Discharged COVID-19 patients testing positive again for SARS-CoV-2 RNA: A minireview of published studies from China

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Abstract
In the ongoing coronavirus disease 2019 (COVID-19) pandemic, one potential cause of concern is that some discharged COVID-19 patients are testing positive again for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA. To better understand what is happening and to provide public health policy planners and clinicians timely information, we have searched and reviewed published studies about discharged patients testing positive again for the SARS-CoV-2 RNA. Our search found 12 reports, all of which described patients in China. Our review of these reports indicates the presence of discharged patients who remain asymptomatic but test positive. However, it is unclear whether they are contagious because a positive reverse transcriptase – polymerase chain reaction (RT-PCR) test does not necessarily indicate the presence of replicating and transmissible virus. Our review suggests the need for timely, parallel testing of different samples, including, for example, fecal specimens, from COVID-19 patients before and after they are discharged from hospitals.

KEYWORDS
coronavirus, infection, pathogenesis, reactivation, respiratory tract, shedding, virus classification

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) results primarily from infection of the respiratory system by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, a member of the beta coronavirus family. Mechanistically, entry is afforded when the surface S (spike) protein of the virus binds to the transmembrane protein, angiotensin-converting enzyme 2, in the plasma membrane of target cells—which include nasal ciliated epithelial cells, nasal goblet/secretory cells, and type II alveolar pneumocytes. The infection initially causes pneumonia-like symptoms, such as cough, fatigue, and myalgia, and later the viral tropism causes damage to the lungs, resulting in ground-glass-opacity (GGO) lesions that can be observed in chest computed tomography (CT) or X-ray images. The diagnosis of COVID-19 considers clinical symptoms, GGO lesions in chest CT or X-ray images, and positive RT-PCR test results for the presence of SARS-CoV-2 RNA in patient samples. For the most part, it is the nasopharyngeal and oropharyngeal swabs that are tested. However, although the reverse transcriptase – polymerase chain reaction (RT-PCR) test is the most widely used method employed for the diagnosis of SARS-CoV-2 infection, a positive result only indicates the presence of viral RNA but is not necessarily proof of the presence of infectious virus.

Most COVID-19 patients recover and are discharged from the hospital. Nevertheless, a small but significant number of COVID-19 patients, especially those with underlying pre-existing conditions, such as hypertension, diabetes, and obesity, die due to complications including acute respiratory distress, respiratory failure, multiorgan failure, and/or shock. The mortality rate of COVID-19 is commonly calculated comparing the numbers of patients who were discharged alive versus those who died by the study end point. In a recent study by Richardson et al employing such methods, of 2634 hospitalized COVID-19 patients in the New York City area, investigators calculated a 21% mortality rate.
For COVID-19 patients to be discharged from hospitals, they must meet strict criteria. For example, the guidelines of the National Health Commission of China state that patients must meet the following four benchmarks before they can be discharged: (a) be afebrile for at least 3 consecutive days, (b) have significantly improved respiratory function, (c) produce two negative SARS-CoV-2 RT-PCR test results at least 24 hours apart, and (d) have significant improvement in lung GGO lesions determined by chest CT or X-ray imaging.\(^\text{11}\) Note that the above discharge standards do not require patients to have complete resolution of lung GGO lesions, rather significant improvement in lung GGO lesions is acceptable when the other criteria are met. In China, it is also required that discharged patients be quarantined for at least 14 days at specific postdischarge quarantine facilities or at home and are monitored for further improvement or any signs of relapse.\(^\text{11}\)

Given these strict discharge criteria, it was surprising to hear the announcement on 25 February 2020 that an estimated 14% of the discharged COVID-19 patients in China’s Guangdong Province tested positive again for SARS-CoV-2 RNA during their postdischarge follow-up examinations. Interestingly, these patients were said to have no COVID-19 symptoms (http://gdio.southcn.com/g/m/2020-02/25/content_190429333.htm). Similarly, the Korean Center for Disease Control and Prevention announced that as of 15 May 2020 there had been 449 individuals who tested positive again after they had been discharged from isolation. Of the 284 individuals for whom symptoms were investigated, 126 (44.7%) showed mild symptoms, such as cough and sore throat (https://www.cdc.go.kr/board/board.es?mid=a30402000000&bid=0030). However, when some of these patients were tested for the presence of SARS-CoV-2 virus, the results were negative. Because of these announcements, several questions emerge—why are there some discharged COVID-19 patients that test positive again for SARS-CoV-2 RNA? Are they discharged from hospitals too early; are they contagious; do they pose a risk to others? Such questions may fuel public fear and uneasiness and call for a careful assessment of public health policies/guidelines regarding the discharge of COVID-19 patients. To learn more about such patients, we conducted a review of identified published reports on the topic of patients who manifest postdischarge RT-PCR positivity for SARS-CoV-2 RNA.

## 2 | MATERIALS AND METHODS

We conducted searches in the PubMed database for reports that describe discharged COVID-19 patients testing positive again for SARS-CoV-2. The following combinations of search keywords were used: recovered patients AND COVID-19; SARS-CoV-2 AND positive again; SARS-CoV-2 AND COVID-19 AND recovered; recovered AND COVID-19 AND positive again; discharged AND COVID-19 AND positive again; discharged AND COVID-19 AND positive; COVID-19 AND recovered AND positive; COVID-19 AND recovered; COVID-19; discharged; and COVID-19 AND positive RT-PCR. As of 27 April 2020, we identified 15 reports, all of which described patients in China. Of the 15 reports, 12 specifically described postdischarge RT-PCR positivity for SARS-CoV-2 RNA in surveillance follow-up examinations. Thus, our review focused on these 12 reports. During the search process, information was extracted by a single reviewer and then confirmed by others.

## 3 | RESULTS

The 12 reports we reviewed describe a total of 90 individuals who tested positive again in postdischarge follow-up examinations.\(^\text{12-24}\) It should be emphasized that all of these patients had confirmed SARS-CoV-2 infection by RT-PCR testing, and most of them had GGO lesions in the lungs and had symptoms such as fever and cough on admission. Furthermore, before being discharged from hospitals, all of them met the four strict discharge criteria, including having at least two negative SARS-CoV-2 RT-PCR test results 24 hours apart.\(^\text{11}\) Therefore, the postdischarge RT-PCR positivity was seen against the backdrop of these two negative RT-PCR results. The discharged patients were quarantined at designated quarantine centers, or in some cases in the same hospital where they had been treated,\(^\text{18}\) or self-quarantine at home in accordance to the postdischarge rules in place.\(^\text{15}\) They all received postdischarge follow-up examinations for signs of clinical symptoms and RT-PCR test for SARS-CoV-2 RNA. In Table 1, we summarize the information about patients who tested positive for SARS-CoV-2 RNA in postdischarge, follow-up examinations in China as described in the 12 published reports.\(^\text{12-24}\) As shown in Table 1, we have included available patient information regarding symptoms and chest CT or X-ray image findings on admission, types of treatment received during hospitalization, and symptoms (or a lack thereof) at the time when the patient tested positive in the postdischarge follow-up examinations. These patients are in all age groups and are of both genders—most of them presented mild to moderate symptoms (fever and cough) on admission, and received treatments with several antiviral drugs, such as oseltamivir, ritonavir, lopinavir, interferon, and arbidol in hospitals (Table 1).\(^\text{12-24}\) Most of the individuals did not have symptoms or worsening of chest CT images when they retested positive (Table 1).\(^\text{12-24}\) In some of the studies, it was stated that patients who tested positive again for SARS-CoV-2 RNA but who were without clinical symptoms were nevertheless readmitted to hospitals for observation. None had symptomatic relapse during the rehospitalization (Table 1).\(^\text{14,16,18,24}\)

In the report by Peng et al.,\(^\text{18}\) it was noted that one patient developed nonorganic insomnia and another patient had increased anxiety during rehospitalization;\(^\text{18}\) in the report by Yuan et al.,\(^\text{20}\) it was noted that eight patients had mild cough at the time of readmission.\(^\text{20}\)

We should point out that except in a few studies\(^\text{12,13}\) it is not clear whether every discharged patient was subjected to RT-PCR test on consecutive days. Nevertheless, we note that in most studies they had tested throat swabs—only a few tested other samples, such as feces, nasopharyngeal swabs, and/or anal swabs—for patients before they were discharged. However, in the postdischarge follow-up examinations, sputum, and anal swabs were the samples mostly tested (Table 1). None of the reports provide any reasons why different
| Authors       | Patient information                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Before discharge                                                                 | RT-PCR specimens tested negative for SARS-CoV-2 RNA before discharge | Postdischarge follow-up                                                                 |
|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------|--------------------------------------------|
| Zhang et al  | A 54-year-old male admitted to a tertiary hospital and then transferred to a designated COVID-19 hospital. His symptoms included fatigue, mild myalgia, fever, and dyspnea. Chest showed bilateral GGO changes in the lungs. He received treatment with arbidol, chloroquine, and low doses of an unspecified hormone. He also received supplemental oxygen. His symptoms and lung lesions were eventually resolved. After hospital discharge, he was quarantined in a medical facility. | Throat swabs                                                                     | Sputum (days 1 and 3)*  
Sputum (days 4, 7-9, 12-13, 15).  
Feces (days 1, 3, and 10). | *Weakly positive  
The Ct (cycle threshold) value for a positive RT-PCR result was <37 and for a weakly positive result it was 37-40. |
| Xing et al   | Patient 1 was a male in his 40 s. On admission, his symptoms included fever, chill, and fatigue, and chest CT showed abnormality in the lower left lobe. He achieved symptom remission and lung CT improvement. After hospital discharge, he was self-quarantine at home, and he did not experience any discomfort.  
Patient 2 was a female in her 20 s. Before admission, her symptoms included headache and pharyngalgia. Chest CT did not show abnormalities in the lungs. After hospital discharge, she was self-quarantine at home, and she did not experience any discomfort. | Throat swabs  
Stool                                                                 | Throat swab (days 4 and 8)*  
Throat swab (day 5).  
Throat swab (day 7). | *Weakly positive  
The Ct value for a positive RT-PCR result was <37 and for a weakly positive result it was 37-40.  
*Weakly positive  
The Ct value for a positive RT-PCR result was <37 and for a weakly positive result it was 37-40. |
| Wang et al   | The patient was an 8-year-old boy. He was admitted to the hospital because of intermittent fever and GGO changes in the lower left lobe on chest CT image. He received unspecified antiviral and symptomatic treatment. After hospital discharge, he was quarantined at home. He was readmitted to the hospital for unexplained fever on postdischarge day 11. After readmission, a chest CT showed disappearance of previous abnormalities. | Throat swabs                                                                     | Throat swab (day 4 of readmission)                                           | Fever  
On the 6th day after readmission, he tested "weakly positive for IgM and strongly positive for IgG antibodies." |
| Lan et al    | This study described four patients (two male and two female) aged 30 to 36 years. Three patients had "fever, cough, or both at onset" and the other was asymptomatic. Their chest CT images showed GGO or mixed GGO and consolidation in the lungs. They had "mild to moderate" symptoms and received treatment with oseltamivir. The symptoms and CT abnormalities of three patients were resolved and CT image of the | Throat swabs                                                                     | Throat swab (on three unspecified dates from days 5 to 13)                 | Absent  
The positive postdischarge RT-PCR results were obtained and duplicated when test kits from two different manufacturers were used.  
In the postdischarge period, all four patients were asymptomatic and chest CT findings showed no change from previous images. They did not have contact with any person. |
### TABLE 1 (Continued)

| Authors | Before discharge | Postdischarge follow-up |
|---------|------------------|-------------------------|
|         | Patient information | RT-PCR specimens tested negative for SARS-CoV-2 RNA before discharge | RT-PCR specimens tested positive for SARS-CoV-2 RNA (postdischarge testing time) | Symptoms | Notes |
| Li et al | 4th patient showed "delicate" patches of GGO. After hospital discharge, all 4 patients were quarantined at home. | Nasal swab, sputum, and feces (on readmission). Stool (unspecified time) | Chest pain and cough | | with respiratory symptoms, and no family members were infected while they were home quarantined. |
| Liu et al | The patient was a 41-year-old male who was "critically ill" and was admitted to ICU. His temperature was 38°C, pulse was 118 beats/min, blood pressure was 121/88 mm Hg, and his pulse oxygen saturation was 90% (oxygen treatment, FIO2, 50%). His chest CT image showed flaky GGO close to the visceral pleura. He received treatment with interferon, traditional Chinese medicine, and oxygen therapy. At the time of his hospital discharge, his chest CT image showed improvement from the first chest CT images. After hospital discharge, he was quarantined at home. On the 18th postdischarge day, he was readmitted to the hospital because of reoccurrence of chest pain and cough. His chest CT showed scattered patches and GGO in both lungs. | Unknown | Nasopharyngeal swab (day 12), anal swab (days 15 and 22) | | The RT-PCR Ct value of ≥40 was defined as a negative test result. |

(Continues)
| Authors          | Patient information                        | Before discharge | RT-PCR specimens tested negative for SARS-CoV-2 RNA before discharge | Postdischarge follow-up | RT-PCR specimens tested positive for SARS-CoV-2 RNA (postdischarge testing time) | Symptoms                        | Notes                                                                 |
|------------------|--------------------------------------------|------------------|-----------------------------------------------------------------------|--------------------------|--------------------------------------------------------------------------------|---------------------------------|----------------------------------------------------------------------|
| Patient 2 (17-year-old female) | Nasopharyngeal swab (day 4), anal swab (11) | Unknown          | Nasopharyngeal swab (day 4), anal swab (11)                          | The RT-PCR Ct value for the nasopharyngeal sample was 35.36 and the anal swab was 35.41. |
| Patient 3 (45-year-old female) | Anal swab (8) | Unknown          | Anal swab (8)                                                        | The RT-PCR Ct value for the nasopharyngeal sample was 28.34. |
| Patient 4 (46-year-old male) | Nasopharyngeal swab (day 8), anal swab (days 10 and 13) | Unknown          | Nasopharyngeal swab (day 8), anal swab (days 10 and 13)             | The RT-PCR Ct value for the nasopharyngeal sample was 32.34 and for the anal swabs were 37.52-39.62. |
| Liu et al<sup>17</sup> | A boy of unspecified age and medical history | Unspecified       | Anal swab (on 9 unspecified days)                                    |                          |                                                                                   |                                 |                                                                      |
| Patient 1 was a 67-year-old male. His symptoms were fever and cough, and his lung X-ray images were abnormal on admission. His symptoms and lung abnormality were resolved during hospitalization. | Unspecified | Samples unspecified (day 11) | Absent                                                                  | He was readmitted to the hospital for 6 days and then discharged. But he was quarantined in the hospital. |
| Patient 2 was the son-in-law of the patient 1. He had fever, chills, and a normal lung X-ray image. During hospitalization, his lung image remained normal and his symptoms were resolved. | Unspecified | Nasopharyngeal swab (day 10) | Nonorganic insomnia and increased anxiety                             | He was readmitted to the hospital for 5 days and then discharged. But he was quarantined in the hospital. |
| Patient 3 was the wife of patient 1. She had cough and a normal lung X-ray image on admission. During hospitalization, her lung image remained normal and her symptoms were resolved. | Unspecified | Nasopharyngeal swab (day 7) | Nonorganic insomnia and increased anxiety                             | She was readmitted to the hospital for 3 days and then discharged. But she was quarantined in the hospital. |
| Patient 4 was the grandson of patient 1. He had cough and a normal lung X-ray image on admission. During hospitalization, his lung image remained normal and symptom was resolved. | Unspecified | Nasopharyngeal swab (day 14) | Absent                                                                  | He was readmitted to the hospital for 5 days and then discharged. But he was quarantined in the hospital. |
| Patient 5 was a 38-year-old female. She presented with fever and normal lung X-ray image on admission. During hospitalization, her lung image remained normal and her symptom was resolved. | Unspecified | Nasal swab (days 4 and 6) | Absent                                                                  | She was readmitted to the hospital with normal CT and without any symptom for 8 days and then discharged. But she was quarantined in the hospital. |
| Patient 6 was a 29-year-old male. He presented with fever and a normal lung X-ray image. During hospitalization, | Unspecified | Throat swab (day 6) and anal swabs (day 7) | Absent                                                                  | He was readmitted to the hospital with normal CT and without any symptoms |
### TABLE 1 (Continued)

| Authors | Before discharge | RT-PCR specimens tested negative for SARS-CoV-2 RNA before discharge | Postdischarge follow-up | RT-PCR specimens tested positive for SARS-CoV-2 RNA (postdischarge testing time) | Symptoms | Notes |
|---------|------------------|---------------------------------------------------------------------|------------------------|---------------------------------------------------------------------------------|---------|-------|
| Tang et al<sup>19</sup> | his lung image remained normal and her symptom was resolved. | | | | for 10 days and then discharged. But he was quarantined in the hospital. | |
| | Patient 7 was a 21-year-old female. She presented with fever, itchy throat, and normal lung X-ray images on admission. During hospitalization, her lung image remained normal and her symptoms were resolved. | | | | She was readmitted to the hospital with an abnormal CT images but without any symptom for 5 days and then discharged. But he was quarantined in the hospital. | |
| Yuan et al<sup>20</sup> | This is a study of postdischarge monitoring of 209 patients. Of the 209 patients, 22 patients tested positive again. No individual patient information before and during hospitalization was provided. | Unspecified | Throat swab (from nine patients at unspecified time) and anal swabs (from 13 patients at unspecified time) | Absent | Unknown | There was no infection discovered among close contacts of these tested positive again patients. A logistic regression model suggested that a high risk of testing positive again was significantly associated with older age and having diarrhea during hospitalization. |
| Li et al<sup>21</sup> | This is a study of postdischarge monitoring of 13 patients. The postdischarge instructions for the patients were: (a) home quarantine for 4 weeks, (b) wear medical masks when going outside and keep distance from others, (c) attend follow-up visit in the first, second, and third week. | Anal swab (unspecified time) and nasopharyngeal swabs (unspecified time) | Eight patients had mild cough | Patients were monitored by RT-PCR analysis of both anal swabs and nasopharyngeal swabs every 3 days. The average time was 7.32 ± 3.86 days from their last negative RT-PCR result to the results turning positive again. An RT-PCR cycle threshold (Ct) value of ≤40 was defined as a positive test result. At the time of tested positive again, 12 patients had improvement in CT image and the other eight patients showed no worsening CT images compared with images before leaving the hospital. During rehospitalization, all patients received treatment with an unspecified lung cleansing and detoxifying herbal medicine. | | |
### TABLE 1 (Continued)

| Authors | Patient information | Before discharge | Postdischarge follow-up |
|---------|---------------------|-----------------|-------------------------|
|         |                     | RT-PCR specimens tested negative for SARS-CoV-2 RNA before discharge | RT-PCR specimens tested positive for SARS-CoV-2 RNA (postdischarge testing time) | Symptoms | Notes |
|         |                     |                  |                         |           |       |

- **Before discharge**
  - fourth week for RT-PCR tests of sputum and fecal samples and routine blood examination and biochemistry tests, and (d) monitor body temperature and other symptoms daily. Of the 13 discharged patients, six tested positive again for SARS-CoV-2 RNA. Before discharge, their symptoms included fever, cough, fatigue, muscle soreness, and sore throat, and their chest CT images showed patchy GGO changes in the lungs. They received treatment with unspecified antiviral and antibiotic, and oxygen inhalation during hospitalization.

- **Postdischarge follow-up**
  - **Patient 1** (female, 72 years old)
    - Respiratory tract
    - Sputum (days 16 and 18)
    - Absent
    - This patient developed a complication of chronic lymphocytic leukemia.

- **Patient 2** (female, 71 years old)
  - Sputum (days 7 and 12)
  - Absent
  - This patient 8 was able to meet discharge criteria again. However, he was tested positive again 7 days after the second discharge.

- **Patient 3** (male, 37 years old)
  - Sputum (days 6 and 7)
  - Absent

- **Patient 4** (male, 73 years old)
  - Sputum (days 5, 6, 8, 16, and 18)
  - Absent

- **Patient 5** (female, 33 years old)
  - Feces (days 8-22)
  - Absent
  - Sputum samples from this patient were repeatedly tested negative. Postdischarge blood and biochemistry tests were normal and CT image was normal.

- **Patient 6** (male, 22 years old)
  - Feces (days 10-24)
  - Absent
  - Sputum samples from this patient repeatedly tested negative. Postdischarge blood and biochemistry tests were normal and CT images was normal.

**Zheng et al**

This was a study of 20 patients (aged 23-57 years, 14 men, 6 women). During hospitalization, all patients had fever, while nine also had cough, and their chest CT images showed GGO and consolidation in the lungs. After hospital discharge, they were quarantined at designated hotels and monitored over a 14-day period.
| Authors | Patient information | Before discharge | RT-PCR specimens tested negative for SARS-CoV-2 RNA before discharge | Postdischarge follow-up | RT-PCR specimens tested positive for SARS-CoV-2 RNA (postdischarge testing time) | Symptoms | Notes |
|---------|---------------------|------------------|---------------------------------------------------------------------|------------------------|------------------------------------------------------------------|---------|-------|
| Patient 1 | Salivary Feces | Feces (day 7) | Absent | All three patients had no increase in their temperature, and had improvement in WBC and lymphocyte counts, as well as their CT images. |
| Patient 2 | Salivary and feces (day 7) | Absent | Compared with the other 17 discharged patients, there were no significant differences in WBC or lymphocyte counts. |
| Patient 3 | Salivary and feces (day 7) | Absent | |

During this period, three patients (see below) tested positive again.

Patient 1 was a 9-year-old boy. His symptoms included fever, sore throat, nasal congestion and runny nose, nausea and gastric appetite, headache, and muscle pain. His chest CT imaging showed cord shadow in the left lower lobe, but the scope was small and limited. He had also had purulent tonsillitis as an underlying condition, and laboratory findings indicated an increased leukocyte count and C-reactive protein level, which were normalized with antibiotic treatment. He received treatment with interferon, unspecified Chinese herbal medicine, vitamin C, and ceftriaxone.

Patient 2 was a 6-year-old boy. His symptoms included fever, nasal congestion and runny nose, and gastric appetite. His chest CT found small GGO changes in the left lower lobe. He had normal range of CRP, WBC, and lymphocyte count but his serum fibrinogen level was lower than normal. He received treatment with interferon, Chinese medicine, and vitamin C.

Patient 3 was an 8-year-old boy. His symptoms included cough and wheezing. His chest CT found light GGO changes in the right lower lobe. He had normal range of CRP, WBC, and lymphocyte count but his serum fibrinogen level was lower than normal. He received treatment with interferon, Chinese medicine, and vitamin C.

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Zhang et al\textsuperscript{23} Patient 1 was a 9-year-old boy. His symptoms included fever, sore throat, nasal congestion and runny nose, nausea and gastric appetite, headache, and muscle pain. His chest CT imaging showed cord shadow in the left lower lobe, but the scope was small and limited. He had also had purulent tonsillitis as an underlying condition, and laboratory findings indicated an increased leukocyte count and C-reactive protein level, which were normalized with antibiotic treatment. He received treatment with interferon, unspecified Chinese herbal medicine, vitamin C, and ceftriaxone.

Patient 2 was a 6-year-old boy. His symptoms included fever, nasal congestion and runny nose, and gastric appetite. His chest CT found small GGO changes in the left lower lobe. He had normal range of CRP, WBC, and lymphocyte count but his serum fibrinogen level was lower than normal. He received treatment with interferon, Chinese medicine, and vitamin C.

Patient 3 was an 8-year-old boy. His symptoms included cough and wheezing. His chest CT found light GGO changes in the right lower lobe. He had normal range of CRP, WBC, and lymphocyte count but his serum fibrinogen level was lower than normal. He received treatment with interferon, Chinese medicine, and vitamin C.

He was readmitted to the hospital without any symptoms or pathological changes in his lungs. He had RT-PCR tests for SARS-CoV-2 RNA in throat swabs on 2 occasions; each time the result was negative.
| Authors     | Patient information                                                                 | Before discharge | RT-PCR specimens tested negative for SARS-CoV-2 RNA before discharge | Postdischarge follow-up | RT-PCR specimens tested positive for SARS-CoV-2 RNA (postdischarge testing time) | Symptoms | Notes                                                                 |
|------------|-------------------------------------------------------------------------------------|------------------|---------------------------------------------------------------------|-------------------------|---------------------------------------------------------------------------------|----------|-----------------------------------------------------------------------|
| Zhang et al | Patient 1 was a 14-year-old male. He was asymptomatic on admission with normal chest CT image. During hospitalization, he received treatment with lopinavir, ritonavir, and arbidol. He also received oxygen via nasal cannula. | Throat swab      | Rectal swab (day 7)                                                 | Absent                  | Chest CT images showed no change from the last scan before discharge. Before retesting positive again, he had not had contact with any suspected or confirmed COVID-19 persons. He was treated with an unspecified Chinese herbal medicine. |
|            | Patient 2 was a 13-year-old male. He was asymptomatic on admission with a normal chest CT image. During hospitalization, he received treatment with oseltamivir, lopinavir, ritonavir, and arbidol. He also received oxygen via nasal cannula. | Throat swab      | Rectal swab (day 5)                                                 | Absent                  | Chest CT images showed no change from the last scan before discharge. Before retesting positive, he had not had contact with any suspected or confirmed COVID-19 person. He was treated with an unspecified Chinese herbal medicine. |
|            | Patient 3 was a 10-month-old female infant with bilateral pneumonia. Her symptoms included fever, dry cough, and malaise. She had a normal chest CT image. During hospitalization, she received treatment with oseltamivir. | Throat swab      | Rectal swab (day 7)                                                 |                        | Chest CT images showed no change from the last scan before discharge. Before retesting positive, she had not had contact with any suspected or confirmed COVID-19 person. She was treated with an unspecified Chinese herbal medicine. |
|            | Patient 4 was a 35-year-old male. He had fever for 1 day and dry cough at onset, a normal chest CT image, and lymphopenia on admission. During hospitalization, he received treatment with oseltamivir, lopinavir, ritonavir, arbidol, and interferon. He also received oxygen via nasal cannula. | Throat swab      | Rectal swab (day 9)                                                 | Absent                  | Chest CT images showed no change from the last scan before discharge. Before retesting positive, he had not had contact with any suspected or confirmed COVID-19 person. He was treated with an unspecified Chinese herbal medicine. |
|            | Patient 5 was a 35-year-old male. He was asymptomatic and had a normal chest CT image on admission. During hospitalization, he received treatment with oseltamivir, lopinavir, ritonavir, arbidol, and interferon. He also received oxygen via nasal cannula. | Throat swab      | Feces (day 11)                                                     | Absent                  | Chest CT images showed no change from the last scan before discharge. Before retesting positive again, he had not had contact with any suspected or confirmed COVID-19 person. He was treated with an unspecified Chinese herbal medicine. |


**TABLE 1** (Continued)

| Authors | Patient information | Before discharge | Postdischarge follow-up |
|---------|---------------------|------------------|-------------------------|
|         |                     | RT-PCR specimens tested negative for SARS-CoV-2 RNA before discharge | RT-PCR specimens tested positive for SARS-CoV-2 RNA (postdischarge testing time) | Symptoms | Notes |
|---------|---------------------|------------------|-------------------------|---------|-------|
| Patient 6 was a 33-year-old male. He was asymptomatic and had a normal chest CT image and lymphopenia on admission. During hospitalization, he received treatment with oseltamivir, lopinavir, ritonavir, arbidol, and interferon. He also received oxygen via nasal cannula. | Throat swab | Throat (day 11) |Absent| Chest CT images showed no change from the last scan before discharge. Before retesting positive, he had not had contact with any suspected or confirmed COVID-19 person. He was treated with an unspecified Chinese herbal medicine. |
| Patient 7 was a 26-year-old male with normal chest CT image on admission. His symptoms included fever, dry cough, and malaise. During hospitalization, he received treatment with oseltamivir, lopinavir, ritonavir, arbidol, and interferon. He also received oxygen via nasal cannula. | Throat swab | • Rectal swab (days 11 and 12) | • Throat swab (day 12) |Absent| Chest CT images showed no change from the last scan before discharge. Before retesting positive, he had not had contact with any suspected or confirmed COVID-19 person. He was treated with an unspecified Chinese herbal medicine. |

Abbreviations: CT, computed tomography; GGO, ground-glass opacity; IgG, immunoglobulin G; WBC, white blood cells.

“*“ is for the explanation in the "Notes" section.
sampling approaches were employed before and after patient discharge.

Most of the reports we reviewed are small case studies and, therefore, do not provide statistics regarding the percentage of patients who retested positive. However, two of the studies examined relatively large numbers of discharged patients. One followed 209 discharged patients and identified 22 patients (10.5%) who tested positive again at least once for SARS-CoV-2 RNA by RT-PCR. The second study followed 172 patients and found 25 patients (14.5%) who similarly retested positive at least once.

### 4 | DISCUSSION

It is somewhat surprising that the studies we found regarding discharged COVID-19 patients testing positive for SARS-CoV-2 RNA described patients in China. It is possible that this results from the strict and vigilant postdischarge monitoring policies in place in China. Although the phenomenon of discharged patients testing positive again for SARS-CoV-2 RNA was officially documented in Korea, our review is limited to published reports from China.

There are several possible explanations for what is happening. First, some of the results could be "false positives." However, a significant number of patients tested positive on different days, and in one report, the positive RT-PCR test results were confirmed for all patients with testing kits from a different manufacturer. Thus, it is unlikely that all results reported were false positives. Second, there remains the possibility that residual virus became active again after the patients had been discharged. Consider the findings from a postmortem pathological examination of the pulmonary tissues from a deceased 78-year-old female COVID-19 patient in China. In this case, the patient met all the discharge criteria, including negative nasopharyngeal swab RT-PCR test results (on 3 consecutive days). Indeed, she would have been discharged from the hospital it was not for the fact that she suddenly died of cardiac arrest. In postmortem examinations, digital PCR test identified SARS-CoV-2 RNA in her lung samples and electron microscopic examination of her lung samples found characteristic coronavirus particles in the ciliated bronchiolar epithelial cells and type II alveolar pneumocytes. The authors of this postmortem study recommend RT-PCR test for SARS-CoV-2 RNA in bronchoalveolar lavage fluid (BALF) for patients because such tests give more reliable information in comparison to the tests of nasopharyngeal swabs, oropharyngeal swabs, and sputum. However, it is unlikely that this recommendation will be adopted because it involves an invasive procedure, which is not suitable solely for a diagnostic purpose.

Our analysis indicates that many of the discharged patients tested positive for SARS-CoV-2 RNA when feces or anal swabs were employed, even though they tested negative at the same time when nasopharyngeal or oropharyngeal or sputum samples were examined. This agrees with other studies showing prolonged presence of SARS-CoV-2 RNA in the gastrointestinal tract of some infected individuals long after they had tested negative in respiratory samples. The positive RT-PCR test result for the presence of SARS-CoV-2 RNA in anal swabs (from discharged patients) is significant because Xiao et al have demonstrated the presence of infectious SARS-CoV-2 virus in the stool samples. In one patient, they demonstrated that the viral load was higher in feces than in respiratory samples collected from the patient 17 to 28 days after symptom onset. Xiao et al also collected fecal samples from 27 other patients, and they detected SARS-CoV-2 RNA at least once in 11 patients. Moreover, they were able to isolate infectious SARS-CoV-2 virus from two of them, which lead them to suggest that "infectious virus in feces is a common manifestation of COVID-19," and that its presence may be a common feature of COVID-19 and a possible mechanism of fecal-oral transmission or fecal-respiratory transmission. Strikingly, Xiao et al also found the presence of a high level of immunoglobulin G antibodies against spike proteins of the SARS-CoV-2 virus and the presence of SARS-CoV-2-neutralizing antibodies in one patient who tested positive for the presence of infectious SARS-CoV-2 virus in the stool. This suggests that precautions should be taken to avoid potential fecal transmission and underscores the importance of testing fecal samples from COVID-19 patients before and after they are discharged from hospitals. One additional point—it should be noted that the RT-PCR tests in place only detect the presence or absence of SARS-CoV-2 RNA, not whether there is the presence of virus. The RNA could be from living, or dead, or antibody neutralized virus. On the bright side, tests of 108 individuals who tested positive again after they were released from isolation indicated the absence of SARS-CoV-2 virus according to the Korea Center for Disease Control and Prevention.

Future studies of larger numbers of patients are needed to determine whether or not some individuals still harbor (active) SARS-CoV-2 virus either in the respiratory system or the stool—or both—when they are tested in postdischarge examination protocols.

It is also possible that the negative RT-PCR test results some patients received before their hospital discharge are false-negatives. For example, the RT-PCR analysis of 1070 samples collected from COVID-19 patients in China by Wang et al demonstrated the following: the positive rate of BALF was 93%; sputum was 72%; nasal swabs were 63%; fibrobronchoscope brush biopsies were 46%; pharyngeal swabs were 32%; and feces were 29%. Given that the viral RNA level in the sputum samples in the early and symptom-progressing phase was significantly higher than that in the recovery phase, and that there appears to be prolonged presence of SARS-CoV-2 RNA in the gastrointestinal tract of some infected individuals long after they had tested negative in their nasopharyngeal or oropharyngeal swabs, it seems that depending on when, where, and how samples are taken from the body and processed—they may or may not contain sufficient amount of SARS-CoV-2 RNA to meet the detection sensitivity of the RT-PCR assays. Thus, it could be that the negative test results for some of the patients described in Table 1 were likely due to a lack of sufficient SARS-CoV-2 virus in the tested throat swabs and nasopharyngeal swabs at the time when the viral load in the upper respiratory system might be low. Therefore, it is important that respiratory and fecal...
samples from recovering COVID-19 patients are tested at the same time points before individuals are to be released from hospitals or examined in follow-up work.

Finally, we should point out that one of the studies we reviewed describes four discharged health care workers who were self-quarantined at home.\textsuperscript{15} It is stated that they took special care at home and that there was no evidence that they transmitted SARS-CoV-2 viruses to their family members,\textsuperscript{15} suggesting that they were not contagious. This is in agreement with the information from the Korean government stating that the close contacts of those discharged patients who tested positive again for SARS-CoV-2 RNA did not redevelop COVID-19 (https://www.cdc.go.kr/board/board.es?mid=a304020000000&bid=0030). Nevertheless, it is prudent that all patients be educated to exercise strict postdischarge quarantine, take measures to avoid close contact with others, and follow instructions for timely postdischarge follow-up examinations.

ACKNOWLEDGMENTS
We wish to thank Mr Michael H. Oppenheim for his excellent editorial assistance.

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**How to cite this article:** Han Z, Battaglia F, Terlecky SR. Discharged COVID-19 patients testing positive again for SARS-CoV-2 RNA: A minireview of published studies from China. *J Med Virol*. 2021;93:262-274. https://doi.org/10.1002/jmv.26250