Reduction in Chest CT Severity and Improved Hospital Outcomes in SARS-CoV-2 Omicron Compared with Delta Variant Infection

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Conflicts of interest are listed at the end of this article.

Radiology 2023; 306:261–269 • https://doi.org/10.1148/radiol.220533 • Content code: CH

Background: The SARS-CoV-2 Omicron variant demonstrates rapid spread but reduced disease severity. Studies evaluating lung imaging findings of Omicron infection versus non-Omicron infection remain lacking.

Purpose: To compare the Omicron variant with the SARS-CoV-2 Delta variant according to their chest CT radiologic pattern, biochemical parameters, clinical severity, and hospital outcomes after adjusting for vaccination status.

Materials and Methods: This retrospective study included hospitalized adult patients with reverse transcriptase–polymerase chain reaction test results positive for SARS-CoV-2, with CT pulmonary angiography performed within 7 days of admission between December 1, 2021, and January 14, 2022. Multiple readers performed blinded radiologic analyses that included RSNA CT classification, chest CT severity score (CTSS) (range, 0 [least severe] to 25 [most severe]), and CT imaging features, including bronchial wall thickening.

Results: A total of 106 patients (Delta group, n = 66; Omicron group, n = 40) were evaluated (overall mean age, 58 years ± 18 [SD]; 58 men). In the Omicron group, 37% of CT pulmonary angiograms (15 of 40 patients) were categorized as normal compared with 15% (10 of 66 patients) of angiograms in the Delta group (P = .016). A generalized linear model was used to control for confounding variables, including vaccination status, and Omicron infection was associated with a CTSS that was 7.2 points lower than that associated with Delta infection (β = −7.2; 95% CI: −9.9, −4.5; P < .001). Bronchial wall thickening was more common with Omicron infection than with Delta infection (odds ratio [OR], 2.4; 95% CI: 1.01, 5.92; P = .04). A booster shot was associated with a protective effect for chest infection (median CTSS, 5; IQR, 0–11) when compared with unvaccinated individuals (median CTSS, 11; IQR, 7.5–14.0) (P = .03). The Delta variant was associated with a higher OR of severe disease (OR, 4.6; 95% CI: 1.2, 26; P = .01) and admission to a critical care unit (OR, 7.0; 95% CI: 1.5, 66; P = .004) when compared with the Omicron variant.

Conclusion: The SARS-CoV-2 Omicron variant was associated with fewer and less severe changes on chest CT images compared with the Delta variant. Patients with Omicron infection had greater frequency of bronchial wall thickening but less severe disease and improved hospital outcomes when compared with patients with Delta infection.

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Online supplemental material is available for this article.

A novel SARS-CoV-2 variant designated B.1.1.529 (Omicron) was identified in November 2021 in South Africa and subsequently spread rapidly around the world, accounting for a sudden increase in the number of SARS-CoV-2 infections in the United Kingdom in December 2021 (1). Patients with Omicron infection have half the odds of being hospitalized and experiencing severe disease compared with those infected with Delta or a preceding variant (hazard ratio, 0.53; 95% CI: 0.50, 0.57) (1,2). Furthermore, the risk of being admitted to a hospital for an Omicron infection is 65% lower for vaccinated individuals than for unvaccinated individuals, although vaccine effectiveness against symptomatic disease with the Omicron variant is lower than that compared with the Delta variant (51% vs 85% >25 weeks after two vaccinations), and wanes rapidly (1). There are limited data on differential severity and outcomes between variants once patients are admitted to a hospital for SARS-CoV-2.

A recent study has shown that vaccinated individuals with SARS-CoV-2 breakthrough infections have fewer
Abbreviations
CTPA = CT pulmonary angiography, CTSS = chest CT severity score, OR = odds ratio, RT–PCR = reverse transcriptase–polymerase chain reaction

Summary
SARS-CoV-2 Omicron variant chest infections are radiologically and clinically less severe than Delta variant infections and are associated with improved hospital outcomes.

Key Results
- In 106 hospitalized adult patients infected with the SARS-CoV-2 Omicron (n = 40) or Delta (n = 66) variant, patients with Omicron infection had lower chest CT severity score (CTSS) (median, 3.5) than did those with Delta infection (median, 11.8) (P < .001).
- Patients who had received a vaccine booster had lower median CTSS (median, 5.0) than did unvaccinated patients (median, 11.0) (P = .03).
- Bronchial wall thickening was more common with the Omicron variant than with the Delta variant (odds ratio, 2.4; P = .04).

Materials and Methods
Patients
Data from 106 consecutive patients admitted to a large tertiary referral center in the United Kingdom were retrospectively collected. Inclusion criteria were hospitalized adult patient (≥18 years of age), CTPA performed within the study time window between December 1, 2021, and January 14, 2022, and a nasal or throat swab that was positive for SARS-CoV-2 at reverse transcriptase–polymerase chain reaction (RT–PCR) testing within 7 days of admission (Fig 1). Exclusion criteria included technically inadequate or abandoned imaging. The study sample included patients who were admitted for symptoms of infection and those who were incidentally positive for SARS-CoV-2. CTPA was performed after respiratory deterioration, as per our national guidelines (9). Data were extracted and analyzed using permission granted by the institutional review board Health Research Authority and Health and Care Research Wales (IRAS 282670; REC 20/HRA/2546), which waived the requirement for informed consent due to the retrospective nature of the study.

CT Protocol
Analysis of the first CTPA study obtained after patient presentation was performed. All examinations were performed with one of three CT scanners (two Siemens Somatom Drive, Siemens Medical Solutions USA; one GE Revolution GSI, GE Healthcare). All examinations were performed with a 0.625-mm section chest CT findings of pneumonia compared with unvaccinated patients (59% vs 22% had no evidence of pneumonia) (3). However, variant status in this study was unknown, and the applicability to other samples may be limited, as most individuals were immunized with a non-mRNA vaccine.

Establishing intrinsic differences in variant virulence, as opposed to reductions in disease severity over time due to population immunity from vaccination or prior infection, is challenging. However, laboratory studies have shown reduced pathogenesis in animal models (4) and lower replication rates in human lung cells compared with those in the upper respiratory tract for the Omicron versus Delta variant (5). These results lend biologic plausibility to the idea that there is reduced lung involvement and reduced risk of severe respiratory outcomes arising directly from the Omicron variant itself.

Multiple studies have shown the degree of parenchymal involvement on CT images is associated with disease severity and poor hospital outcome, including a study that used a 25-point chest CT severity score (CTSS) of CT pulmonary angiograms (6). Further studies have evaluated the CT imaging characteristics, or signature, of SARS-CoV-2 infection (7,8), but studies evaluating the lung imaging findings of Omicron infection versus non-Omicron infection remain lacking.

In this retrospective analysis, we compared the radiologic pattern, imaging characteristics, and disease severity at initial CT pulmonary angiography (CTPA) in patients infected with the Omicron variant with those in patients infected with the Delta variant. We also compared the imaging severity according to vaccination status and evaluated the study sample with regard to biochemical parameters, clinical disease severity, and hospital outcomes by variant and vaccination status.

Figure 1: Flowchart of study patients. CTPA = CT pulmonary angiography, CTSS = CT severity score, OR = odds ratio, PCR = polymerase chain reaction.
Table 1: Summary of Patient Characteristics

| Characteristic                                      | Delta Group (n = 66) | Omicron Group (n = 40) | P Value |
|-----------------------------------------------------|----------------------|------------------------|---------|
| Age (y)*                                            | 56 ± 18              | 62 ± 19                | .07     |
| Sex                                                 |                      |                        |         |
| Female                                              | 34 (52)              | 14 (35)                | .11     |
| Male                                                | 32 (48)              | 26 (65)                | .11     |
| Ethnicity†                                          |                      |                        |         |
| Other                                               | 19 (29)              | 6 (15)                 | .16     |
| White                                               | 47 (71)              | 34 (85)                | .16     |
| Smoking status                                      |                      |                        |         |
| Current smoker                                      | 4 (6)                | 5 (12)                 | .29     |
| Ex-smoker                                           | 15 (23)              | 14 (35)                | .18     |
| Never smoked                                        | 47 (71)              | 21 (52)                | .06     |
| Any comorbidity                                     | 30 (45)              | 25 (62)                | .09     |
| Hypertension                                        | 17 (26)              | 13 (32)                | .46     |
| Diabetes mellitus                                   | 6 (9)                | 8 (20)                 | .11     |
| Ischemic heart disease                              | 4 (6)                | 10 (25)                | .01     |
| Active malignancy or within past 5 years            | 7 (11)               | 7 (18)                 | .31     |
| Asthma                                              | 8 (12)               | 6 (15)                 | .67     |
| COPD                                                | 7 (11)               | 6 (15)                 | .55     |
| Medical condition–induced immunosuppression         | 9 (14)               | 13 (32)                | .02     |
| BMI (kg/m²)†                                        | 31 ± 10              | 29 ± 8                 | .17     |
| Drug-induced immunosuppression                      | 11                   | 4                      |         |
| Any drug prescribed to treat COVID-19               | 4 (6.1)              | 4 (10)                 | .47     |
| Dexamethasone                                       | 49 (74)              | 23 (57)                | .07     |
| Remdesivin                                          | 2 (3%)               | 0 (0)                  | .53     |
| Missing                                             | 47 (72)              | 23 (57)                | .12     |
| Missing                                             | 1                    | 0                      |         |
| Tocilizumab                                         | 29 (44)              | 17 (42)                | .88     |
| Ronapreve                                           | 34 (52)              | 7 (18)                 | <.001   |
| Ronapreve                                           | 12 (18)              | 1 (2)                  | .02     |

Note.—Unless otherwise indicated, data are number of findings, and data in parentheses are percentages. Statistics were generated with either the Wilcoxon rank sum test (age and body mass index [BMI]) or the Fisher exact test (all other variables). BMI = body mass index, COPD = chronic obstructive pulmonary disease, COVID-19 = coronavirus disease 2019.

* Data are mean ± SD.
† For ethnicity, the category “other” includes Asian—any other Asian background, Asian or Asian British–Bangladeshi, Asian British–Pakistani, Black or Black British–African, Black or Black British–Caribbean, Chinese. Not stated, Other—not known. The ethnicity category “White” includes White—any other White background, White-British, White-Irish. For detailed ethnicity data, see Table E2 (online).

Imaging Analysis

RSNA categorization, assessment for bronchial wall thickening, and CTSS analysis were performed by one radiologist with 15 years of thoracic imaging experience (R.E.B.) and one radiologist in training (S.J.S.) who independently interpreted every imaging study while blinded to variant status, clinical information, and other radiologist scoring, within 1 week. Images were categorized according to the RSNA Expert Consensus Statement as negative, typical, indeterminate, or atypical for SARS-CoV-2 pneumonia (10). The dichotomous outcome of bronchial wall thickening was determined after inspection of bronchi throughout all lung lobes. Final RSNA categories and the presence or absence of bronchial wall thickening were determined in consensus with a third radiologist (H.P., 5 years of thoracic imaging experience) in cases of interobserver discrepancy (seven cases for RSNA categorization, 26 cases for bronchial wall thickening). Studies categorized as negative, typical, or indeterminate (n = 100) were evaluated in terms of severity using the semiquantitative chest CT severity score (CTSS), as in previous studies (6). The resulting global CT score was the sum of each individual lobar score, from 0 to 25, with the mean CTSS between the two radiologists used for analysis (consensus CTSS). There was a high level of agreement between observers (weighted Cohen κ = 0.77; 95% CI: 0.72, 0.83; P < .001).

Further blinded analysis for additional imaging characteristics was undertaken by one radiologist with 4 years of thoracic imaging experience (L.W.) and one radiologist with 2 years of thoracic imaging experience (C.X.), with conclusions reached in consensus with a third radiologist with 20 years of thoracic imaging experience (F.K.M.) in cases of interobserver discrepancy.

Clinical and Biochemical Data

Electronic patient records were used to capture patient demographics, vaccination status (typically with an mRNA vaccine or a ChAdOx1 vaccine for the first two doses, with an mRNA booster, where given), comorbidities, immunosuppression status, laboratory findings, in-hospital treatments, and clinical outcomes. The date of vaccination was not consistently recorded and could not be included. Oxygen saturation and requirements were used to calculate the World Health Organization ordinal progression score. Patients with severe disease were defined as those patients reaching point 6 or higher during the assessment period (11). Mortality data were collected for individuals who died by 30 days after CTPA; admission to critical care was defined as admission to either a high-dependency unit or an intensive care unit during hospitalization.
RT-PCR and Variant Status

RT-PCR analysis was performed with a TaqPath assay (Thermo Fisher). Infections with S gene target failure are used as a surrogate for Omicron status, as previously reported (1). The study was performed prior to the spread of the BA.2 Omicron variant, which does not exhibit S gene target failure.

Statistical Analyses

All analyses were conducted with R software (version 4.0.5; https://www.r-project.org/). For the primary analysis of CTSS by variant and vaccination status, we used the Wilcoxon rank sum test to determine the differences between scores, and the median and IQR were reported. Multivariable linear regression analysis was used to assess associations, controlling for confounding features, and full information is given in Appendix E1 (online). For analysis of CT imaging characteristics, we used the Fisher exact test to determine differences in proportions between groups, with odds ratios (ORs) and CIs reported. A logistic regression model was used to control for confounding variables (Appendix E1 [online]) for bronchial wall thickening. For survival analysis, using the outcome of 30-day admission to critical care or death, we fitted survival models using Cox proportional hazard regression. Power calculation was performed assuming a CTSS reduction by four points for Omicron infection on the basis of pilot data ($\alpha = 0.05$, 80% power). $P < .05$ was indicative of a significant difference.

Results

Patient Clinical Characteristics by Variant and Vaccination Status

Data from 106 adult patients with SARS-CoV-2 infection
Tsakok and Watson et al (Delta, \(n = 66\); Omicron, \(n = 40\)) (mean age, 58 years ± 18 [SD]; 58 men) and available CTPA images were analyzed (Fig 1). Body mass index and ethnicity were similar across groups. As expected with the ongoing vaccine rollout, there were differences by variant in vaccination status, with a greater proportion of admissions due to the Delta variant in patients who were unvaccinated (Delta, 34 of 62 patients [55%]; Omicron, seven of 32 patients [22%]), and a greater proportion of patients with Omicron infection had received a booster (Delta, 10 of 62 patients [16%]; Omicron, 13 of 32 patients [41%]) (Table 1). There was no evidence of a difference in smoking status between variant groups, nor was there a difference in any comorbidity other than ischemic heart disease and immunosuppression (Table 1). A greater proportion of those who had received a booster had active malignancy, chronic obstructive pulmonary disease, or immunosuppression and were, on average, 20 years older, which would be in keeping with the stage of booster rollout in the United Kingdom at the time of our study (Table E1 [online]).

**CT Patterns**

We evaluated CT findings according to the RSNA CT classification of SARS-CoV-2 pneumonia (Fig 2). More studies were categorized as normal in patients with Omicron infection (37%, 15

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**Table 2: Uni- and Multivariable Linear Regression Models for the Association between CTSS and Listed Variables**

| Variable                        | Univariable Model | Multivariable Model |
|---------------------------------|-------------------|---------------------|
|                                 | \(\beta\) Coefficient | 95% CI   | \(P\) Value | \(\beta\) Coefficient | 95% CI   | \(P\) Value |
| Omicron variant (ref: Delta variant) | -6.8               | -9.3, -4.3          | <.001      | -7.2               | -9.9, -4.5          | <.001      |
| Age                             | -0.083             | -0.16, -0.01        | .03        | -0.055             | -0.13, 0.021        | .16        |
| Current smoker (ref: never smoked) | -3.5               | -8.2, 1.2           | .15        | -1.7               | -6.2, 1.6           | .44        |
| Ex-smoker (ref: never smoked)   | 1                  | -2.1, 4.1           | .52        | 3.1                | 0.36, 5.8           | .03        |
| Presence of immunosuppression   | 1.2                | -1.9, 4.3           | .46        | 5.6                | 2.5, 8.7            | <.001      |
| Single or double vaccinated (ref: unvaccinated) | -1.8               | -4.9, 1.3           | .29        | -1.3               | -4.1, 1.4           | .37        |
| Booster vaccinated (ref: unvaccinated) | -3.9               | -7.4, -0.37         | .03        | -3.6               | -7.3, 0.12          | .06        |

Note.—All listed variables were included as covariates in the multivariable model, which was determined by backward selection with an exit \(P\) value > .1 (Appendix E1 [online]). CTSS = chest CT severity score, ref = reference.
CT Imaging Characteristics
Bronchial wall thickening was more common in patients with the Omicron variant than in those with the Delta variant, both before (OR, 2.4; 95% CI: 1.01, 5.92; \( P = .04 \)) and after adjusting for covariates (Table E4 [online]). There were no additional lung CT findings that were more common in patients with the Delta variant than in those with the Omicron variant (Table E5 [online]).

Biochemical and Clinical Severity
Omicron infection was associated with higher lymphocyte and monocyte counts compared with Delta infection (Fig 6A), while no difference in C-reactive protein or platelet level was seen (Fig E3 [online]). Severe disease (indicated by a World Health Organization score ≥ 6, requiring noninvasive ventilation, high-flow oxygen administration, or more) was more likely with the Delta variant as opposed to the Omicron variant (OR, 4.6; 95% CI: 1.2, 26.0; \( P = .01 \)) (Fig 6B). Critical care admission was also more likely with the Delta variant versus the Omicron variant (OR, 7.0; 95% CI: 1.5, 66; \( P = .004 \)) (Fig 6C).

High CTSS Correlates with Poorer Clinical Outcomes across Both Variants
In analyses adjusting for age per the original linear model, a high CTSS was associated with a composite outcome of admission to critical care or death within 30 days of CTPA (27 events; adjusted hazard ratio, 3.8; 95% CI: 1.1, 14.0; \( P = .04 \)) (Table 3). Only one patient with Omicron infection had a CTSS higher than 14.

Figure 5: The proportion of patients with bronchial wall thickening by variant. \( P \) values were generated with the Fisher exact test.
Table 3: Uni- and Multivariable Cox Proportional Hazard Models for the Relationship between High CTSS and Admission to Critical Care or Death

| Variable                              | Univariable Model | Multivariable Model |
|---------------------------------------|-------------------|---------------------|
|                                       | HR    | 95% CI | P Value | HR    | 95% CI | P Value |
| High CTSS (≥14)                       | 3.4   | 1.4, 7.9 | .006   | 3.8   | 1.1, 14 | .04    |
| Omicron variant (ref: Delta variant)  | 0.54  | 0.18, 1.6 | .27    | 0.64  | 0.094, 4.3 | .64    |
| Age                                   | 0.99  | 0.97, 1.0 | .65    | 0.99  | 0.96, 1   | .71    |
| Current smoker (ref: never smoked)    | 0.97  | 0.075, 4.3 | .59    | 1.2   | 0.13, 10 | .90    |
| Ex-smoker (ref: never smoked)         | 0.82  | 0.32, 2.1 | .69    | 1.1   | 0.35, 3.6 | .85    |
| Presence of immunosuppression         | 1.4   | 0.57, 3.5 | .46    | 2.4   | 0.63, 9.1 | .20    |
| Single or double vaccinated (ref: unvaccinated) | 1     | 0.34, 3.0 | .99    | 0.56  | 0.15, 2.1 | .38    |
| Booster vaccinated (ref: unvaccinated) | 0.53  | 0.11, 2.4 | .41    | 0.51  | 0.07, 3.7 | .51    |

Note.—All listed variables were included as covariates in the multivariable model. CTSS = CT severity score, HR = hazard ratio, ref = reference.

Discussion

The SARS-CoV-2 Omicron variant demonstrates rapid spread but with lower rates of hospital admission and reduced disease severity. Studies evaluating lung CT findings in patients with Omicron infection versus CT findings in patients with non-Omicron infection are lacking. In this report, we examined the CT features and biochemical and clinical outcomes for patients hospitalized with SARS-CoV-2 infection due to either the Omicron or the Delta variant. More CT pulmonary angiograms were categorized as normal in patients with Omicron infection...
than in patients with Delta infection (37% [15 of 40 patients] vs 15% [10 of 66 patients], respectively; \( P = .016 \)). Omicron infection was associated with a CTSS that was 7.2 points lower than that associated with Delta infection (\( \beta = -7.2 \) points; 95% CI: -9.9, -4.5; \( P < .001 \)) in an adjusted multivariable linear regression analysis. Bronchial wall thickening was more common with Omicron infection than with Delta infection (OR, 2.4; 95% CI: 1.01, 5.9; \( P = .04 \)). Patients who received a booster had less severe disease on CT scans versus unvaccinated patients (median CTSS, 5; [IQR, 0.0–11.5] vs 11 [IQR, 7.5–14.0]; \( P = .03 \)). The Delta variant was associated with more severe disease (OR, 4.6; 95% CI: 1.2, 26.0; \( P = .01 \)) and critical care admission (OR, 7.0; 95% CI: 1.5, 66.2; \( P = .004 \)) than the Omicron variant. We also found that infection with the Omicron variant was associated with both higher lymphocyte and monocyte counts in the peripheral blood. Lower levels of these parameters have been associated with more severe disease (12,13); thus, this finding is consistent with Omicron infection causing less severe illness.

Previous reports have shown vaccination reduces the relative risk of hospitalization in patients with Delta infection but not in those with Omicron infection (1,14). Within this context, our results suggest that Omicron infection is intrinsically less severe than Delta infection, as evidenced by the significant difference in disease severity among unvaccinated individuals during our study period and the robust findings from the generalized linear model across the entire sample. The persistence of effect in just the typical subgroup suggests that the lower CTSS in patients with Omicron infection is not simply explained by a greater proportion of normal scans. The fact that a large and significant difference continued to be observed regardless of whether the scores were taken from an experienced or a trainee radiologist indicates the utility and relevance of these findings for everyday clinical practice. Further, the high proportion of scans negative for pneumonia in those with Omicron infection suggests the reduced utility of CT as a diagnostic tool in the context of this variant, while the wide range of CTSS in just typical cases demonstrates a range of severity within this category, suggesting that CTSS provides substantially more information rather than simple classification.

We were also able to show that a cutoff CTSS of 14, as previously described (6), enables accurate prediction of critical care admission or death within 30 days in this study sample, further validating this previous finding and demonstrating the utility of CTPA findings in the radiologic assessment of SARS-CoV-2 pneumonia.

Our study had limitations. First, over the study period, case rates and vaccination status fluctuated, with differences noted in the underlying demographics of those who had received a booster vaccination; thus, comparisons regarding different levels of vaccination status are limited. Vaccination efficacy varies not only according to variant type but also according to the time since vaccination, vaccination type, and the percentage of the population vaccinated—variables for which we were unable to control in our study. Second, we were unable to establish the frequency of previous infection with SARS-CoV-2 within our study sample. The Omicron variant is associated with a higher rate of reinfection (15), and it is possible that a larger proportion of Omicron cases, as compared with Delta cases, represented reinfections, and this may have contributed to the reduced severity of Omicron infections. Third, detection of bronchial wall thickening is subjective and reduced in those with higher CTSS due to background ground-glass opacification, potentially leading to a reduction in the number of patients with Delta infection identified as having bronchial wall thickening. Fourth, threshold to imaging may differ between variants. Finally, our study sample contained patients with SARS-CoV-2 infection; however, not all were admitted for SARS-CoV-2 infection; therefore, outcome data should be interpreted with caution. In conclusion, in this small series of hospitalized patients with reverse transcriptase–polymerase chain reaction (rt-PCR) findings positive for SARS-CoV-2 with CT pulmonary angiography (CTPA) performed within 7 days of admission, we found that Omicron infection is less likely to be associated with SARS-CoV-2 pneumonia and that when pneumonia does occur, it is less severe on chest CT scans. In agreement with chest CT patterns, Omicron infection was associated with reduced clinical and biochemical markers of severity and improved hospital outcomes.

**Author contributions:** Guarantors of integrity of entire study, M.T.T., R.E.B., F.G.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature search, M.T.T., R.A.W., S.J.S., L.W.; clinical studies, M.T.E., R.A.W., S.J.S., M.K., C.X., H.P., R.A.W., N.P.T.; statistical analysis, M.T.E., R.A.W., S.J.S., D.W.E.; and manuscript editing, all authors

**Disclosures of conflicts of interest:** M.T.T. No relevant relationships. R.A.W. Fellowship received from The Wellcome Trust. S.J.S. No relevant relationships. M.K. No relevant relationships. C.X. No relevant relationships. H.P. No relevant relationships. L.W. No relevant relationships. E.K.M. No relevant relationships. B.S. No relevant relationships. N.P.T. No relevant relationships. R.E.B. No relevant relationships. D.W.E. Research fellowship from the Robertson Foundation; lecture fees from Gilead. F.G. Grants from the National Institute for Health and Care Research for the EXPLAIN Study, co-applicant for ICOVID H2020, chief investigator for Innovate UK, Integrated Diagnostics 2019—The Integration and Analysis of Data using Artificial Intelligence to Improve Patient Outcomes with Thoracic Diseases (DART) Consortium; consulting fees from Sensyne; lectures for Polarean and GlassSmithKline; president of the European Society of Thoracic Imaging; stock in RAIQC; material from Polarean.

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