We acknowledge that our assessment could be limited by the application of retrospective and descriptive methods involving analyses of publicly available surveillance data. It is possible that the temporal relationship between the seasonal influenza pattern and social distancing strategy implementation had occurred coincidentally by chance because heterogeneity of influenza seasons is a well-known phenomenon. Previous research suggested that despite the marked fluctuations of peak amplitudes and peak times, epidemic duration is often conserved (*2*). However, occurrence of a deformed seasonal pattern in the setting of the outbreak of infection with SARS-CoV-2 served as a natural experiment for supporting the evaluation of the impacts of social distancing in mitigating influenza virus transmission (*6*,*7*).

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Three Patients with COVID-19 and Pulmonary Tuberculosis, Wuhan, China, January–February 2020

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During January–February 2020, coronavirus disease (COVID-19) and tuberculosis were diagnosed for 3 patients in Wuhan, China. All 3 patients had COVID-19 pneumonia. One severely ill patient died after acute respiratory distress syndrome developed. Clinicians and public health officials should be aware of underlying chronic infections such as tuberculosis in COVID-19 patients.

The leading cause of death from a single infectious agent is tuberculosis (TB) (*1*). Globally, an estimated 1.7 billion persons are infected with *Mycobacterium*

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tuberculosis (*2*), and a country with one of the highest TB burdens in the world is China (*2*,*3*). Co-infection with severe acute respiratory syndrome coronavirus (*4*,*5*) or Middle East respiratory syndrome coronavirus (*6*) and *M. tuberculosis* has been associated with intensive care unit admission. As severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerges, we report 2 patients with COVID-19 and laboratory-confirmed TB and 1 with COVID-19 and clinically diagnosed TB in China.

Patient 1 was a 50-year-old man who became ill with fever and productive cough on December 25, 2019. Pulmonary TB had been diagnosed for this patient 20 years ago, for which he received anti-TB treatment for 6 months (Table; Appendix Figure 1, https://wwwnc.cdc.gov/EID/article/26/11/20-1536-App1.pdf). At hospital admission, chest auscultation detected bilateral rhonchi and wet rales. While hospitalized, the patient experienced continuous fever, respiratory distress, and hypoxia. A computed tomography (CT) scan of his chest showed bilateral emphysema, bullous cysts, and right pleural effusion. The pleural effusion contained elevated concentrations of adenosine deaminase (ADA) and lactate dehydrogenase (LDH), and results of a Rivalta test for pleural effusion and *M. tuberculosis* DNA tests were positive. Sputum samples were positive for acid-fast bacilli (AFB) and for *M. tuberculosis* DNA and RNA. On January 28, 2020, a chest CT scan showed progression of bilateral patchy ground-glass opacities (Appendix Figure 2). The diagnosis was severe pneumonia, laboratory-confirmed active pulmonary TB, anemia, and hypoproteinemia. The patient received anti-TB and corticosteroid treatments and oxygen therapy. The patient's dyspnea gradually deteriorated; subsequently, acute respiratory distress syndrome developed. On January 29, he died of respiratory and circulatory failure; a throat swab sample taken that day was positive for SARS-CoV-2 RNA.

Patient 2 was a 44-year-old man who became ill with fever, fatigue, headache, and dry cough on January 16. Chest CT scan showed bilateral patchy ground-glass opacities and pleural effusion (Appendix Figure 3). On February 14, a chest CT scan showed signs of cavitation, which according to the patient's medical records were new, and a throat swab sample tested positive for SARS-CoV-2 RNA. At admission, the patient had tachycardia. A TB purified protein derivative skin test showed an induration of 7 × 10 mm. Rivalta test was positive for pleural effusion, which contained elevated concentrations of C-reactive protein, LDH, and ADA (35.1 U/L) and was infiltrated with lymphocytes. Sputum and pleural effusion AFB smears were negative. The clinical diagnosis was active pulmonary TB, tuberculous pleuritis, and pleural effusion. While hospitalized, the patient received antiviral drugs and a fixed-dose combination of isoniazid, rifampicin, pyrazinamide and ethambutol. After admission, the patient was found to have type 2 diabetes mellitus, for which acarbose and metformin were prescribed. His signs and symptoms improved after treatment, and he was discharged on March 3 with anti-TB treatment to be continued.

Patient 3 was a 57-year-old man with a 3-year history of diabetes mellitus who on January 16 became ill with cough. In 2001, pulmonary TB had been diagnosed and considered cured. On January 27, 2020, according to the patient's medical records, a chest CT scan showed signs of TB. On February 3, another CT scan showed bilateral patchy ground-glass opacities (Appendix Figure 4). On February 5, the patient was transferred to Wuhan Pulmonary Hospital, Wuhan, China, where a test for SARS-CoV-2 was positive. At admission, the patient had tachypnea and a peripheral capillary oxygen saturation of 90%. His sputum was positive for *M. tuberculosis* DNA. The diagnosis was severe COVID-19 pneumonia and latent pulmonary TB. While hospitalized, the patient received antibiotics, antiviral drugs, corticosteroids, and oxygen support. On February 7, a chest CT scan showed progression of the ground-glass opacities. Immunoglobulin was administered. Additional CT scans showed gradual improvement, and the patient was discharged on March 2.

All 3 patients with SARS-CoV-2 infection and pulmonary TB had COVID-19 pneumonia; illness was moderate for 1 patient and severe for the other 2. The patient in whom acute respiratory distress syndrome developed died of respiratory and circulatory failure.

In consideration of the high disease burden of TB and the rapid spread of COVID-19, the potential effects of a possible interaction between the 2 infections requires attention (*7*; P. Glaziou, unpub. data, https://www.medrxiv.org/content/10.1101/2020.04.28.20079582v1). As for general COVID-19 patients, the spectrum of disease for COVID-19 patients with TB can vary from moderate to severe respiratory illness and even death. Underlying conditions including chronic obstructive pulmonary disease, diabetes, hypertension, and malignancy have been associated with more severe outcomes in COVID-19 patients (*8*). However, in our study, the outcome for 1 of the 3 co-infected patients was severe despite his having no other known conditions thought to predispose him to severe COVID-19. Clinicians and public health officials should remain aware of heightened risks caused by chronic infections such as TB in COVID-19 patients.

Table. Clinical characteristics and laboratory results for 3 patients with COVID-19 and TB, Wuhan, China, January–February 2020*

Characteristics	Patient 1	Patient 2	Patient 3
Age, y	50	44	57
Smoker	+	+	–
Underlying medical conditions†	–	+	+
Signs and symptoms‡			
Fever	+	+	+
Cough	+	+	+
Fatigue	+	+	+
Wheeze	+	+	+
Chills	–	+	–
Weight loss	+	+	+
Night sweats	NA	+	–
Vomiting	–	–	–
Diarrhea	–	–	–
Tachycardia	–	+	–
Tachypnoea	+	–	+
Laboratory findings§			
Leukocyte count, × 10^9 cells/L (reference range 3.5–9.5 × 10^9 cells/L)	10.4 (↑)	6.86	8.86
Neutrophil count, ×10^9 cells/L (reference range 1.8–6.3 × 10^9 cells/L)	8.74 (↑)	4.35	7.74 (↑)
Lymphocyte count ×10^9 cells/L (reference range 1.1–3.2 × 10^9 cells/L)	0.73 (↓)	1.75	0.74 (↓)
T-cell count, cells/μL (reference range 690–2,540 cells/μL)	NA	1,092.92	282.12 (↓)
CD4+ T-cell percentage (reference range 40%–57%)	NA	25.3 (↓)	25.91 (↓)
CD4+ T-cell count, cells/μL (reference range 410–1,590 cells/μL)	NA	415.51	138.91 (↓)
CD8+ T-cell percentage (reference range 8%–37%)	NA	36.67	19.37
CD8+ T-cell count, cells/μL (reference range 190–1,140 cells/μL)	NA	602.14	103.8 (↓)
CD4+ to CD8+ T-cell count ratio (reference range 0.71–2.78)	NA	0.69 (↓)	1.34
Hemoglobin, g/L (reference range 130–175 g/L)	83 (↓)	127 (↓)	134
Platelet count, ×10^9/L (reference range 125–350 10^9/L)	430 (↑)	280	218
Activated partial thromboplastin time, s (reference range 27–45 s)	45.5 (↑)	36.4	30.8
Prothrombin time, s (reference range 11–16 s)	18.4 (↑)	13.3	16.29
International normalized ratio (reference range 0.8–1.3)	1.44 (↑)	1.03	1
Fibrinogen, g/dL (reference range 2–4 g/dL)	8.01 (↑)	4.5 (↑)	5.07 (↑)
D–dimer, μg/L (reference range 0–0.5 μg/L)	1.58 (↑)	3.7 (↑)	NA
Alanine aminotransferase, U/L (reference range 9–50 U/L)	9	12	52 (↑)
Aspartate aminotransferase, U/L (reference range 15–40 U/L)	3 (↓)	11 (↓)	45 (↑)
Albumin, g/L (reference range 35–55 g/L)	29.9 (↓)	36.7	35.6
Bilirubin, μmol/L (reference range 0–21 μmol/L)	2.56	5	4.15
Creatinine, μmol/L (reference range 44–115 μmol/L)	38 (↓)	NA	64
Lactate dehydrogenase, U/L (reference range 106–245 U/L)	170	NA	367 (↑)
Creatine kinase, U/L (reference range 24.0–194.0 U/L)	31	24.7	45.1
Creatine kinase isoenzyme, U/L (reference range 0–24 U/L)	9	12.6	22.6
Bicarbonate, mmol/L (reference range 22–27 mmol/L)	21.4	29.9 (↑)	29.8 (↑)
C-reactive protein, mg/L (reference range 0.0–5.0 mg/L)	293.8 (↑)	3.99	44.4 (↑)
Procalcitonin, ng/mL (reference range 0.00–0.25 ng/mL)	0.14	0.04	0.04
Erythrocyte sedimentation rate, mm/h (reference range 0–15 mm/h)	123 (↑)	81 (↑)	53 (↑)
Chest CT findings			
Ground-glass opacities	+	+	+
Pleural effusion	+	+	–
Treatment			
Antibiotics	+	+	+
Anti-TB therapy	+	+	–
Lopinavir/ritonavir	–	+	+
Umifenovir hydrochloride	–	+	–
Interferon–α	–	+	+
Corticosteroid	+	–	+
Immunoglobulin	–	–	+
Oxygen support	+	–	+
Duration of hospitalization, d	22	26	27
Time from illness onset to discharge or death, d	35	47	46
Clinical severity	Severe	Moderate	Severe
Outcome	Died	Survived	Survived

*All patients were male. COVID-19, coronavirus disease; CT, computed tomography; NA, not available; TB, tuberculosis; ↑, values higher than reference range; ↓, values lower than reference range.; +, positive; –, negative.
†Patients 2 and 3 had type 2 diabetes mellitus.
‡At admission to the original hospital.
§Test results after transfer to the Wuhan Pulmonary Hospital.

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H.Y., Y. L., and Z.Y. supervised the study. Z.Y., J. N., H.H., Y.W., and L. Li recruited the patients; collected specimens; and collected demographic, clinical, and laboratory data. J.C., Q.W., and L. Liang plotted the figures; J.C., Q.W., W.L., Q.Z., and Y.L. analyzed the data; H.Y., Y.L., and Z.Y. interpreted the results; J.C. and Q.W. wrote the initial drafts of the manuscript. All authors read and approved the final report.

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Detection of SARS-CoV-2 in Hemodialysis Effluent of Patient with COVID-19 Pneumonia, Japan

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We report detection of severe acute respiratory syndrome coronavirus 2 RNA in hemodialysis effluent from a patient in Japan with coronavirus disease and prolonged inflammation. Healthcare workers should observe strict standard and contact precautions and use appropriate personal protective equipment when handling hemodialysis circuitry from patients with diagnosed coronavirus disease.

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Three Patients with COVID-19 and Pulmonary Tuberculosis, Wuhan, China, January–February 2020

Appendix

Methods

Study Design and Participants

In early 2000, China launched its hospital-based management model for TB, mandating tuberculosis-specific hospitals to diagnose and treat TB patients (*1*). In the region of Wuhan, the Wuhan Pulmonary Hospital (also known as Wuhan Tuberculosis Control Institute) and the Wuhan Jinyintan Hospital are the two designated hospitals for the treatment of TB patients. Due to the outbreak of COVID-19, Wuhan Jinyintan Hospital was converted to provide surge medical care of COVID-19 on January 3, 2020. Since then, the Wuhan Pulmonary Hospital is the only hospital providing medical care for TB patients.

Wuhan Pulmonary Hospital was one of the first COVID-19 designated hospitals. For suspected COVID-19 patients presenting to outpatient departments, or admitted to Wuhan Pulmonary Hospital, respiratory specimens were collected and tested for SARS-CoV-2. Laboratory-confirmed COVID-19 patients who had clinically diagnosed or laboratory-confirmed TB were admitted to Wuhan Pulmonary Hospital, and patients initially hospitalized in other hospitals in Wuhan were transferred. Between January 3 and March 3, 2020, all COVID-19 cases who had clinically diagnosed or laboratory-confirmed TB and were hospitalized in Wuhan Pulmonary Hospital were enrolled in this study.

Diagnoses of Pulmonary tuberculosis and COVID-19

The diagnosis of pulmonary tuberculosis (PTB) was made based on clinical presentation, chest radiography, and laboratory investigation, according to the diagnostic guidelines for PTB issued by the National Health Commission (NHC) of China (*2*). An adult was clinically diagnosed with PTB if the following clinical criteria were met:

i) typical radiographic findings indicating a high clinical probability of PTB;

ii) suspicious symptoms (cough for >2 weeks, with or without night sweats, fatigue, weight loss, chest pain, dyspnea) or signs (tubular breath sound or wet rales on chest auscultation) of PTB, or tuberculosis purified protein derivative (PPD) skin test positive.

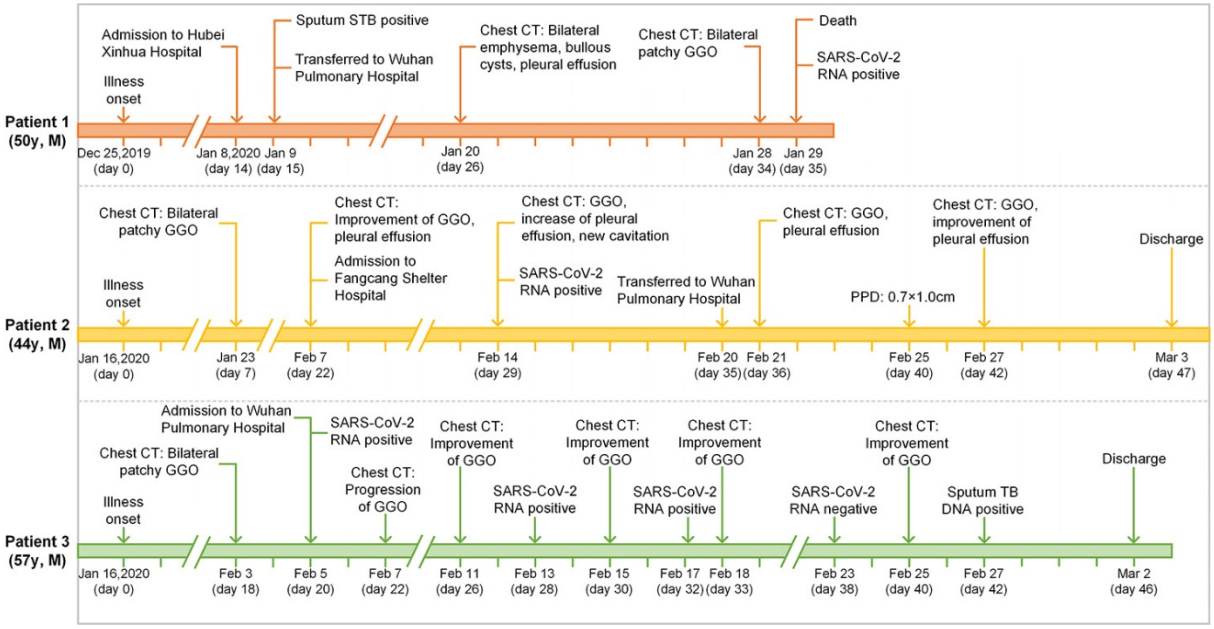
Patients with typical radiographic findings indicating PTB and laboratory detected *Mtb* in their specimens (culture or nucleic acid amplification testing) were classified as laboratory-confirmed PTB cases. Suspected and laboratory-confirmed COVID-19 cases were defined according to the guidelines for COVID-19 issued by China NHC (*3*).

Procedure and Data Collection

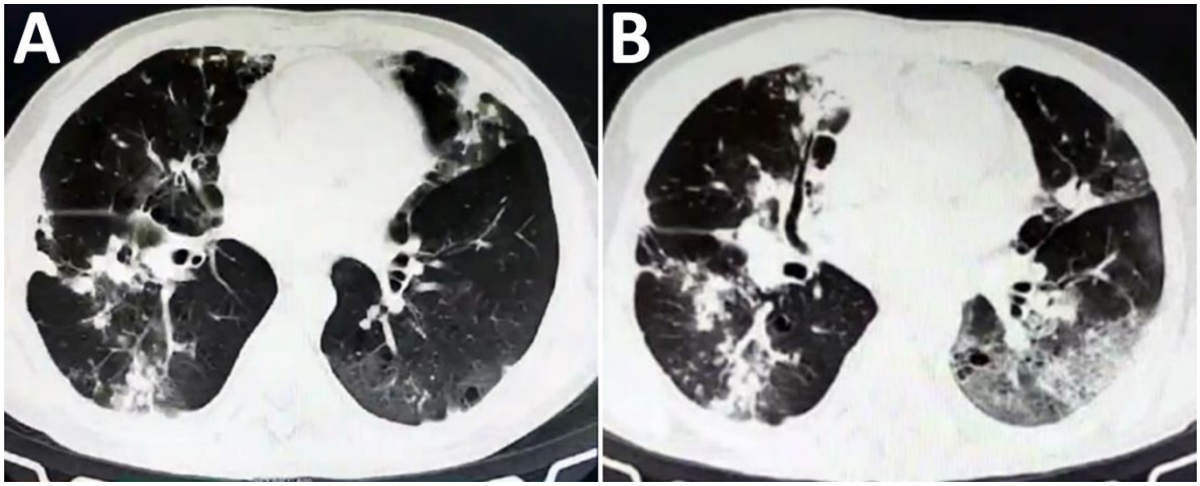
Demographic, clinical, laboratory and radiological data were reviewed from medical records. Data available included detailed information on comorbidities, clinical presentation, complications, and treatments for both COVID-19 and TB. The date of illness onset was defined as the day when COVID-19 symptoms were first noticed and was interpreted as “day 0”.

Ethics

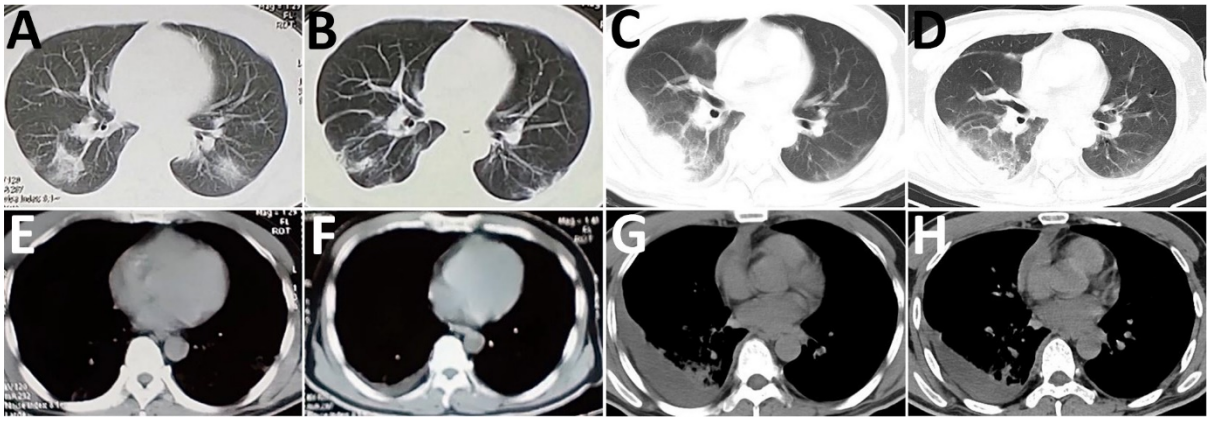
The study protocol was reviewed and approved by the ethics committee of Wuhan Pulmonary Hospital. Written informed consent was obtained from each patient.



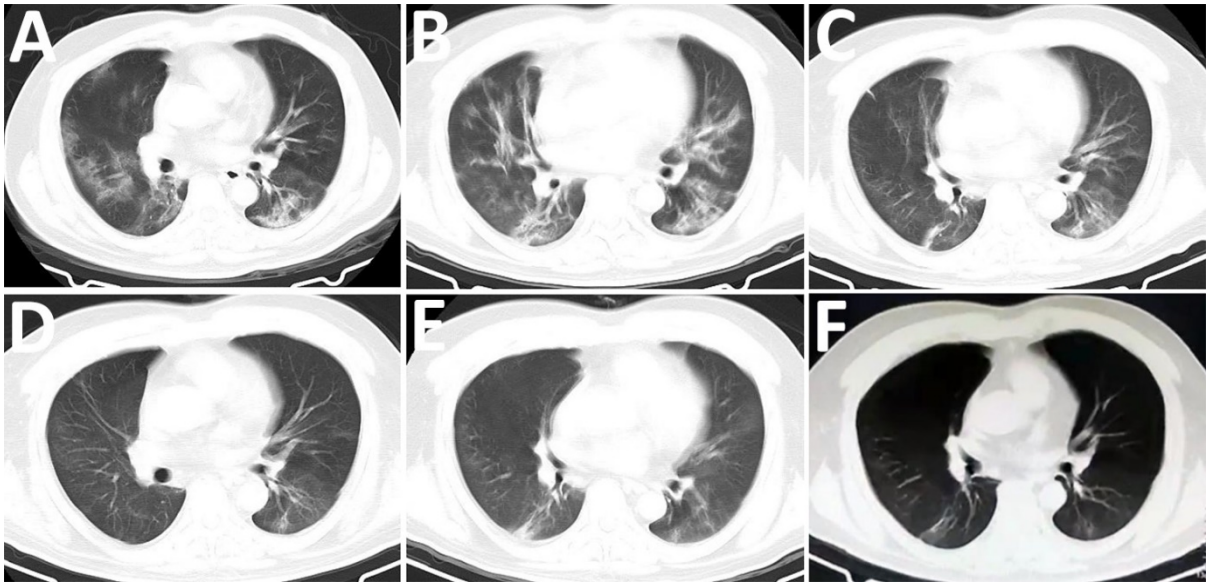
Appendix Figure 1. The clinical course of three patients with SARS-CoV-2 and TB coinfections.



Appendix Figure 2. Chest CT scan images of patient 1. Representative chest CT scan images on January 20 and January 28, both were taken during the patient's hospitalization in Wuhan Pulmonary Hospital.



Appendix Figure 3. Chest CT scans of patient 2. Representative chest CT scan images showing bilateral patchy ground-glass opacities (GGO) in the lung on January 23, and gradual improvement of GGO on February 7, 21, and 27 (upper panels). Representative chest CT scans showing pleural effusion in the lung on February 7, increased pleural effusion on February 21, and improvement on February 27 (lower panels). CT scans were performed in Huangpi District People's Hospital on January 23, in Wuhan Jinyintan Hospital on February 7, and in Wuhan Pulmonary Hospital on February 21 and 27.



Appendix Figure 4. Chest CT scans of patient 3. Representative chest CT scans showing bilateral patchy ground-glass opacities (GGO) in the lung on February 3, a progression of GGO on February 7 and gradual improvement of GGO on February 11, 15, 18, and 25. All CT scans were performed in Wuhan Pulmonary Hospital.

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