

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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. after being given inhaled ciclesonide;10 however, no control group was used and it is not known whether these patients would have improved spontaneously. Yet, the possibility that inhaled corticosteroids might prevent (at least partly) the development of symptomatic infection or severe presentations of COVID-19 cannot be ignored. By contrast, a systematic review on the use of systemic corticosteroids to treat SARS, once established, showed no benefit but possible harm.<sup>11</sup>

The potential benefits or harms of inhaled corticosteroids and other treatments for people at risk of SARS-CoV-2 infection or patients with COVID-19 are unclear at present, and no changes to the treatment or management of chronic respiratory conditions, including COPD and asthma, should be considered at this stage. However, collecting accurate data for the comorbidities and previous therapy of patients with COVID-19 will be essential to understanding risk factors for becoming infected, developing symptoms, and being diagnosed, as well as enabling answers to questions about possible benefits or harms of therapy for asthma and COPD during the COVID-19 pandemic. This could be achieved using a standard dataset as advocated by WHO, including information about the presence and severity of comorbidities and all medication that was being taken at the time of infection.

DMGH has received personal fees from AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Pfizer, and Sanofi, and non-financial support from Boehringer Ingelheim and Novartis, outside of the submitted work. RF has received grants from GlaxoSmithKline and Menarini, outside of the submitted work. AA has received grants from AstraZeneca, GlaxoSmithKline, and Menarini, and personal fees from AstraZeneca, Chiesi, GlaxoSmithKline, and Menarini. outside of the submitted work. OS and JRB declare no competing interests.

## \*David M G Halpin, Rosa Faner, Oriol Sibila, Joan Ramon Badia, Alvar Aqusti d.halpin@nhs.net

University of Exeter Medical School, College of Medicine and Health, University of Exeter, Exeter EX1 2LU, UK (DMGH); Respiratory Institute, Hospital Clinic, August Pi i Sunyer Biomedical Research Institute, University of Barcelona and National Spanish Network for Respiratory Research, Barcelona, Spain (RF, OS, JRB, AA)

- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497-506.
- Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of 2 pneumonia. Respirology 2018; 23: 130-37.
- Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of 3 patients dying in relation to COVID-19 in Italy. JAMA 2020; published online March 23. DOI:10.1001/jama.2020.4683.
- CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 - United States, February 12-March 28, 2020. 2020. https://www.cdc.gov/mmwr/volumes/69/wr/pdfs/mm6913e2-H.pdf (accessed April 2, 2020).
- 5 The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)-China, 2020. China CDC Weekly 2020; 2: 113-22
- Liu Y, Liu G, Wu H, Jian W, Wild SH, Gasevic D. Sex differences in non-6 communicable disease prevalence in China: a cross-sectional analysis of the China Health and Retirement Longitudinal Study in 2011. BMJ Open 2017; 7: e017450.
- Su N, Lin J, Chen P, et al. Evaluation of asthma control and patient's perception of asthma: findings and analysis of a nationwide questionnairebased survey in China. J Asthma 2013; 50: 861-70.
- Yamaya M, Nishimura H, Deng X, et al. Inhibitory effects of glycopyrronium, formoterol, and budesonide on coronavirus HCoV-229E replication and cytokine production by primary cultures of human nasal and tracheal epithelial cells. Respir Investig 2020; published online Feb 21. DOI:10.1016/j.resinv.2019.12.005
- Matsuyama S, Kawase M, Nao N, et al. The inhaled corticosteroid ciclesonide blocks coronavirus RNA replication by targeting viral NSP15. bioRxiv 2020; published online March 12. DOI:10.1101/2020.03.11.987016 (preprint)
- 10 Iwabuchi K, Yoshie K, Kurakami Y, Takahashi K, Kato Y. Morishima T. COVID-19. Three cases improved with inhaled ciclesonide in the early to middle stages of pneumonia. 2020. http://www.kansensho.or.jp/uploads/ files/topics/2019ncov/covid19 casereport 200310.pdf (accessed March 27, 2020; in Japanese)
- Stockman LJ, Bellamy R, Garner P. SARS: systematic review of treatment 11 effects. PLoS Med 2006; 3: e343.



## (M) The role of CT in case ascertainment and management of COVID-19 pneumonia in the UK: insights from high-incidence regions

Published Online March 25, 2020 https://doi.org/10.1016/ 52213-2600(20)30132-6 Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the seventh pathogenic human coronavirus to be identified and the third with a predilection for causing potentially fatal pneumonia, after severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome coronavirus. Coronavirus disease (COVID-19) infection is highly transmissible but has a relatively low death rate (1.0-3.5%), except in older people (aged >70 years) with comorbidities.<sup>1,2</sup> It is estimated that 15-20% of people infected develop severe pneumonia and 5-10% require critical care.<sup>2</sup>

COVID-19 preparedness in countries with a surge in new cases have prioritised containment, rapid diagnosis, and fastidious contact tracing. With sustained community transmission, real-time RT-PCR (rtRT-PCR) of viral nucleic acid could be supported by

more versatile diagnostic tools because of concern over false-negative results and limited availability. It has been suggested that CT could play a role in COVID-19 case ascertainment. Driven by a sustained daily increase in new cases, the diagnostic criteria in China originally included CT.

CT abnormalities might predate rtRT-PCR positivity in symptomatic patients and in those without symptoms who subsequently test positive by rtRT-PCR.<sup>3-5</sup> Nevertheless, albeit in a few people, patients who test positive by rtRT-PCR but have a clear CT scan (likely to represent very early infection) have been recognised. Of 36 patients scanned within the first 2 days of symptoms, CT was healthy in half (56%), despite most (>90%) patients testing positive by rtRT-PCR.6

The most common CT features reported in COVID-19 pneumonia are bilateral and subpleural areas of ground-glass opacification, consolidation affecting the lower lobes, or both.<sup>3,6-8</sup> Foci of abnormality might be well demarcated, sometimes with a rounded configuration.<sup>3,5,7,9,10</sup> In the intermediate phase of infection (4-14 days from symptom onset), a so-called crazy-paving pattern might be seen. Other CT findings (eq, a tree-in-bud pattern, nodules, cysts, cavitation, and large volume lymphadenopathy) are uncommon. Differences in the frequency of individual features between pneumonia caused by SARS-CoV-2 and other viruses are beginning to be studied.<sup>11</sup>

However, several aspects of the utility of CT in COVID-19 infection are worth noting. In one study,<sup>2</sup> ground-glass opacification was evident in nearly all 15 people who were asymptomatic (but tested positive by rtRT-PCR) and had been in close contact with patients with confirmed COVID-19. The extent of pulmonary involvement, defined as affected lung segments, was less than in the symptomatic group and more frequently unilateral.

Pan and colleagues,<sup>9</sup> employing serial CTs, described the radiological time course of 21 patients with confirmed mild to moderate infection who survived to discharge. Peak radiological abnormalities occurred at around day 10, followed by gradual regression starting 2 weeks after symptom onset. In a separate analysis, Ai and colleagues<sup>3</sup> reported radiological improvement predating rtRT-PCR becoming negative in 24 (42%) of 57 patients recovering from COVID-19 pneumonia.

Two studies have specifically compared the performance of CT with rtRT-PCR. In a cohort of just over 1000 cases,<sup>3</sup> CT was reported to have a diagnostic sensitivity of 97%, positive predictive value of 65%, and negative predictive value of 83%. CT was abnormal in 308 (75%) of 413 patients who initially tested negative by rtRT-PCR, but were clinically assessed as likely to have (147 [48%] patients) or probably did have (103 [33%] patients) COVID-19 pneumonia. A similar CT sensitivity of 98% (vs 71% for rtRT-PCR; p<0.001) was found in a smaller study of 51 patients, in which just under a third (15 [29%] patients) tested negative on the initial rtRT-PCR.<sup>10</sup>

There are few descriptions of COVID-19 pneumonia in individuals with premorbid pulmonary conditions. Shi and colleagues<sup>4</sup> reported that nine (11%) of 81 patients with confirmed COVID-19 had underlying lung disease; although, the specific details are not known. The potential effect of COVID-19 pneumonia on patients with established respiratory conditions remains unclear at this time.

CT is likely to become increasingly important for the diagnosis and management of COVID-19 pneumonia, given the continuing increase in global cases. The observed evolution from pneumonic injury to respiratory death in this disease suggests a pathological pathway that might be amenable to early CT detection, particularly if the patient is scanned 2 or more days after developing symptoms. Additionally, a negative CT 1 week after the onset of symptoms is reported to have a high negative predictive value for COVID-19 pneumonia. The prognostic value of CT would be further enhanced if it was able to define early radiological abnormalities or patterns that portend a poor outcome. Strict requirements for cleaning of scanning suites in between cases will, however, place considerable challenges on patient throughput. In the rapidly changing landscape of this pandemic, new data are emerging from affected regions on an almost daily basis. In this context, the British Society of Thoracic Imaging have issued guidance that underscores the importance of clinical, laboratory, and radiographic assessment in suspected COVID-19 cases, with CT reserved for patients who are critically ill and for when there is diagnostic uncertainty.<sup>12</sup> Emerging data will clarify if CT also has a role to play in prognostication and disease monitoring.



We declare no competing interests

\*Felix Chua, Darius Armstrong-James, Sujal R Desai, Joseph Barnett, Vasileios Kouranos, Onn Min Kon, Ricardo José, Rama Vancheeswaran, Michael R Loebinger, Joyce Wong, Maria Teresa Cutino-Moquel, Cliff Morgan, Stephane Ledot, Boris Lams, Wing Ho Yip, Leski Li, Ying Cheong Lee, Adrian Draper, Sze Shyang Kho, Elisabetta Renzoni, Katie Ward, Jimstan Periselneris, Sisa Grubnic, Marc Lipman, Athol U Wells, Anand Devaraj f.chua@rbht.nhs.uk

Interstitial Lung Disease Unit, Department of Respiratory Medicine (FC, VK, ER, AUW), Department of Infectious Disease and Medical Mycology (DA-J), Department of Radiology (SRD, ADe), Host Defence Unit, Department of Respiratory Medicine (RJ, MRL), Department of Cardiology, Harefield Hospital (JW), Adult Intensive Care Unit (CM, SL), Royal Brompton Hospital, Royal Brompton and Harefield NHS Foundation Trust, London SW3 6NP, UK: Department of Radiology (JB) and Department of Respiratory Medicine (ML), Royal Free Hospital, Royal Free London NHS Foundation Trust, London, UK; Department of Respiratory Medicine, St Mary's Hospital, Imperial College Healthcare NHS Trust, London, UK (OMK); Department of Integrated Respiratory Medicine, West Hertfordshire Hospitals NHS Trust, Watford, UK (RV); Department of Diagnostic Virology, Barts Health NHS Trust, London, UK (MTC-M): Respiratory Medicine and Intensive Care Unit, Guy's and St Thomas' NHS Foundation Trust, London, UK (BL); Division of Respiratory Medicine, Prince of Wales Hospital, Hong Kong Special Administrative Region, China (WHY); Department of Radiology, Princess Margaret Hospital, Hong Kong Special Administrative Region, China (LL, YCL); Department of Respiratory Medicine (ADr) and Department of Radiology (SG), St George's University Hospitals NHS Foundation Trust, London, UK; Department of Medicine, Sarawak General Hospital, Sarawak, Malaysia (SSK); Department of Respiratory Medicine, Hammersmith Hospital, Imperial College Healthcare NHS Trust, London, UK (KW); and Department of Respiratory Medicine, King's College Hospital NHS Foundation Trust, London, UK (JP)

WHO. Who Director-General's opening remarks at the media briefing on COVID-19. March 3, 2020. https://www.who.int/dg/speeches/detail/whodirector-general-s-opening-remarks-at-the-media-briefing-on-covid-19---3-march-2020 (accessed March 6, 2020).

- Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, on behalf of the Chinese Centre for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)-China, 2020. CCDC Weekly 2020; 2: 113-22.
- 3 Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases Radiology 2020; published online Feb 26. DOI:10.1148/radiol.2020200642.
- Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with 4 COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020; published online Feb 24. DOI:10.1016/51473-3099(20)30086-4.
- Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for typical 2019-nCoV pneumonia: relationship to negative RT-PCR testing. Radiology 2020; published Feb 12. DOI:10.1148/radiol.2020200343
- 6 Bernheim A, Mei X, Huang M, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiology 2020; published Feb 20. DOI:10.1148/radiol.2020200463.
- Chung M, Bernheim A, Mei X, et al. CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology 2020; published online Feb 4. DOI:10.1148/radiol.2020200230.
- Kanne JP, Little BP, Chung JH, et al. Essentials for radiologists on COVID-19: 8 an update-Radiology Scientific Expert Panel. Radiology 2020; published online Feb 27. DOI:10.1148/radiol.2020200527.
- Pan F, Ye T, Sun P, et al. Time course of lung changes on chest CT during 9 recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology 2020; published online Feb 13. DOI:10.1148/radiol.2020200370
- 10 Fang Y. Zhang H. Xie I. et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology 2020; published Feb 19. DOI:0.1148/ radiol.2020200432.
- Bai HX, Hsieh B, Xiong Z, et al. Performance of radiologists in 11 differentiating COVID-19 from viral pneumonia on chest CT. Radiology 2020; published online March 10. DOI:10.1148/radiol.2020200823.
- British Society of Thoracic Imaging. Radiology decision tool for suspected 12 COVID-19. https://www.bsti.org.uk/media/resources/files/NHSE\_BSTI\_ APPROVED\_Radiology\_on\_CoVid19\_v6\_ucQ1tNv.pdf (accessed March 19, 2020).

## (M) Monitoring the COVID-19 epidemic in the context of widespread local transmission

Published Online April 2, 2020 https://doi.org/10.1016/ \$2213-2600(20)30162-4 Coronavirus disease 2019 (COVID-19) is a novel viral disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first detected in Wuhan, China, in December, 2019.1 Given the fast spread, the severity of disease, the increasing number of cases outside China, and the number of affected countries, WHO declared the rapid spread of SARS-CoV-2 a pandemic on March 11, 2020.<sup>2</sup> The availability of reliable surveillance platforms is crucial to monitor the COVID-19 epidemic in a timely manner and to respond with adequate control measures. Since the beginning of the outbreak, different countries have used different testing approaches and criteria, depending on their resources and capacity.

Most national and international public health agencies are publicly reporting epidemic curves, focusing on laboratory-confirmed COVID-19 cases, as well as deaths by COVID-19. However, epidemic curves based on laboratory-confirmed cases, regardless of whether they are presented on a logarithmic or linear scale, show detection of the disease in population groups defined by changing testing criteria and are not representative of the COVID-19 burden in the community in a specific region or country. The absolute number of cases provides a misleading picture of how the epidemic evolves and does not allow comparisons by country or by region within a country.

In almost all countries, COVID-19 testing capacity is low. When no or few cases of disease have been reported in a country, laboratory testing is restricted to travellers presenting with an acute respiratory