (0.8-1.3)
Healthcare worker					
Physician	7	0.3%	164	2.0%	0.2 (0.1-0.4)
Yes, but not physician	323	15.8%	1400	17.2%	0.9 (0.8-1.01)
No	1709	83.8%	6589	80.8%	Ref
Living with persons at age<16	452	22.2%	1506	18.5%	1.3 (1.1-1.4)
Living with persons at age≥65	647	31.8%	2994	36.7%	0.8 (0.7-0.9)
Have you had a flu shot within the past year?	1039	51%	5998	73.6%	0.4 (0.3-0.4)
Self-reported history of COVID-19					
Yes (I tested positive)	48	0.6%	10	0.5%	0.8 (0.4-1.7)
Yes (I had the symptoms but did not receive a positive test)	60	0.7%	23	1.1%	1.5 (0.9-2.5)
No	8045	80%	2006	98.4%	Ref
Have you had any vaccine side-effects?					
Yes	331	16.2%	644	7.9%	2.5 (2.2-2.9)
No	1424	69.8%	7051	86.5%	Ref
Unsure	284	13.9%	458	5.6%	3.1 (2.6-3.6)
Pregnancy status					
Pregnant	31	1.5%	36	0.4%	3.3 (2.0-5.3)
Not pregnant	1072	52.57 %	4087	50.1%	Ref
Desire to be pregnant	84	4.1%	144	1.8%	2.2 (1.7-2.9)
Not applicable	852	41.8%	3886	47.7%	0.8 (0.8-0.9)

Ref: reference NA: Logistic regression was not performed due to too small number (n≤3)

Conclusion. Corowa-kun reduced vaccine hesitancy by providing COVID-19 vaccine information in a messenger app. Mobile messenger apps could be leveraged to increase COVID-19 vaccine acceptance.

Disclosures. **All Authors**: No reported disclosures

440. Detection of COVID-19 Patients Requiring Escalation to ICU Status Using a Naïve Bayes Classifier

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Session: P-21. COVID-19 Research

Background. A naïve Bayes classifier is a popular tool used in assigning variables an equal and independent contribution to a binary decision. With respect to COVID-19 severity, the naïve Bayes classifier can consider different variables, such as age, gender, race/ethnicity, comorbidities, and initial laboratory values to determine the probability a patient may need to be admitted or transferred to an intensive care unit (ICU). The aim of this study was to develop a screening tool to detect COVID-19 patients that may require escalation to ICU status.

Methods. Patients hospitalized with COVID-19 were gathered from the end of March 2020 to the end of May 2020 from four hospitals in our metropolitan area. We began searching for potential variables to include in the classification model using chi-square analysis or calculating the optimal cutpoint to separate ICU and non-ICU status. After identifying significant variables, we began using standard procedures to construct a classifier. The dataset was split 7:3 to create samples for training and testing. To appraise the model's performance, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), area under the curve (AUC), and the Matthew's correlation coefficient (MCC) were calculated.

Table 1. Univariate analysis of variables in the COVID-19 dataset dichotomized by ICU status

Variable	Non-ICU (n = 397)	ICU (n=177)	P value
Age ≥ 55 years	260 (65.5)	150 (84.7)	<0.001
Male	175 (44.1)	101 (57.1)	0.005
African American	143 (36.0)	63 (35.6)	0.997
Hypertension	276 (69.5)	132 (74.6)	0.257
Chronic kidney disease	67 (16.9)	60 (33.9)	<0.001
Chronic obstructive pulmonary disease	58 (14.6)	40 (22.6)	0.026
Obstructive sleep apnea	49 (12.3)	42 (23.7)	0.001
Diabetes mellitus type II	136 (34.3)	91 (51.4)	<0.001
Presenting with fever	252 (63.5)	122 (68.9)	0.242
Presenting with diarrhea	123 (31.0)	37 (20.9)	0.017
C-reactive protein ≥ 10 mg/L	39 (9.8)	35 (19.8)	0.002
Lactate dehydrogenase ≥ 400 U/L	145 (36.5)	95 (53.7)	<0.001
Ferritin ≥ 550 ng/mL	162 (40.8)	104 (58.8)	<0.001
Troponin-I ≥ 0.1 ng/mL	27 (6.8)	45 (25.4)	<0.001

Results. A total of 574 COVID-19 patients were included in the study. There were 402 patients in the training sample and 172 patients in the testing sample. The naïve Bayes classifier demonstrated an overall accuracy result of 75.6% (95% CI; 68.5% – 81.8%) using the 14 variables listed in Table 1. The model was able to correctly classify 84.9% of ICU status patients (sensitivity), but only 54.7% of non-ICU status patients (specificity). The PPV and the NPV were 80.1% and 61.7%, respectively. The AUC was 0.717 (95% CI; 0.629 – 0.805) and the MCC was 0.410.

Conclusion. Our naïve Bayes classifier operates by recognizing certain aspects of severe COVID-19 cases and looking for the probability of the variables in said patients. We present a classification model that potentially could be used alongside other tools to screen patients with COVID-19 early in their hospital course to identify those needing escalation to ICU level care.

Disclosures. **All Authors**: No reported disclosures

441. The Effects of Race and Comorbidity Burden on Inflammatory Biomarkers Among Persons Hospitalized with COVID-19.

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