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.

approved method for diagnosis of COVID-19, as per WHO recommendations.[10] To re-emphasise, the management of any patient with suspected COVID-19 is one or both of RT-PCR testing and isolation, irrespective of RSNA or CO-RADS category. Typical does not mean specific for COVID-19.

CT remains a powerful diagnostic tool in the context of COVID-19 and should be used to trouble-shoot problematic cases like the one presented by Harkin and colleagues. Clinicians are still in the early stages of understanding COVD-19 and need to acknowledge the shortcomings of research to date. CT has been studied primarily in regions with a high prevalence of COVID-19, but its performance in lower-prevalence environments that we are likely to see in the coming months is not clear. A well designed, cross-sectional study is needed to define the sensitivity of typical CT findings and their specificity when multiple other disease processes are at play.

We declare no competing interests.

*Mark M Hammer, Constantine A Raptis, Travis S Henry, Amar Shah, Sanjeev Bhalla, *Michael D Hope*
michael.hope@ucsf.edu

Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA (MMH); Mallinckrodt Institute of Radiology, Washington University School of Medicine in Saint Louis, Saint Louis, MO, USA (CAR, SB); Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA 94143, USA (TSH, MDH); Department of Radiology, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY, USA (AS); and Department of Radiology, San Francisco Veterans Affairs Medical Center, San Francisco, CA, USA (MDH)

1 Harkin TJ, Rurak KM, Martins J, Eber C, Szporn AH, Beasley MB. Delayed diagnosis of COVID-19 in a 34-year-old man with atypical presentation. *Lancet Respir Med* 2020; published online May 18. https://doi.org/10.1016/S2213-2600(20)30232-0.

2 Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. *AJR Am J Roentgenol* 2020; published online March 14. DOI:10.2214/AJR.20.23034.

3 Das KM, Lee EY, Langer RD, Larsson SG. Middle East respiratory syndrome coronavirus: what does a radiologist need to know? *AJR Am J Roentgenol* 2016; **206:** 1193–201.

4 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.

5 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 online Feb 20. DOI:10.1148/radiol.2020200463.

6 Inui S, Fujikawa A, Jitsu M, et al. Chest CT findings in cases from the cruise ship "Diamond Princess" with coronavirus disease 2019 (COVID-19). *Radiol Cardiothorac Imaging* 2020; **2:** e200110.

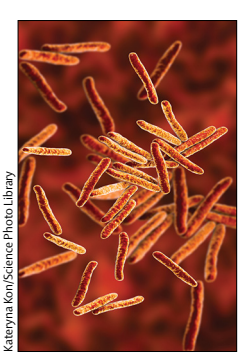
7 Simpson S, Kay FU, Abbara S, et al. Radiological Society of North America expert consensus statement on reporting chest CT findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. *J Thorac Imaging* 2020; **2:** e200152.

8 Prokop M, van Everdingen W, van Rees Vellinga T, et al. CO-RADS – a categorical CT assessment scheme for patients with suspected COVID-19: definition and evaluation. *Radiology* 2020; published online April 27. DOI:10.1148/radiol.2020201473.

9 American College of Radiology. ACR recommendations for the use of chest radiography and computed tomography (CT) for suspected COVID-19 infection. March 22, 2020. https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for-Suspected-COVID19-Infection (accessed March 24, 2020).

10 WHO. Global surveillance for human infection with coronavirus disease (COVID-19). Feb 27, 2020. https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov) (accessed April 27, 2020).

Tackling two pandemics: a plea on World Tuberculosis Day



Kateryna Kon/Science Photo Library

Published **Online** March 24, 2020 https://doi.org/10.1016/S2213-2600(20)30151-X

We are facing an unprecedented pandemic. A quarter of the world's population is infected and, between 2020 and 2021, it is predicted that 10 million people will have fallen ill, 3 million will not have been diagnosed or received care, and more than 1 million—mainly the most vulnerable—will have died.[1] This pandemic is not COVID-19 but tuberculosis. On World Tuberculosis Day, it is worth comparing the COVID-19 and tuberculosis pandemics to ensure that, while we focus on the former, we do not forget the latter.

A pandemic is defined as a disease that spreads across whole countries or the whole world. Tuberculosis and COVID-19 are both pandemics that show ongoing, sustained community transmission across continents. Indeed, no country is tuberculosis-free and this is likely to be the case soon for COVID-19.

There are striking similarities between the two pandemics. Both cause major infection-related morbidity and mortality around the world. Tuberculosis was the leading cause of mortality from an infectious disease worldwide in 2018, causing 1·2 million deaths.[1] COVID-19 has infected more than 300 000 people and caused over 13 000 deaths in the first quarter of 2020 alone.[2] Both COVID-19 and tuberculosis can present with respiratory symptoms, and diagnosis and treatment of people with tuberculosis, or tuberculosis and COVID-19 co-infection, are likely to be compromised during the COVID-19 pandemic. Older people and those with comorbidities are at increased risk of severe disease and adverse outcomes in both diseases.[3,4] And, as we are discovering for COVID-19, both diseases have considerable social impact—including stigma,

discrimination, and isolation—in addition to the economic impact from country productivity losses and catastrophic costs to individuals and households.[5]

There are also stark differences. While tuberculosis is a slow pandemic and has accompanied humankind for millennia,[6] the coronavirus (SARS-CoV-2) that causes COVID-19 is new and spreading rapidly around the world. Tuberculosis has been labelled a pandemic many times over the past three centuries, whereas this is the first COVID-19 pandemic. Children are less severely affected by COVID-19, whereas 1·1 million children had tuberculosis disease in 2018, of whom 200 000 died.[1] The vast majority of cases and deaths from tuberculosis occur in low-income and middle-income countries, whereas high-income countries have low rates.[1] By contrast, Europe became the second epicentre of COVID-19 after China, which might explain, in part, why COVID-19 can be expected to mobilise more global resources and person-power in a year than tuberculosis has in decades. However, underprepared and vulnerable countries in sub-Saharan Africa and Central and South America might soon see substantial rises in COVID-19 cases and deaths, and concerted, collective action must be taken now to avoid catastrophe.[7]

There are many unknowns. The clinical and epidemiological interactions of COVID-19 with tuberculosis (with or without HIV) are likely to be highly complex. Simply put, tuberculosis transmission might rise because of increased respiratory symptoms associated with COVID-19, or decline owing to COVID-19-related self-isolation and quarantine. There is increasing recognition of the millions of people treated for tuberculosis who have residual, long-term lung damage[8] who are likely to be at a higher risk of severe disease and death from COVID-19. Because of extreme pressures on health systems, exacerbated by COVID-19, people with tuberculosis are likely to face decreased access to diagnostic and treatment services, which might also result in adverse outcomes.

Tuberculosis disproportionately affects men and boys compared with women and girls.[9] Early data show that more men are dying from COVID-19, potentially due to sex-based immunological differences or gender-based factors such as prevalence of smoking.[10] The association between COVID-19 and poverty is also unclear but, as more data become available, we will be able to better understand the differential effects of COVID-19 according to socioeconomic position. COVID-19, like tuberculosis, will almost certainly be associated with the medical poverty trap, in which poorer people have a higher likelihood of infection, disease, and adverse outcomes. Moreover, unemployed populations and informal or so-called zero-hours contract workers will experience further impoverishment, which increases risk of tuberculosis.[5]

Amid the expanding COVID-19 pandemic, our plea on World Tuberculosis Day is that we do not forget the tuberculosis pandemic, which, at present, is still the leading cause of infectious disease mortality. We need to continue to mobilise funding for research for better tuberculosis diagnostics, vaccine development, novel therapeutics, equitable access to care, and innovative social protection interventions for tuberculosis-affected households.[5] We should drastically increase and sustain investment in health systems that are responsive to the needs of the poor and resilient to the threat of infections, especially those that are air-borne and require isolation facilities. We need to continue to inform, advocate for, and empower local communities and to lobby governments and policymakers to ensure that tuberculosis, as well as COVID-19, remain high on the global agenda. These two pandemics, one old and one new, remind us of the need to be proactive and long-sighted, to plan ahead, and to not become complacent.

We declare no competing interests. TW is supported by grants from the Wellcome Trust, UK (209075/Z/17/Z), the Academy of Medical Sciences, UK, and the Swedish Health Research Council, Sweden. LEC is supported by grants from the European and Developing Countries Clinical Trial Partnership (EDCTP, DRIA2014-309), the Medical Research Council (MRC), UK, the TB REACH Initiative of the Stop TB Partnership (STBP/TBREACH//GSA/W5-07), the Wellcome Trust (contract pending), and the Health Protection Research Unit for Emerging and Zoonotic Infections (HPRU EZI). PM is funded by the Wellcome Trust (206575/Z/17/Z). KAM is supported by a grant from the Department for International Development, UK. SBS is supported by the NIHR Global Health Research Unit on Lung Health and TB in Africa at the Liverpool School of Tropical Medicine (16/136/35).

Tom Wingfield, Luis E Cuevas, Peter MacPherson, Kerry A Millington, S Bertel Squire
tom.wingfield@lstmed.ac.uk

Departments of Clinical Sciences and International Public Health, Liverpool School of Tropical Medicine, Liverpool L3 5QA, UK (TW, LEC, PM, KAM, SBS); Social Medicine, Infectious diseases, and Migration (SIM) Group, Department of Global Public Health Sciences, Karolinska Institutet, Stockholm, Sweden (TW); Tropical and Infectious Disease Unit, Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK (TW, SBS); Zankli Research Centre, Bingham University, Nasarawa State, Nigeria (LEC); Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Blantyre, Malawi (PM); and Clinical Research Department, London School of Hygiene and Tropical Medicine, London, UK (PM).

1 WHO. Global tuberculosis report 2019. https://www.who.int/tb/global-report-2019/ (accessed March 19, 2020).

2 Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6 (accessed March 19, 2020).

3 The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus disease (COVID-19)—China. 2020. *China CDC Wkly* 2020; **2:** 113–22.

4 Negin J, Abimbola S, Marais BJ. Tuberculosis among older adults—time to take notice. *Int J Infect Dis* 2015; **32:** 135–37.

5 Wingfield T, Tovar MA, Datta S, Saunders MJ, Evans CA. Addressing social determinants to end tuberculosis. *Lancet* 2018; **391:** 1129–32.

6 Saleem A, Azher M. The next Pandemic - Tuberculosis: The oldest disease of mankind rising one more time. *Br J Med Pract* 2013; **6:** a615.

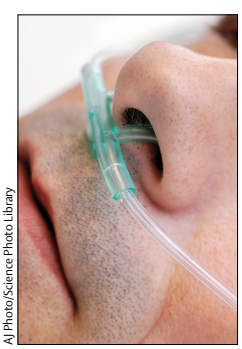
7 Gilbert M, Pullano G, Pinotti F, et al. Preparedness and vulnerability of African countries against importations of COVID-19: a modelling study. *Lancet Infect Dis* 2020; **395:** 871–77.

8 Meghji J, Lesosky M, Joekes E, et al. Patient outcomes associated with post-tuberculosis lung damage in Malawi: a prospective cohort study. *Thorax* 2020; **75:** 269–78.

9 Horton KC, MacPherson P, Houben RMGJ, White RG, Corbett EL. Sex differences in tuberculosis burden and notifications in low- and middle-income countries: a systematic review and meta-analysis. *PLoS Med* 2016; **13:** e1002119.

10 Wenham C, Smith J, Morgan R, the Gender and COVID-19 Working Group. COVID-19: the gendered impacts of the outbreak. *Lancet* 2020; **395:** 846–48.

COVID-19: Respiratory support outside the intensive care unit



A J Photo/Science Photo Library

Published **Online**
April 9, 2020
https://doi.org/10.1016/S2213-2600(20)30176-4

For **NHS guidelines** see https://www.england.nhs.uk/coronavirus/secondary-care/other-resources/specialty-guides/#adult-critical-care

For **Irish Thoracic Society guidelines** see https://irishthoracicsociety.com/2020/03/irish-thoracic-society-covid-19-guidelines-for-managing-respiratory-care/

For **ARDSnet guidelines** see https://www.thoracic.org/statements/resources/cc/ards-guidelines.pdf

The optimal mode of respiratory support for individuals with severe coronavirus disease 2019 (COVID-19) before invasive mechanical ventilation (IMV) is currently a subject of much debate. Recently published guidelines[1] and a Comment[2] differ substantially to other guidelines in this regard, with some advocating high flow nasal cannulae (HFNC) over non-invasive ventilation (NIV),[1,2] or vice versa (NHS guidance). This debate is understandable given the paucity of data and need for rapid generation of guidance, but it is a cause of confusion among respiratory physicians.

Much of the data guiding practice in this area derive from the critical care setting. In acute respiratory distress syndrome (ARDS), early intubation was associated with survival benefit when PaO_2/FiO_2 ratio was <150 when compared with NIV.[3] Some COVID-19 guidelines have therefore suggested NIV as a bridging therapy only, before transfer to the intensive care unit (ICU) and IMV. However, up to 50% of patients with COVID-19 admitted to the ICU did not subsequently require IMV.[4] Given the considerable resource limitations imposed by the current unprecedented viral pandemic, it is important to ascertain whether selected patients can be safely managed outside of the ICU.

To our knowledge, there have been no randomised control trials in the use of either HFNC or NIV in coronavirus-related pneumonia. It has been reported that use of NIV during the Middle Eastern respiratory syndrome outbreak was associated with a 92% risk of requiring IMV, thus suggesting futility.[5] This study was based in the ICU, however, and patients enrolled had a median PaO_2/FiO_2 ratio of 110 (IQR 62–160), indicating a degree of severity that likely warranted initial management with IMV. Conversely, data from only one study[6] on the severe acute respiratory syndrome (SARS) outbreak suggest that NIV can successfully avoid intubation.

HFNC has received much interest since the FLORALI trial.[7] Acute hypoxaemic respiratory failure (AHRF) in this study was largely secondary to community or hospital-acquired pneumonia. Though the primary outcome of intubation at day 28 was negative, HFNC reduced requirement for intubation in a subgroup of patients with PaO_2/FiO_2 ratio <200 and was associated with a reduction in mortality when compared with NIV or regular oxygen face mask. The NIV group of this study involved NIV use for an average of only 8 h per day, however, and a relatively high target tidal volume of 7–10 mL/kg. FLORALI also utilised a flow rate of 50 L/min with HFNC. To ameliorate potential aerosol generation, a flow limit of 30 L/min in COVID-19 has been proposed. The level of positive end-expiratory pressure (PEEP) supplied is consequently reduced. Notably, with regards to aerosol generation and risk to health-care workers, intubation poses a greater risk than NIV and a risk with HFNC has not been established.[8]

Concern regarding ward oxygen flow rates and hospital oxygen reserves is probably the most important cause for hesitancy over advocating HFNC (Irish Thoracic Society Guidelines). A major benefit of PEEP is that it might allow for down-titration of FiO_2, mitigating against over-consumption of hospital oxygen supply and avoiding hyperoxia-related lung injury. Anecdotal reports and our own experience of COVID-19-related lung injury suggests a good response to application of PEEP, perhaps related