antibiotics against Gram-negative bacterial infections with DTR under the existing economic model. The FDA has approved eight antibiotics since 2014. Companies behind five of 15 antibacterials approved since 2009 have gone bankrupt or exited antimicrobial development.

Several large pharmaceutical companies are creating a $1 billion global for-profit venture to acquire or invest in small antibiotic companies and their products. Although industry re-engagement is welcome, economically viable antibiotic development will require substantial market reforms. Small markets and responsible stewardship mandate that reforms, at least partly, delink antibiotic use from reimbursement. Subscription models, in which governments pay fees for access to priority antibiotics, are being piloted in the UK and considered by the US Congress (PASTEUR Act). Ultimately, however, multifaceted international strategies will probably be necessary to salvage antibiotic development.

CJC reports grants and other from Merck, Astellas, and Cidara; grants from Melinta; and other from Medicines Company, Sycexus, Shionogi, and Opex, outside the submitted work. MNH reports grants and other from Merck, Astellas, and Cidara; grants from Melinta; and other from Medicines Company, Sycexus, and Shionogi, outside the submitted work.

*Corneilus J Clancy, M Hong Nguyen
cjc76@pitt.edu

Department of Medicine, Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, USA (CJC); and Department of Medicine, University of Pittsburgh, Pittsburgh, PA, USA (CJC, MNH)

1 Strich JR, Warner S, LaiYL, et al. Needs assessment for novel Gram-negative antibiotics in US hospitals: a retrospective cohort study. Lancet Infect Dis 2020; published online June 4. https://doi.org/10.1016/S1473-3099(20)30352-5

2 Clancy CJ, Nguyen MH. Estimating the size of the United States market for new antibiotics with activity against carbapenem-resistant Enterobacteriaceae. Antimicrob Agents Chemother 2019; 63: AK02733-19

3 Clancy CJ, Potoski BA, Buehrle DJ, Nguyen MH. Estimating the treatment of carbapenem-resistant Enterobacteriaceae infections in the United States using antibiotic prescription data. Open Forum Infect Dis 2019; 6: ofz244.

4 Rex JH. Assessing antibiotic value: DTR, fire extinguishers, and a view from Australia. AMR Solutions blog. 2020. https://amrsolutions2020/06/07/assessing-antibiotic-value-dtr-fire-extinguishers-and-a-view-from-australia/ (accessed July 4, 2020).

5 Silverman E. Pharma giants to unveil major $1 billion venture to push novel antibiotics. STAT. 2020. https://www.statnews.com/pharmalet/2020/06/29/antibiotics-merek-lilly-pfizer-whoo/ (accessed July 4, 2020).

6 Clancy CJ, Nguyen MH. Coronavirus disease 2019, superinfections, and antimicrobial development: what can we expect? Clin Infect Dis 2020; published online May 1. https://doi.org/10.1093/cid/ciaa524.

CT screening for early diagnosis of SARS-CoV-2 infection

Heshui Shi and colleagues reported chest CT image characteristics of subclinical and clinical stages among 81 patients confirmed to have acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Undoubtedly, their work is important for clinical management of coronavirus disease 2019 (COVID-19) pneumonia. However, from an epidemiological perspective, interpretation of CT for early identification of SARS-CoV-2 infection needs to be done with caution.

First, the sensitivity and specificity of CT for screening and diagnosing SARS-CoV-2 infection are unknown. Shi and colleagues reported that the CT findings of 14 (93%) of 15 preclinical patients had ground-glass opacification. However, this study did not include suspected cases that were SARS-CoV-2 negative. RT-PCR results—the gold standard for diagnosing SARS-CoV-2 infection—corresponding to the CT findings were also not reported. Thus, the concordance between CT findings and laboratory tests was unknown. Another study showed a contradictory finding that seven (37%) of 19 asymptomatic cases had positive RT-PCR results for SARS-CoV-2 in the absence of CT changes. Therefore, we have adequate reason to doubt whether CT is suitable for screening asymptomatic infections.

Second, the use of CT for screening and diagnosing COVID-19 might have a disproportionate risk-benefit ratio. Large-scale use of CT will increase radiation exposure of the population, which increases the probability of uncertain biological effects in the long term. Use of CT might also increase the risk of cross-infection if disinfection is not properly implemented. Furthermore, studies have shown that the secondary attack rate among close contacts is 9·6% (95% CI 7·9–11·8), and asymptomatic patients account for only 1·2% of total SARS-CoV-2 infections. These data show the little additional value CT screening has for early diagnosis of COVID-19.

The feasibility of applying CT for early diagnosis of SARS-CoV-2 infection needs more supportive evidence. We believe that use of CT in screening or early diagnosis in high-risk groups should balance risks and benefits to reduce radiation dose and potential disease burden. On the basis of current evidence and experience, we suggest that there should be clear criteria for the use of CT in diagnosis of SARS-CoV-2 infection. One criterion would be to have symptoms or signs of infection or to identify close contacts and have a nucleic acid screening test; another would be to treat or determine the course of the disease. Otherwise, CT should not be recommended for screening or early diagnosis.

We declare no competing interests. YH and WC contributed equally to this work.

Yongshun Huang, Weibin Cheng, Na Zhao, Hongying Qu,* Junzhang Tian
jz.tian@163.com

Department of Clinical Laboratory (YH, NZ, HQ) and Guangdong Provincial Key Laboratory of Occupational Disease Prevention and Treatment (YH, NZ, HQ), Guangdong Province Hospital for Occupational Disease Prevention and Treatment, Guangzhou, Guangdong, China; and Institute for Healthcare Artificial Intelligence Application, Guangdong Second Provincial General Hospital, Guangzhou, Guangdong 510337, China (WC, JT)

1 Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020; published online Feb 24. https://doi.org/10.1016/S1473-3099(20)30085-4.
Correspondence

2 Zhibin H, Song C. Screening and management of asymptomatic infection of coronavirus disease 2019 (COVID-19). Chin J Prev Med 2020; published online March 9. DOI:10.3760/cma.j.cn112150-20200229-00220.

3 Fernandez-Antoran D, Piedrafita G, Murai K, et al. Outpacing p53 mutant cells in the normal esophagus by redox manipulation. Cell Stem Cell 2019; 25: 29–41.

4 Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in Shenzhen China: analysis of 391 cases and 1285 of their close contacts. medRxiv 2020; published online March 4. DOI:10.1101/2020.03.03.20028423 (preprint).

5 Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus disease (COVID-19) in China. Zhonghua Lixue Bingxue Za Zhi 2020; 41: 145–51 (in Chinese).

Authors’ reply

We appreciate the concerns raised by Yongshun Huang and colleagues regarding our Article on radiological findings in coronavirus disease 2019 (COVID-19). During the outbreak of COVID-19 in China in January, and February, 2020, timely diagnosis was a crucial step for infection control, especially in the epidemic area of Wuhan, Hubei province. However, RT-PCR kits were not sufficiently provided to hospitals in Wuhan until Jan 16, 2020. Before then, there was less capacity of kits to meet the rapidly increasing clinical demand. Furthermore, the total positive rate of RT-PCR for throat swab samples was reported to be less than 60%. The diagnostic sensitivity of viral pneumonia by chest radiography was relatively low, whereas CT had a high sensitivity for diagnosis of COVID-19, making it a potential primary tool for COVID-19 detection in epidemic areas. Additionally, according to the guideline for diagnosis and treatment of COVID-19 by the Chinese Ministry of Health (fifth trial edition), clinically suspected cases in Hubei province were mainly those with imaging features consistent with pneumonia.

We agree that there should be clear criteria for CT use in diagnosis of COVID-19. In fact, we do not recommend CT for screening or early diagnosis in all areas or for all populations. In our study, group 1 (preclinical) included health-care workers (ten nurses and five physicians) from two hospitals in Wuhan, who were on the frontline during the outbreak peak. All 15 participants had close contact with confirmed cases and willingly underwent CT scanning as a screening measure. Our Article retrospectively included this group, mainly to illustrate the imaging findings in the subclinical phase, which might also be incidentally found in patients who are imaged for other reasons. Based on this discovery in an epidemic area, we have proposed the potential role of CT in asymptomatic high-risk individuals with a history of exposure to COVID-19 patients in epidemic areas. Compared with another recent publication, the discrepancy in CT positive rates might be attributed to variable sample sizes, different demographic features, and potential retrospective selection bias.

In the epidemic area, all CT scans were done in accordance with strict infection control protocol to avoid cross-infection. We agree that use of CT for screening or diagnosis has a disproportionate risk-benefit ratio. Fortunately, under well controlled epidemic conditions in Wuhan, the RT-PCR assay or severe acute respiratory syndrome coronavirus 2 antibody test are the first choices for screening for COVID-19 at present.

We declare no competing interests.

Heshui Shi, Xiaoyu Han, Yukun Cao, Osamah Alwailid, *Chuansheng Zheng
hqczxh@sina.com
Department of Radiology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei 430022, China (HS, XH, YC, OA, CZ); and Hubei Province Key Laboratory of Molecular Imaging, Wuhan, Hubei, China (HS, XH, YC, OA, CZ)
1 Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020; published online Feb 24. https://doi.org/10.1016/S1473-3099(20)30086-4.
2 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.202002642.

3 Franquet T. Imaging of pulmonary viral pneumonia. Radiology 2011; 260: 18–39.
4 General Office of National Health Committee. Notice on the issuance of a program for the diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (fifth trial edition). Feb 5, 2020. http://www.nhc.gov.cn/jylj/s9520/202002/e84bd30142ab4d8982326326e4db22ea.shtml (accessed March 20, 2020).
5 Zhibin H, Song C. Screening and management of asymptomatic infection of coronavirus disease 2019 (COVID-19). Chin J Prev Med 2020; published online March 8. DOI:10.3760/cma.j.cn112150-20200229-00220.

Invisible spread of SARS-CoV-2

We read with interest Adam Kucharski and colleagues’ mathematical modelling study of the early dynamics of coronavirus disease 2019 (COVID-19). We agree that a stochastic transmission model might best fit with the reality around the Huanan Seafood Wholesale Market, which was the origin of the COVID-19 outbreak and 1 mile away from our hospitals in Wuhan. We appreciate the work making use of different datasets and considering travel. However, we have concerns about the clinical and strategic values of this work.

First, the authors separated exposed (and not yet symptomatic) individuals from infectious (and symptomatic) individuals. Clinically, both groups are contagious. We wonder if they considered separately for these two groups the correlation of variation in the viral genome with speed of spread.

Second, epidemiological modelling depends primarily on the use of a realistic and dynamic basic reproduction number ($R_0$), such as those in a previous study, in which the reported $R_0$ varied from greater than 7 before, to less than 1 after, control measures were introduced.

Third, it is unclear to us whether the Wuhan-based stochastic transmission model can accommodate variation in cultures and lifestyles, which often affects adherence to social distancing, which is crucial for prevention of respiratory transmission.