Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Short Communication

Clinical Characteristics of Patients with Coronavirus Disease (COVID-19): Preliminary Baseline Report of Japan COVID-19 Task Force, a Nationwide Consortium to Investigate Host Genetics of COVID-19 ☆

Hiromu Tanaka [1], Ho Lee [1], Atsuho Morita [1], Ho Namkoong [2,#], Shotaro Chubachi [1], Hiroki Kabata [1], Hirofumi Kamata [1], Makoto Ishii [1], Naoki Hasegawa [2], Norihiro Harada [3], Tetsuya Ueda [4], Soichiro Ueda [5], Takashi Ishiguro [6], Ken Arimura [7], Fukuki Saito [8], Takashi Yoshiyama [9], Yasushi Nakano [10], Yoshikazu Mutoh [11], Yusuke Suzuki [12], Koji Murakami [13], Yukinori Okada [14,15,16,17], Ryuji Koike [18], Yuko Kitagawa [19], Katsushi Tokunaga [20], Akinori Kimura [21], Seiya Imoto [22], Satoru Miyano [23], Seishi Ogawa [24,25,26], Takanori Kanai [27], Koichi Fukunaga [1], The Japan COVID-19 Task Force

[1] *Division of Pulmonary Medicine, Department of Medicine, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan*
[2] *Department of Infectious Diseases, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan*
[3] *Department of Respiratory Medicine, Juntendo University Faculty of Medicine and Graduate School of Medicine, Tokyo, Japan*
[4] *Department of Respiratory Medicine, Osaka Saiseikai Nakatsu Hospital, Osaka, Japan*
[5] *JCHO (Japan Community Health Care Organization) Saitama Medical Center, Internal Medicine, Saitama, Japan*
[6] *Department of Respiratory Medicine, Saitama Cardiovascular and Respiratory Center, Kumagaya, Japan*
[7] *Department of Respiratory Medicine, Tokyo Women's Medical University, Tokyo, Japan*
[8] *Department of Emergency and Critical Care Medicine, Kansai Medical University General Medical Center, Moriguchi, Japan*
[9] *Fukujuji Hospital, Kiyose, Japan*
[10] *Kawasaki Municipal Ida Hospital, Department of Internal Medicine, Kawasaki, Japan*
[11] *Department of Infectious Diseases, Tosei General Hospital, Seto, Japan*
[12] *Department of Respiratory Medicine, Kitasato University, Kitasato Institute Hospital, Tokyo, Japan*
[13] *Department of Respiratory Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan*
[14] *Department of Statistical Genetics, Osaka University Graduate School of Medicine, Suita, Japan*
[15] *Integrated Frontier Research for Medical Science Division, Institute for Open and Transdisciplinary Research Initiatives, Osaka University, Suita, Japan*
[16] *The Center for Infectious Disease Education and Research (CiDER), Osaka University, Suita, Japan*
[17] *Laboratory of Statistical Immunology, Immunology Frontier Research Center (WPI-IFReC), Osaka University, Suita, Japan*
[18] *Medical Innovation Promotion Center, Tokyo Medical and Dental University, Tokyo, Japan*
[19] *Department of Surgery, Keio University School of Medicine, Tokyo, Japan*
[20] *Genome Medical Science Project (Toyama), National Center for Global Health and Medicine, Tokyo, Japan*
[21] *Institute of Research, Tokyo Medical and Dental University, Tokyo, Japan*
[22] *Division of Health Medical Intelligence, Human Genome Center, the Institute of Medical Science, the University of Tokyo, Tokyo, Japan*
[23] *M&D Data Science Center, Tokyo Medical and Dental University, Tokyo, Japan*
[24] *Department of Pathology and Tumor Biology, Kyoto University, Kyoto, Japan*
[25] *Institute for the Advanced Study of Human Biology (WPI-ASHBi), Kyoto University, Kyoto, Japan*
[26] *Department of Medicine, Center for Hematology and Regenerative Medicine, Karolinska Institute, Stockholm, Sweden*
[27] *Division of Gastroenterology and Hepatology, Department of Medicine, Keio University School of Medicine, Tokyo, Japan*

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ABSTRACT

Background and design: The coronavirus disease (COVID-19) pandemic is having a devastating effect worldwide. Host genome differences between populations may influence the severity of COVID-19.

The Japan COVID-19 Task Force is conducting host genome analysis of hospitalized patients with COVID-19 from more than 70 institutions nationwide in Japan. This report describes the clinical characteristics of patients enrolled to date.

☆ Details are given in the "author information" section.

Corresponding author: Ho Namkoong, MD, PhD. Department of Infectious Diseases, Keio University School of Medicine, 35 Shinanomachi, Shinjuku, Tokyo 160-8582, Japan.

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Results: The median (interquartile range) age of the 1674 patients included in the analysis was 59 (45–71) years, and more than half of the patients (66.2%) were male. Less than half of the patients (41.2%) had severe disease. The case fatality rate was 3.2%.
Conclusions: Since this is a hospital-based study, the number of severe cases was relatively high, but the case fatality rate was relatively low, when compared to that of other countries. In the future, we will continue to enroll patients and conduct genome analyses of patients with COVID-19.

The coronavirus disease (COVID-19) pandemic has had a devastating effect worldwide, including in Japan (see https://www.mhlw.go.jp/stf/covid-19/kokunainohasseijoukyou.html)(Ministry of Health, Labour and Welfare 2021). Host genome differences between populations may influence disease severity. This may explain why Asians, including Japanese, may have a lower risk of death (Price-Haywood, 2020; Zeberg and Pääbo, 2020). The Japan COVID-19 Task Force was established in early 2020 as a nationwide multicenter consortium. We collected and analyzed clinical specimens from patients in more than 70 institutions nationwide since February 2020 and reported the results of a genome-wide association study (Namkoong H et al., 2021).

This cross-sectional study aimed to determine the clinical characteristics of Japanese patients with COVID-19. The study facilities provide coverage for the most populous prefectural capital cities in Japan. We included 1645 (98.3%) patients with reverse transcription polymerase chain reaction (RT-PCR)-confirmed COVID-19, 10 (0.6%) patients with rapid antigen test-confirmed COVID-19, and 19 (1.1%) patients who were considered as highly suspicious for COVID-19 by the physician. We collected information on patient demographics, laboratory test data, radiographic imaging, treatment, comorbidities, and outcomes for 1674 cases to construct a database for the Japan COVID-19 Task Force. The cases were not limited to inpatients; however, 1668 (99.6%) patients were hospitalized patients. All the patients in this study provided appropriate informed consent, which was approved by the ethics committee of the affiliated institutes. Symptoms and signs included not only those reported on referral or admission but also those observed during hospitalization. Laboratory and radiographic data were collected within 48 hours of the initial visit or admission. Disease outcome during hospitalization was assessed for fatality rate. We obtained information regarding any support using oxygen devices, invasive mechanical ventilation (IMV), and extracorporeal membrane oxygenation (ECMO) during the clinical course to determine the disease severity. In this report, disease severity was defined as follows: most severe, patients requiring support using high-flow oxygen devices, IMV, ECMO, or death; severe, patients requiring support using low-flow oxygen devices; mild, symptomatic patients not requiring oxygen support; asymptomatic, asymptomatic patients not requiring oxygen support (World Health Organization, 2020).

The patients' clinical characteristics are shown in Table 1. Their median (interquartile range) age was 59 (45–71) years, 66.2% were male, and most patients were Japanese. Comorbidities included hypertension (34.6%), diabetes mellitus (22.9%), coronary artery disease (9.9%), and chronic kidney disease (7.0%). Moreover, 231 cases were categorized as most severe (13.8%), 459 cases as severe (27.4%), 933 cases as mild (55.7%), and 51 cases as asymptomatic (3.0%). The most common symptom was fever (≥37.5°C), which was observed in 79.3% of patients. Cough, sputum, shortness of breath, dysgeusia, and dysosmia were observed in 58.2%, 24.7%, 30.7%, 18.7%, and 17.0% of patients, respectively. Most patients were enrolled in April 2020 (first wave), August 2020 (second wave), and December 2020 (third wave) (Figure 1). Supplementary Table 1 shows the patients' characteristics in each epidemic. There was a high prevalence of elderly males among patients in the third epidemic. They also had a higher prevalence of comorbidities such as hypertension, diabetes, and chronic kidney disease, and a low prevalence of dysgeusia and dysosmia.

Laboratory findings showed an elevated inflammatory response, with median ferritin and C-reactive protein levels of 376 ng/mL and 2.69 mg/dL, respectively. Regarding radiographic findings, 81.3% of patients had ground glass opacity (GGO), and 39.8% had consolidation on chest computed tomography. The bilateral spread of GGOs was generally present during the acute phase of COVID-19.

A total of 19.0% of patients were admitted to the intensive care unit, 11.1% were intubated, and 2.3% required ECMO. The fatality rate was 3.2%. Complications included bacterial infection and thrombosis in 11.9% and 3.6% of patients, respectively. The most commonly used antivirals were favipiravir and remdesivir, which were used in 35.9% and 18.9% of patients, respectively. Systemic corticosteroids were used in 40.9% of patients, especially in 58.9% of patients in the third epidemic.

Clinical characteristics of patients in this study were similar to those of other previously reported large-sample studies in Asian populations (Guan, 2020; Matsunaga N et al., 2020). The proportion of male patients was higher in this study than in other studies, which may be due to the relatively high disease severity in males (Chen N et al., 2020). The proportion of patients with comorbidities such as hypertension, diabetes, and chronic kidney disease was higher than that reported in another registry in Japan (Matsunaga N et al., 2020). We believe that this finding is due to a large number of patients registered in the third epidemic, unlike

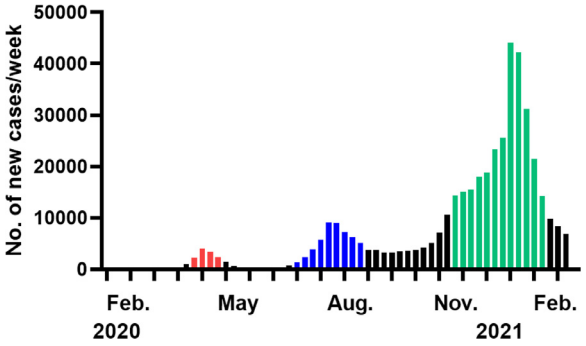

Figure 1. Coronavirus disease (COVID-19) epidemic trend in Japan, from February 2020 to February 2021. The epidemic curve shows the three epidemic waves during 1 year in Japan. Red bar shows the first wave including 89 patients in this study; from April 1 to 28, 2020. Blue bar shows the second wave including 468 patients in this study; from July 1 to September 1, 2020. Green bar shows the third wave including 564 patients in this study; from November 18, 2020 to February 9, 2021. ■ Black bar shows the number of new patients during the period not included in the three epidemic waves. We created this figure using GraphPad Prism 9 (GraphPad Software, San Diego, California).

Table 1
Characteristics of 1674 patients with COVID-19 in Japan

Parameters	Number of patients with data	Subcategories	n (%) or median and IQR
Severity classification	1674		
		Asymptomatic	51 (3.0)
		Mild	933 (55.7)
		Severe	459 (27.4)
		Most severe	231 (13.8)
Death at discharge	1633		52 (3.2)
Age, years	1674		59 (45–71)
Sex	1674		
		Male	1109 (66.2)
		Female	565 (33.8)
Population	1674		
		Japanese	1629 (97.3)
		Others	45 (2.7)
BMI, kg/m^2	1525		23.9 (21.6–26.9)
Smoking history	1547		
		Never	840 (54.3)
		Previously or currently	707 (45.7)
Chronic medical conditions			
Hypertension	1643		569 (34.6)
Diabetes mellitus	1654		379 (22.9)
Coronary artery disease	1657		164 (9.9)
Malignancy	1640		97 (5.9)
Autoimmune disease	1653		61 (3.7)
COPD	1651		67 (4.1)
Chronic liver disease	1592		53 (3.3)
Chronic kidney disease	1579		110 (7.0)
Symptoms at referral			
Fever (≥37.5°C)	1653		1311 (79.3)
Cough	1648		959 (58.2)
Sputum	1642		405 (24.7)
Sore throat	1628		387 (23.8)
Rhinorrhea	1634		232 (14.2)
Dysgeusia	1635		305 (18.7)
Dysosmia	1634		278 (17.0)
Shortness of breath	1616		496 (30.7)
Fatigue	1642		811 (49.4)
Laboratory tests			
WBC [cells/μL]	1613		5200 (4100–6700)
LDH [IU/L]	1634		237 (190–314)
Ferritin [ng/mL]	1269		376 (171–711)
KL-6 [U/mL]	1213		234 (178–350)
PCT [ng/mL]	1165		0.06 (0.04–0.11)
CRP [mg/dL]	1628		2.69 (0.51–6.87)
Radiographic imaging			
Chest radiography findings	1556	Bilateral thoracic opacities	834 (53.6)
		Unilateral thoracic opacities	180 (11.6)
	1539	Bilateral thoracic consolidation	305 (19.8)
		Unilateral thoracic consolidation	121 (7.9)
Chest CT findings	1480	Bilateral GGO	1055 (71.3)
		Unilateral GGO	148 (10.0)
	1445	Bilateral consolidation	465 (32.2)
		Unilateral consolidation	110 (7.6)
Complications after referral			
Bacterial infection	1653		196 (11.9)
Heart failure	1641		36 (2.2)
Thrombosis	1623		59 (3.6)
COVID-19 treatment			
ICU admission	1650		314 (19.0)
Intubation	1649		183 (11.1)
ECMO	1641		37 (2.3)
Antiviral drugs			
	1657	Favipiravir	595 (35.9)
	1645	Ritonavir	7 (0.4)
	1648	Remdesivir	311 (18.9)
Hydroxychloroquine	1647		18 (1.1)
Tocilizumab	1643		118 (7.2)
Systemic corticosteroid	1663		680 (40.9)

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease; CRP, C-reactive protein; CT, computed tomography; ECMO, extracorporeal membrane; GGO, ground glass opacity; ICU, intensive care unit; IQR, interquartile range; KL-6, Krebs von den Lungen-6; LDH, lactate dehydrogenase; PCT, procalcitonin; WBC, white blood cell.

the situation in the previously reported registry. Our study suggests that the number of hospitalized older male patients with more comorbidities has gradually increased in Japan during the past year. Compared with the recent meta-analyses in other countries (Macedo A et al., 2021), we believe that the lower fatality rate in this study and in the previous report (Matsunaga N et al., 2020) may be explained by reasons specific to Japan. We consider the possibility that many inpatient cases of our study would have been treated as outpatients in other countries, because in Japan, the public health centers coordinated the hospitalization of many patients, including those with mild disease. The low fatality rate may also reflect the unique genetic characteristics of the Japanese. For example, the effect of DOCK2 on disease severity of COVID-19 has been reported (Namkoong H et al., 2021). Our study had a large group of patients treated with remdesivir, especially in the third epidemic. A relatively high proportion of patients were treated with systemic corticosteroids, based on the results of the RECOVERY trial (Horby, 2021). These treatments may have resulted in a lower fatality rate in this study than that in previous reports.

With this clinical information, characterization of the host genomic factors in a representative sample of Japanese patients may provide insights into new treatment approaches.

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Ethics Approval

This study was approved by the ethics committee of Keio University School of Medicine (20200061) and affiliated institutes.

Author Information

Japan COVID-19 Task Force are composed of more than 70 institutions nationwide in Japan. The members who contributed to the collection and analysis of cases at each institution are shown as coauthors in the following list.

Hiromu Tanaka[1], Ho Lee[1], Atsuho Morita[1], Ho Namkoong[2], Shotaro Chubachi[1], Hiroki Kabata[1], Hirofumi Kamata[1], Makoto Ishii[1], Naoki Hasegawa[2], Kazuhisa Takahashi[3], Norihiro Harada[3], Toshio Naito[4], Makoto Hiki[5,6], Yasushi Matsushita[7], Haruhi Takagi[3], Ryousuke Aoki[8], Ai Nakamura[3], Sonoko Harada[3,9], Hitoshi Sasano[3], Katsunori Masaki[1], Shinnosuke Ikemura[1], Satoshi Okamori[1], Hideki Terai[1], Takanori Asakura[1], Junichi Sasaki[10], Hiroshi Morisaki[11], Yoshifumi Uwamino[12], Kosaku Nanki[13], Yohei Mikami[13], Sho Uchida[2], Shunsuke Uno[2], Rino Ishihara[13], Yuta Matsubara[13], Tomoyasu Nishimura[2,14], Takunori Ogawa[1], Toshiro Sato[15], Tetsuya Ueda[16], Masanori Azuma[16], Ryuichi Saito[16], Toshikatsu Sado[16], Yoshimune Miyazaki[16], Ryuichi Sato[16], Yuki Haruta[16], Tadao Nagasaki[16], Yoshinori Yasui[17], Yoshinori Hasegawa[16], Soichiro Ueda[18], Ai Tada[18], Masayoshi Miyawaki[18], Masaomi Yamamoto[18], Eriko Yoshida[18], Reina Hayashi[18], Tomoki Nagasaka[18], Sawako Arai[18], Yutaro Kaneko[18], Kana Sasaki[18], Takashi Ishiguro[19], Taisuke Isono[19], Shun Shibata[19], Yuma Matsui[19], Chiaki Hosoda[19], Kenji Takano[19], Takashi Nishida[19], Yoichi Kobayashi[19], Yotaro Takaku[19], Noboru Takayanagi[19], Etsuko Tagaya[20], Masatoshi Kawana[21], Ken Arimura[20], Yasushi Nakamori[22], Kazuhisa Yoshiya[22], Fukuki Saito[22], Tomoyuki Yoshihara[22], Daiki Wada[22], Hiromu Iwamura[22], Syuji Kanayama[22], Shuhei Maruyama[22], Takanori Hasegawa[23], Kunihiko Takahashi[23], Tatsuhiko Anzai[23], Satoshi Ito[23], Akifumi Endo[24], Yuji Uchimura[25], Yasunari Miyazaki[26], Takayuki Honda[26], Tomoya Tateishi[26], Shuji Tohda[27], Naoya Ichimura[27], Kazunari Sonobe[27], Chihiro Tani Sassa[27], Jun Nakajima[27], Masumi Ai[28], Takashi Yoshiyama[29], Ken Ohta[29], Hiroyuki Kokuto[29], Hideo Ogata[29], Yoshiaki Tanaka[29], Kenichi Arakawa[29], Masafumi Shimoda[29], Takeshi Osawa[29], Yasushi Nakano[30], Yukiko Nakajima[30], Ryusuke Anan[30], Ryosuke Arai[30], Yuko Kurihara[30], Yuko Harada[30], Kazumi Nishio[30], Yoshikazu Mutoh[31], Tomonori Sato[32], Reoto Takei[32], Satoshi Hagimoto[32], Yoichiro Noguchi[32], Yasuhiko Yamano[32], Hajime Sasano[32], Sho Ota[32], Yusuke Suzuki[33], Sohei Nakayama[33], Keita Masuzawa[33], Tomomi Takano[34], Kazuhiko Katayama[35], Koji Murakami[36], Mitsuhiro Yamada[36], Hisatoshi Sugiura[36], Hirohito Sano[36], Shuichiro Matsumoto[36], Nozomu Kimura[36], Yoshinao Ono[36], Hiroaki Baba[37], Rie Baba[38], Daisuke Arai[38], Takayuki Ogura[38], Hidenori Takahashi[38], Shigehiro Hagiwara[38], Genta Nagao[38], Shunichiro Konishi[38], Ichiro Nakachi[38], Hiroki Tateno[39], Isano Hase[39], Shuichi Yoshida[39], Shoji Suzuki[39], Miki Kawada[40], Hirohisa Horinouchi[41], Fumitake Saito[42], Keiko Mitamura[43], Masao Hagihara[44], Junichi Ochi[42], Tomoyuki Uchida[44], Ryuya Edahiro[45,46], Yuya Shirai[45,46], Kyuto Sonehara[46,47], Tatsuhiko Naito[46], Kenichi Yamamoto[46], Shinichi Namba[46], Ken Suzuki[46], Takayuki Shiroyama[45], Yuichi Maeda[45], Takuro Nii[45], Yoshimi Noda[45], Takayuki Niitsu[45], Yuichi Adachi[45], Takatoshi Enomoto[45], Saori Amiya[45], Reina Hara[45], Toshihiro Kishikawa[46,48,50], Shuhei Yamada[49], Shuhei Kawabata[49], Noriyuki Kijima[49], Masatoshi Takagaki[49,54], Noa Sasa[46,48], Yuya Ueno[48], Motoyuki Suzuki[48], Norihiko Takemoto[48], Hirotaka Eguchi[48], Takahito Fukusumi[48], Takao Imai[48], Munehisa Fukushima[48,53], Haruhiko Kishima[49], Hidenori Inohara[48], Kazunori Tomono[51], Kazuto Kato[52], Haruhiko Hirata[45], Yoshito Takeda[45], Atsushi Kumanogoh[45,47,54,55], Naoki Miyazawa[56], Yasuhiro Kimura[56], Reiko Sado[56], Hideyasu Sugimoto[56], Akane Kamiya[57], Naota Kuwahara[58], Akiko Fujiwara[58], Tomohiro Matsunaga[58], Yoko Sato[58], Takenori Okada[58], Takashi Inoue[59], Toshiyuki Hirano[59], Keigo Kobayashi[59], Hatsuyo Takaoka[59], Koichi Nishi[60], Masaru Nishitsuji[60], Mayuko Tani[60], Junya Suzuki[60], Hiroki Nakatsumi[60], Hidefumi Koh[61], Tadashi Manabe[61], Yohei Funatsu[61], Fumimaro Ito[61], Takahiro Fukui[61], Keisuke Shinozuka[61], Sumiko Kohashi[61], Masatoshi Miyazaki[61], Tomohisa Shoko[62], Mitsuaki Kojima[62], Tomohiro Adachi[62], Motonao Ishikawa[63], Kenichiro Takahashi[64], Kazuyoshi Watanabe[65], Yoshihiro Hirai[66], Hidetoshi Kawashima[66], Atsuya Narita[66], Kazuki Niwa[67], Yoshiyuki Sekikawa[67], Hisako Sageshima[68], Yoshihiko Nakamura[69], Kota Hoshino[69], Junichi Maruyama[69], Hiroyasu Ishikura[69], Tohru Takata[70], Takashi Ogura[71], Hideya Kitamura[71], Eri Hagiwara[71], Kota Murohashi[71], Hiroko Okabayashi[71], Takao Mochimaru[72,73], Shigenari Nukaga[72], Ryosuke Satomi[72], Yoshitaka Oyamada[73], Nobuaki Mori[74], Tomoya Baba[75], Yasutaka Fukui[75], Mitsuru Odate[75], Shuko Mashimo[75], Yasushi Makino[75], Kazuma Yagi[76], Mizuha Hashiguchi[76], Junko Kagyo[76], Tetsuya Shiomi[76], Kodai Kawamura[77], Kazuya Ichikado[77], Kenta Nishiyama[77], Hiroyuki Muranaka[77], Kazunori Nakamura[77], Satoshi Fuke[78], Hiroshi Saito[78], Tomoya Tsuchida[79], Shigeki Fujitani[80], Mumon Takita[80], Daiki Morikawa[80], Toru Yoshida[80], Takehiro Izumo[81], Minoru Inomata[81], Naoyuki Kuse[81], Nobuyasu Awano[81], Mari Tone[81], Akihiro Ito[82], Toshio Odani[83], Masaru Amishima[84], Takeshi Hattori[84], Yasuo Shichinohe[85], Takashi Kagaya[86], Toshiyuki Kita[86], Kazuhide Ohta[86], Satoru Sakagami[86], Kiyoshi Koshida[86], Morio Nakamura[86], Koutaro Yokote[87], Taka-Aki Nakada[88], Ryuzo Abe[88], Taku Oshima[88], Tadanaga Shimada[88], Kentaro Hayashi[89], Tetsuo Shimizu[89], Yutaka Kozu[89], Hisato Hiranuma[89], Yasuhiro Gon[89], Namiki Izumi[90], Kaoru Nagata[90], Ken Ueda[90], Reiko Taki[90], Satoko Hanada[90], Naozumi Hashimoto[91], Keiko Wakahara[91], Koji Sakamoto[91], Norihito Omote[91], Akira Ando[91], Yu Kusaka[92], Takehiko Ohba[92], Susumu Isogai[92], Aki Ogawa[92],

Takuya Inoue[92], Nobuhiro Kodama[93], Yasunari Kaneyama[93], Shunsuke Maeda[93], Takashige Kuraki[94], Takemasa Matsumoto[94], Masahiro Harada[95], Takeshi Takahashi[95], Hiroshi Ono[95], Toshihiro Sakurai[95], Takayuki Shibusawa[95], Yusuke Kawamura[96], Akiyoshi Nakayama[96], Hirotaka Matsuo[96], Yoshifumi Kimizuka[97], Akihiko Kawana[97], Tomoya Sano[97], Chie Watanabe[97], Ryohei Suematsu[97], Makoto Masuda[98], Aya Wakabayashi[98], Hiroki Watanabe[98], Suguru Ueda[98], Masanori Nishikawa[98,], Ayumi Yoshifuji[99], Kazuto Ito[99], Saeko Takahashi[100], Kota Ishioka[100], Yusuke Chihara[101], Mayumi Takeuchi[101], Keisuke Onoi[101], Jun Shinozuka[101], Atsushi Sueyoshi[101], Yoji Nagasaki[102], Masaki Okamoto[103,104], Sayoko Ishihara[105], Masatoshi Shimo[105], Yoshihisa Tokunaga[103,104], Masafumi Watanabe[106], Sumito Inoue[106], Akira Igarashi[106], Masamichi Sato[106], Nobuyuki Hizawa[107], Yoshiaki Inoue[108], Shigeru Chiba[109], Kunihiro Yamagata[110], Yuji Hiramatsu[111], Hirayasu Kai[110], Satoru Fukuyama[112], Yoshihiro Eriguchi[113], Akiko Yonekawa[113], Keiko Kan-o[112], Koichiro Matsumoto[112], Kensuke Kanaoka[114], Shoichi Ihara[114], Kiyoshi Komuta[114], Koichiro Asano[115], Tsuyoshi Oguma[115], Yoko Ito[115], Satoru Hashimoto[116], Masaki Yamasaki[116], Yu Kasamatsu[117], Yuko Komase[118], Naoya Hida[118], Takahiro Tsuburai[118], Baku Oyama[118], Yuichiro Kitagawa[119], Tetsuya Fukuta[119], Takahito Miyake[119], Shozo Yoshida[119], Shinji Ogura[119], Minoru Takada[120], Hidenori Kanda[120], Shinji Abe[121], Yuta Kono[121], Yuki Togashi[121], Hiroyuki Takoi[121], Ryota Kikuchi[121], Shinichi Ogawa[122], Tomouki Ogata[122], Shoichiro Ishihara[122], Arihiko Kanehiro[123,124], Shinji Ozaki[123], Yasuko Fuchimoto[123], Sae Wada[123], Nobukazu Fujimoto[124], Kei Nishiyama[125], Mariko Terashima[126], Satoru Beppu[126], Kosuke Yoshida[126], Osamu Narumoto[127], Hideaki Nagai[127], Nobuharu Ooshima[127], Mitsuru Motegi[128], Akira Umeda[129], Kazuya Miyagawa[130], Hisato Shimada[131], Mayu Endo[132], Yoshiyuki Ohira[133], Hironori Sagara[133], Akihiko Tanaka[133], Shin Ohta[133], Tomoyuki Kimura[133], Yoko Shibata[134], Yoshinori Tanino[134], Takefumi Nikaido[134], Hiroyuki Minemura[134], Yuki Sato[134], Yuichiro Yamada[135], Takuya Hashino[135], Masato Shinoki[135], Hajime Iwagoe[136], Hiroshi Takahashi[137], Kazuhiko Fujii[137], Hiroto Kishi[137], Tomoo Ishii[138], Masayuki Kanai[139], Tomonori Imamura[139], Tatsuya Yamashita[139], Masakiyo Yatomi[140], Toshitaka Maeno[140], Shinichi Hayashi[141], Mai Takahashi[141], Mizuki Kuramochi[141], Isamu Kamimaki[141], Yoshiteru Tominaga[141], Mitsuyoshi Utsugi[142], Akihiro Ono[142], Toru Tanaka[143], Takeru Kashiwada[143], Kazue Fujita[143], Yoshinobu Saito[143], Masahiro Seike[143], Masahiro Kanai[144], Ryunosuke Saiki[145], Takayoshi Hyugaji[146], Eigo Shimizu[146], Kotoe Katayama[146], Satoru Miyawaki[147], Meiko Takahashi[148], Fumihiko Matsuda[148], Yosuke Omae[149], Yasuhito Nannya[145], Takafumi Ueno[150], Yukinori Okada[46,47,55,151], Ryuji Koike[152], Yuko Kitagawa[153], Katsushi Tokunaga[149], Akinori Kimura[154], Seiya Imoto[146], Satoru Miyano[23], Seishi Ogawa[145,155,156], Takanori Kanai[13], Koichi Fukunaga[1]

1 Division of Pulmonary Medicine, Department of Medicine, Keio University School of Medicine, Tokyo, Japan
2 Department of Infectious Diseases, Keio University School of Medicine, Tokyo, Japan.
3 Department of Respiratory Medicine, Juntendo University Faculty of Medicine and Graduate School of Medicine, Tokyo, Japan.
4 Department of General Medicine, Juntendo University Faculty of Medicine and Graduate School of Medicine, Tokyo, Japan.
5 Department of Emergency and Disaster Medicine, Juntendo University Faculty of Medicine and Graduate School of Medicine, Tokyo, Japan.
6 Department of Cardiovascular Biology and Medicine, Juntendo University Faculty of Medicine and Graduate School of Medicine, Tokyo, Japan.
7 Department of Internal Medicine and Rheumatology, Juntendo University Faculty of Medicine and Graduate School of Medicine, Tokyo, Japan.
8 Department of Nephrology, Juntendo University Faculty of Medicine and Graduate School of Medicine, Tokyo, Japan.
9 Atopy (Allergy) Research Center, Juntendo University Graduate School of Medicine, Tokyo, Japan.
10 Department of Emergency and Critical Care Medicine, Keio University School of Medicine, Tokyo, Japan
11 Department of Anesthesiology, Keio University School of Medicine, Tokyo, Japan.
12 Department of Laboratory Medicine, Keio University School of Medicine, Tokyo, Japan
13 Division of Gastroenterology and Hepatology, Department of Medicine, Keio University School of Medicine, Tokyo, Japan.
14 Keio University Health Center
15 Department of Organoid Medicine, Keio University School of Medicine, Tokyo, Japan.
16 Department of Respiratory Medicine, Osaka Saiseikai Nakatsu Hospital, Osaka, Japan.
17 Department of Infection Control, Osaka Saiseikai Nakatsu Hospital, Osaka, Japan.
18 JCHO (Japan Community Health Care Organization) Saitama Medical Center, Internal Medicine, Saitama, Japan.
19 Department of Respiratory Medicine, Saitama Cardiovascular and Respiratory Center, Kumagaya, Japan.
20 Department of Respiratory Medicine, Tokyo Women's Medical University, Tokyo, Japan.
21 Department of General Medicine, Tokyo Women's Medical University, Tokyo, Japan.
22 Department of Emergency and Critical Care Medicine, Kansai Medical University General Medical Center, Moriguchi, Japan.
23 M&D Data Science Center, Tokyo Medical and Dental University, Tokyo, Japan.
24 Clinical Research Center, Tokyo Medical and Dental University Hospital of Medicine, Tokyo, Japan.
25 Department of Medical Informatics, Tokyo Medical and Dental University Hospital of Medicine, Tokyo, Japan.
26 Respiratory Medicine, Tokyo Medical and Dental University, Tokyo, Japan.
27 Clinical Laboratory, Tokyo Medical and Dental University Hospital of Medicine, Tokyo, Japan.
28 Department of Insured Medical Care Management, Tokyo Medical and Dental University Hospital of Medicine, Tokyo, Japan
29 Fukujuji Hospital, Kiyose, Japan.
30 Kawasaki Municipal Ida Hospital, Department of Internal Medicine, Kawasaki, Japan.
31 Department of Infectious Diseases, Tosei General Hospital, Seto, Japan.
32 Department of Respiratory Medicine and Allergy, Tosei General Hospital, Seto, Japan.
33 Department of Respiratory Medicine, Kitasato University Kitasato Institute Hospital, Tokyo, Japan.
34 School of Veterinary Medicine, Kitasato University, Towada, Japan.
35 Laboratory of Viral Infection I, Department of Infection Control and Immunology, Ōmura Satoshi Memorial Institute & Graduate School of Infection Control Sciences, Kitasato University, Tokyo, Japan.
36 Department of Respiratory Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan
37 Department of Infectious Diseases, Tohoku University Graduate School of Medicine, Sendai, Japan
38 Saiseikai Utsunomiya Hospital, Utsunomiya, Japan.

39 Department of Pulmonary Medicine, Saitama City Hospital, Saitama, Japan.
40 Department of Infectious Diseases, Saitama City Hospital, Saitama, Japan.
41 Department of General Thoracic Surgery, Saitama City Hospital, Saitama, Japan.
42 Department of Pulmonary Medicine, Eiju General Hospital, Tokyo, Japan.
43 Division of Infection Control, Eiju General Hospital, Tokyo, Japan.
44 Department of Hematology, Eiju General Hospital, Tokyo, Japan.
45 Department of Respiratory Medicine and Clinical Immunology, Osaka University Graduate School of Medicine, Suita, Japan.
46 Department of Statistical Genetics, Osaka University Graduate School of Medicine, Suita, Japan.
47 Integrated Frontier Research for Medical Science Division, Institute for Open and Transdisciplinary Research Initiatives, Osaka University, Suita, Japan.
48 Department of Otorhinolaryngology-Head and Neck Surgery, Osaka University Graduate School of Medicine, Suita, Japan.
49 Department of Neurosurgery, Osaka University Graduate School of Medicine, Suita, Japan
50 Department of Head and Neck Surgery, Aichi Cancer Center Hospital, Nagoya, Japan.
51 Division of Infection Control and Prevention, Osaka University Hospital, Suita, Japan.
52 Department of Biomedical Ethics and Public Policy, Osaka University Graduate School of Medicine, Suita, Japan.
53 Department of Otolaryngology and Head and Neck Surgery, Kansai Rosai Hospital, Hyogo, Japan
54 Department of Immunopathology, Immunology Frontier Research Center (WPI-IFReC), Osaka University, Suita, Japan.
55 The Center for Infectious Disease Education and Research (CiDER), Osaka University, Suita, Japan.
56 Department of Respirtory Medicine, Saiseikai Yokohamashi Nanbu Hospital, Yokohama, Japan.
57 Department of Clinical Laboratory, Saiseikai Yokohamashi Nanbu Hospital, Yokohama, Japan.
58 Internal Medicine, Internal Medicine Center, Showa University Koto Toyosu Hospital, Tokyo, Japan.
59 Internal Medicine, Sano Kosei General Hospital, Sano, Japan.
60 Ishikawa Prefectural Central Hospital, Kanazawa, Japan.
61 Tachikawa Hospital, Tachikawa, Japan.
62 Department of Emergency and Critical Care Medicine, Tokyo Women's Medical University Medical Center East, Tokyo, Japan.
63 Department of Medicine, Tokyo Women's Medical University Medical Center East, Tokyo, Japan.
64 Department of Pediatrics, Tokyo Women's Medical University Medical Center East, Tokyo, Japan.
65 Japan Community Health care Organization Kanazawa Hospital, Kanazawa, Japan.
66 Department of Respiratory Medicine, Japan Organization of Occupational Health and Safety, Kanto Rosai Hospital, Kawasaki, Japan.
67 Department of Generai Internal Medicine, Japan Organization of Occupational Health and Safety, Kanto Rosai Hospital, Kawasaki, Japan.
68 Sapporo City General Hospital, Sapporo, Japan.
69 Department of Emergency and Critical Care Medicine, Faculty of Medicine, Fukuoka University, Fukuoka, Japan.
70 Department of Infection Control, Fukuoka University Hospital, Fukuoka, Japan.
71 Kanagawa Cardiovascular and Respiratory Center, Yokohama, Japan.
72 Department of Respiratory Medicine, National Hospital Organization Tokyo Medical Center, Tokyo, Japan.
73 Department of Allergy, National Hospital Organization Tokyo Medical Center, Tokyo, Japan.
74 Department of General Internal Medicine and Infectious Diseases, National Hospital Organization Tokyo Medical Center, Tokyo, Japan.
75 Department of Respiratory Medicine, Toyohashi Municipal Hospital, Toyohashi, Japan.
76 Keiyu Hospital, Yokohama, Japan.
77 Division of Respiratory Medicine, Social Welfare Organization Saiseikai Imperial Gift Foundation, Inc., Saiseikai Kumamoto Hospital, Kumamoto, Japan.
78 KKR Sapporo Medical Center, Department of respiratory medicine, Sapporo, Japan.
79 Division of General Internal Medicine, Department of Internal Medicine, St. Marianna University School of Medicine, Kawasaki, Japan.
80 Departmet of Emergency and Critical Care Medicine, St. Marianna University School of Medicine, Kawasaki, Japan.
81 Japanese Red Cross Medical Center, Tokyo, Japan.
82 Matsumoto City Hostpital, Matsumoto, Japan.
83 Department of Rheumatology, National Hospital Organization Hokkaido Medical Center, Sapporo, Japan.
84 Department of Respiratory Medicine, National Hospital Organization Hokkaido Medical Center, Sapporo, Japan.
85 Department of Emergency and Critical Care Medicine, National Hospital Organization Hokkaido Medical Center, Sapporo, Japan.
86 NHO Kanazawa Medical Center, Kanazawa, Japan.
87 Department of Endocrinology, Hematology and Gerontology, Chiba University Graduate School of Medicine, Chiba, Japan.
88 Department of Emergency and Critical Care Medicine, Chiba University Graduate School of Medicine, Chiba, Japan.
89 Nihon University School of Medicine, Department of Internal Medicine, Division of Respiratory Medicine, Tokyo, Japan.
90 Musashino Red Cross Hospital, Musashino, Japan.
91 Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan.
92 Ome Municipal General Hospital, Ome, Japan.
93 Fukuoka Tokushukai Hospital, Department of Internal Medicine, Kasuga, Japan.
94 Fukuoka Tokushukai Hospital, Respiratory Medicine, Kasuga, Japan.
95 National Hospital Organization Kumamoto Medical Center, Kumamoto, Japan.
96 Department of Integrative Physiology and Bio-Nano Medicine, National Defense Medical College, Tokorozawa, Japan.
97 Division of Infectious Diseases and Respiratory Medicine, Department of Internal Medicine, National Defense Medical College, Tokorozawa, Japan.
98 Department of Respiratory Medicine, Fujisawa City Hospital, Fujisawa, Japan.
99 Department of Internal Medicine, Tokyo Saiseikai Central Hospital, Tokyo, Japan.
100 Department of Pulmonary Medicine, Tokyo Saiseikai Central Hospital, Tokyo, Japan.
101 Uji-Tokushukai Medical Center, Uji, Japan.
102 Department of Infectious Disease and Clinical Research Institute, National Hospital Organization Kyushu Medical Center, Fukuoka Japan.
103 Department of Respirology, National Hospital Organization Kyushu Medical Center, Fukuoka, Japan.

104 Division of Respirology, Rheumatology, and Neurology, Department of Internal Medicine, Kurume University School of Medicine, Kurume, Japan.
105 Department of Infectious Disease, National Hospital Organization Kyushu Medical Center, Fukuoka Japan.
106 Department of Cardiology, Pulmonology, and Nephrology, Yamagata University Faculty of Medicine, Yamagata, Japan.
107 Department of Pulmonary Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan.
108 Department of Emergency and Critical Care Medicine, Facualty of Medicine, University of Tsukuba, Tsukuba, Japan.
109 Departmentof Hematology, Facualty of Medicine, University of Tsukuba, Tsukuba, Japan.
110 Department of Nephrology, Facualty of Medicine, University of Tsukuba, Tsukuba, Japan.
111 Department of Cardiovascular Surgery, Facualty of Medicine, University of Tsukuba, Tsukuba, Japan.
112 Research Institute for Diseases of the Chest, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.
113 Department of Medicine and Biosystemic Science, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan.
114 Daini Osaka Police Hospital, Osaka, Japan.
115 Division of Pulmonary Medicine, Department of Medicine, Tokai University School of Medicine, Isehara, Japan.
116 Department of Anesthesiology and Intensive Care Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan.
117 Department of Infection Control and Laboratory Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan.
118 Department of Respiratory Internal Medicine, St. Marianna University School of Medicine, Yokohama-City Seibu Hospital, Yokohama, Japan.
119 Gifu University School of Medicine Graduate School of Medicine, Emergency and Disaster Medicine, Gifu, Japan.
120 KINSHUKAI Hanwa The Second Hospital, Osaka, Japan.
121 Department of Respiratory Medicine, Tokyo Medical University Hospital, Tokyo, Japan.
122 JA Toride medical hospital, Toride, Japan.
123 Okayama Rosai Hospital, Okayama, Japan.
124 Himeji St. Mary's Hospital, Himeji, Japan.
125 Emergency & Critical Care, Niigata University, Niigata, Japan.
126 Emergency & Critical Care Center, National Hospital Organization Kyoto Medical Center, Kyoto, Japan.
127 National Hospital Organization Tokyo National Hospital, Kiyose, Japan.
128 Fujioka General Hospital, Fujioka, Japan.
129 Department of General Medicine, School of Medicine, International University of Health and Welfare Shioya Hospital, Ohtawara Japan.
130 Department of Pharmacology, School of Pharmacy, International University of Health and Welfare Shioya Hospital, Ohtawara Japan.
131 Department of Respiratory Medicine, International University of Health and Welfare Shioya Hospital, Ohtawara Japan.
132 Department of Clinical Laboratory, International University of Health and Welfare Shioya Hospital, Ohtawara Japan.
133 Department of General Medicine, School of Medicine, International University of
134 Health and Welfare, Narita Japan.
135 Department of Pulmonary Medicine, Fukushima Medical University, Fukushima, Japan.
136 Kansai Electric Power Hospital, Osaka, Japan.
137 Department of Infectious Diseases, Kumamoto City Hospital, Kumamoto, Japan.
138 Department of Respiratory Medicine, Kumamoto City Hospital, Kumamoto, Japan.
139 Tokyo Medical University Ibaraki Medical Center, Inashiki, Japan.
140 Department of Emergency and Critical Care Medicine, Tokyo Metropolitan Police Hospital, Tokyo, Japan.
141 Department of Respiratory Medicine, Gunma University Graduate School of Medicine, Maebashi, Japan.
142 National hospital organization Saitama Hospital, Wako, Japan.
143 Department of Internal Medicine, Kiryu Kosei General Hospital, Kiryu, Japan.
144 Department of Pulmonary Medicine and Oncology, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan
145 Department of Biomedical Informatics, Harvard Medical School, Boston, MA, USA.
146 Department of Pathology and Tumor Biology, Kyoto University, Kyoto, Japan.
147 Division of Health Medical Intelligence, Human Genome Center, the Institute of Medical Science, the University of Tokyo, Tokyo, Japan.
148 Department of Neurosurgery, Faculty of Medicine, the University of Tokyo, Tokyo, Japan.
149 Center for Genomic Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan.
150 Genome Medical Science Project (Toyama), National Center for Global Health and Medicine, Tokyo, Japan.
151 Department of Biomolecular Engineering, Graduate School of Tokyo Institute of Technology, Tokyo, Japan.
152 Laboratory of Statistical Immunology, Immunology Frontier Research Center (WPI-IFReC), Osaka University, Suita, Japan.
153 Medical Innovation Promotion Center, Tokyo Medical and Dental University, Tokyo, Japan.
154 Department of Surgery, Keio University School of Medicine, Tokyo, Japan.
155 Institute of Research, Tokyo Medical and Dental University, Tokyo, Japan.
156 Institute for the Advanced Study of Human Biology (WPI-ASHBi), Kyoto University, Kyoto, Japan.
157 Department of Medicine, Center for Hematology and Regenerative Medicine, Karolinska Institute, Stockholm, Sweden.

Declaration of Competing Interest

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