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## A systematic review and metanalysis of diagnostic yield of BAL for detection of SARS-CoV-2

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### ABSTRACT

**Background:** The gold standard for diagnosing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is microbiological confirmation by reverse transcriptase-polymerase chain reaction (RT-PCR)<sup>1</sup> most commonly done using oropharyngeal (OP) and nasopharyngeal swabs (NP). But in suspected cases, where these samples are false-negative, bronchoalveolar lavage (BAL) may prove diagnostic.

**Objectives:** Hence, the diagnostic yield of BAL for detection of SARS-CoV-2 in cases of non-diagnostic upper respiratory tract samples is reviewed.

**Methods:** Databases such as MEDLINE, Scopus, and Google Scholar were searched using a systematic search strategy. The current study has been in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and has been registered with the International Prospective Registry of Systematic Reviews (CRD42020224088).

**Results:** 911 records were identified at initial database extraction, of which 317 duplicates were removed and, 596 records were screened for inclusion eligibility. We included total 19 studies in the systematic review, and 17 were included in metanalysis. The pooled estimate of SARS-CoV-2 positivity in BAL was 11% (95%CI: 0.01–0.24). A sensitivity analysis also showed that the results appear to be robust and minimal risk of bias amongst the studies.

**Conclusion:** The current study demonstrates that BAL can be used to diagnose additional cases primary disease and superadded infections in patients with severe COVID-19 lower respiratory tract infection.

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### Introduction

Microbiological confirmation by reverse transcriptase-polymerase chain reaction (RT-PCR) is considered the gold standard for diagnosing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.<sup>1</sup> Oropharyngeal (OP) and nasopharyngeal swabs (NP) were most frequently used samples. While OP and NP swabs are the least invasive method of obtaining samples in patients with a contagious respiratory disease, false-negative results may result from sampling error or low amounts of virus in the collected sample (due to early or late sampling or patient having mild disease<sup>2</sup>).

Studies have been done to evaluate the role of Bronchoalveolar lavage (BAL) in cases where NP and or OP swabs were non-diagnostic.

In Italy, Turriziani et al. described 15% ( $n = 55$ ) positivity in 367 BAL specimens to detect SARS-CoV-2 virus.<sup>3</sup> In the United States, Chang et al. described 206 BAL specimens, reporting a positivity rate of zero percent.<sup>4</sup> Yet, studies from China have shown BAL positivity between 93 and 100%.<sup>5,6</sup> Given the variability of these results, we conducted a systematic review and meta-analysis to assess the diagnostic yield of BAL for detection of SARS-CoV-2 in cases of non-diagnostic upper respiratory tract samples.

### Methods

#### Search strategy

Databases such as MEDLINE, Scopus, and GoogleScholar were searched using a systematic search strategy [Box1]. The search period included was from inception to 1st September 2021. Also, the

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reference lists of selected articles were manually screened for potential articles eligible for inclusion. There were no restrictions regarding date or language in our search strategy. A re-run of the search strategy was done prior to the final analysis.

**Box 1: Search Strategy**  
**MEDLINE**  
 ("Bronchoalveolar Lavage"[Mesh]"bronchoalveolar lavage"[MeSH Terms] OR "Bronchoalveolar lavage"[Text Word]) AND ("COVID-19" OR "SARS" OR "severe acute respiratory syndrome" OR "COVID-19 diagnostic testing" [Supplementary Concept])  
**SCOPUS**  
 (TITLE-ABS-KEY (bronchoalveolar AND lavage) AND TITLE-ABS-KEY ("COVID-19" OR "SARS"))  
**GoogleScholar**  
 All in title: bronchoalveolar lavage SARS

**Eligibility criteria**

Case-series and hospital-based cross-sectional studies describing patients with known COVID-19 (diagnosed by RTPCR positive on nasopharyngeal specimens) or suspected COVID-19 disease (high-risk of COVID-19 based on physician assessment of exposure history, symptoms and/or radiological features) and undergoing BAL for any indication were eligible for inclusion in this study.

**Data extraction**

Two reviewers independently screened records for potential inclusion. Disagreements were resolved after discussion with a third reviewer. Rayyan software was used for cataloguing and screening studies. Two independent reviewers used data extraction using a standardised format for the following variables: author name, place, study settings, patient demographic characteristics, clinical descriptions, and outcomes in terms of SARS-CoV-2 positivity. Disagreements in data extraction were resolved by discussion with a third reviewer. In case of missing or incomplete data, the authors were contacted for further details. Data extraction was done using a standard format in Microsoft Excel software (Table 1).

**Risk of bias**

Two independent reviewers critically appraised the selected cross-sectional studies for risk of bias using the Appraisal tool for Cross-Sectional Studies (AXIS) tool which evaluates various aspects of methodological quality using a 20 item questionnaire. The appraisal was qualitative and colour coded as green (no risk of bias), yellow (unclear risk of bias) or, red (high risk of bias).

The current study has been in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines<sup>7</sup> and has been registered with the International Prospective Registry of Systematic Reviews (CRD42020224088)

**Statistical analysis**

A random effects model was used to pool the percentage of BAL specimens that were positive for SARS-CoV-2. Study heterogeneity was estimated using the I-squared statistic. Small study effects and publication bias were explored using Doi plot and Luis Furuya-Kanamori (LFK) index. Sensitivity analysis was done to assess the robustness of the pooled estimate. MetaXL software was used for the statistical analysis. A p value of less than 0.05 was considered significant. Studies with samples size less than 10 were excluded, and total 17 studies were included in final meta-analysis.

**Table 1**  
 Data Extraction Sheet of 19 studies included in systematic review.

| S.No | Study/place                    | Study Settings | Patient number; Age; Males; Comorbidities | Intervention | Outcome   | BAL morphological findings   | Other Microorganisms in BAL  | Clinical Outcomes | Time                          |
|------|--------------------------------|----------------|---|--------------|---|--|--|-------------------|-------------------------------|
| 1    | Baron A <sup>16</sup> / France | Single centre, | n = 24; NA; NA; NA                        | BAL (n = 28) | 1. To confirm SARS-CoV-2 infection (n = 2; 7%), after one and three negative RT-PCR on nasopharyngeal (NP) swab.<br>2. Suspicion of ventilator-associated pneumonia (n = 11; 39%).<br>3. Suspicion of invasive aspergillosis (n = 4, 14%).<br>4. To rule out a super-infection before starting a corticosteroid course (n = 12; 43%). | Cell count/ $\mu$ L = 540 (305–775)<br>Macrophage% = 21 (14–46)<br>Neutrophils% = 54 (39–75)<br>Lymphocytes% = 6 (2–14)<br>Activated lymphocytes present = 14 (54)<br>Eosinophils% = 1 (0–1) | Global microbiological yield of BAL 24 (86)<br>Aspergillus (culture and/or PCR) 7 (25) | NA                | March 31st and June 3rd, 2020 |

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**Table 1** (Continued)

| S. No | Study/place                      | Study Settings                     | Patient number; Age; Males; Comorbidities  | Intervention  | Outcome  | BAL morphological findings | Other Microorganisms in BAL  | Clinical Outcomes | Time                              |
|-------|----------------------------------|------------------------------------|--|---------------|--|----------------------------|--|-------------------|-----------------------------------|
| 2     | Yang Y <sup>19</sup> / China     | Single centre study                | n = 410<br>median age: 47.5 (2–86)<br>M: 47.1%; 120 (29.3%); NA                          | BAL (n = 66)  | 5. BAL fluid neutrophil vs lymphocytic: 24:4<br>BAL positive 45/66 (68.18%)  | NA                         | NA   | NA                | NA                                |
| 3     | Patrucco F <sup>21</sup> /Italy  | Multicentre, retrospective         | n = 131<br>median age; 64.65 (53.71–73.98)<br>M: 71%; NA                                 | BAL (n = 131) | 1. BAL positive 43/131 (32.8%)<br>2. virus other than SARS-CoV-2 in COVID 19 patients: 7%, Bacteria: 23%, Fungi: 7%                        | NA                         | At least 1 pathogen* = 46 (35.11)<br>Virus (non-SARS-CoV-2) = 10 (7.75)<br>Bacteria = 30 (22.90)<br>Fungi = 19 (14.50)   | NA                | March 16th and May 27th, 2020.    |
| 4     | Abid MB <sup>15</sup> / USA      | Single centre, retrospective       | N = 1516;<br>(FOB=53)<br>Ages: 76, 78, 77<br>All males;<br>All had underlying malignancy | BAL=3         | BAL positive = 3   | NA                         | NA   | NA                | March 13, 2020 and June 11, 2020. |
| 5     | Mondoni M <sup>20</sup> , Italy  | Multicentre, retrospective         | N = 109<br>(FOB=109)<br>mean±SD age 60.0 ± 13.6 years<br>M: 71%                          | BAL=78        | Bronchoscopy positive = 43/78 (55.1%)<br>BAL positive = 35/61 (57.4%)<br>Bronchial washing positive = 8/17 (47.1%)<br>Fungal infections: 4 | NA                         | Lower respiratory tract coinfection (n = 4)  | NA                | March 1, and April 15, 2020       |
| 6     | Geri P <sup>23</sup> , Italy     | Single centre, retrospective       | N = 79<br>Mean age 65 ± 17 years<br>M: 75%   | BAL=79        | BAL positive = 2/79  | NA                         | NA   | NA                | 14 March 2020 and 4 May 2020      |
| 7     | Vannucci J <sup>24</sup> , Italy | Single centre, retrospective study | N = 81<br>Mean age: 68.3 ± 16.2<br>M: 62%; NA  | BAL=81        | BAL positive = 3/81 (3.7%)<br>Associated infections: 0   | NA                         | Haemophilus parainfluenzae 4 (4.9)<br>Staphylococcus aureus 3 (3.7)<br>Pseudomonas aeruginosa 3 (3.7)<br>Klebsiella pneumoniae 2 (2.5)<br>Enterobacter aerogenes 1 (1.2)<br>Enterococcus faecium 1 (1.2)<br>Streptococcus pneumoniae 1 (1.2)<br>Haemophilus influenzae 1 (1.2) | NA                | NA                                |

(continued on next page)

Table 1 (Continued)

| S. No | Study/place                       | Study Settings                           | Patient number;<br>Age; Males;<br>Comorbidities   | Intervention               | Outcome  | BAL morphological<br>findings | Other<br>Microorganisms in<br>BAL  | Clinical Outcomes | Time   |
|-------|-----------------------------------|--|---|----------------------------|--|-------------------------------|--|-------------------|--|
| 8     | Ora J <sup>25</sup> , Italy       | Single Centre                            | N = 28<br>mean ± SD: age<br>65 ± 16<br>M: 57%; NA   | BAL=28                     | BAL positive = 0   | NA                            | Candida albicans<br>n = 4<br>Pneumocystis jiro-<br>vecii n = 2<br>Candida glabrata<br>n = 1<br>Streptococcus pneu-<br>moniae n = 1<br>Staphylococcus epi-<br>dermidis n = 2<br>Klebsiella pneumo-<br>niae n = 2<br>Enterococcus fae-<br>cium n = 1 | NA                | March 13th and<br>April 30th, 2020,          |
| 9     | Ramos KJ, <sup>26</sup> USA       | Single centre                            | N = 16<br>Mean age±SD:<br>59 ± 14, M: 50%;<br>NA  | BAL=16                     | BAL positive = 3/16<br>(19%)                               | NA                            | NA   | NA                | March 26 - April 17,<br>2020                 |
| 10    | Wang W <sup>5</sup> , China       | Multicenter                              | N = 205<br>FOB=28<br>Mean age:<br>44 years, range:<br>5–67years<br>M: 68%   | BAL=15<br>Brush Biopsy =13 | BAL positive=14/15<br>(93%)<br>Brush Biopsy =6/<br>13(46%) | NA                            | NA   | NA                | January 1 through<br>February 17, 2020       |
| 11    | Liu R <sup>6</sup> , China        | Single centre,<br>retrospective<br>study | N = 4880<br>FOB=5<br>Median Age was<br>50 years<br>(IQR=27);<br>M = 46.13%; NA  | BAL=5                      | BAL positive =5/5<br>(100%)                                | NA                            | NA   | NA                | January 22 to Febru-<br>ary 14, 2020         |
| 12    | Turriziani O <sup>3</sup> , Italy | Single Centre                            | N = 6565<br>FOB=367<br>median age was<br>57, IQR: 41–73   | BAL=367                    | BAL positive = 55/<br>367 (15%)                            | NA                            | NA   | NA                | 6 March through 4<br>May 2020                |
| 13    | Chang J <sup>4</sup> , USA        | Single centre                            | N = 177<br>(FOB=206)<br>Mean age ± SD:<br>59.0 ± 14.5<br>M: 54%;<br>Lung Transplant<br>66 (37.3%) COPD/<br>Asthma 36<br>(20.3%)<br>Interstitial Lung<br>Disease 32 (18.1) | BAL=206                    | BAL positive = 0   | NA                            | NA   | NA                | April 13, 2020, and<br>July 10, 2020         |
| 14    | Challener D <sup>27</sup> , USA   | Single centre                            | N = 34; NA;<br>M: 53%; NA   | BAL=34                     | BAL positive = 0   | NA                            | Fungal n = 5<br>Viral n = 4<br>Bacterial n = 7<br>Mycobacteria<br>n = 2  | NA                | February 6, 2020<br>and February 20,<br>2020 |
| 15    |                                   |  |   |                            |  | NA                            |  | NA                | NA   |

(continued on next page)

**Table 1** (Continued)

| S. No | Study/place                             | Study Settings                     | Patient number; Age; Males; Comorbidities  | Intervention                            | Outcome  | BAL morphological findings | Other Microorganisms in BAL  | Clinical Outcomes | Time                               |
|-------|---|------------------------------------|--|---|--|----------------------------|--|-------------------|------------------------------------|
|       | Catherine Gao et al., <sup>28</sup> USA | Single centre, retrospective study | N = 123<br>Median Age: 63years, IQR: 46–70<br>M: 68%; NA   | Total BAL=123, BAL in NP negative= 48   | BAL positive: 9<br>Bacterial infection: (18/79)<br>22.8% |                            | Bacterial co-infection: 42/123 (34.1%)                                   |                   | (continued on next page)           |
| 16    | Barberi et al., <sup>8</sup> Italy      | Single centre, retrospective study | N = 198<br>Median Age: 70years, IQR:58–78<br>M = 54%; NA   | Total BAL=198<br>BAL in NP negative=198 | BAL positive:32 (16%)                                    | NA                         | NA   | NA                | March 1, 2020 until April 30, 2020 |
| 17    | Clercq et al., <sup>11</sup> Belgium    | Single centre, retrospective study | N = 405;<br>Mean age: 56.8 ± 13.3 years<br>M:59.3%;<br>Any concomitant disease 16 (80%)<br>Hypertension 4 (20%)<br>Malignancy 7 (35%)<br>Chronic kidney disease 6 (30%)<br>Chronic cardiac disease 6 (30%)<br>Chronic pulmonary disease, not asthma 4 (20%)<br>Asthma 4 (20%)  | Total BAL=27<br>BAL in NP negative=27   | BAL positive = 7   | NA                         | H. influenzae =3<br>S. Pneumoniae = 1<br>M. Pneumoniae =1<br>E coli. = 2 | NA                | 19 March 2020 and 30 April 2020    |
| 18    | Mahmood et al., <sup>9</sup> USA        | Multicentre, retrospective study   | N = 53;<br>Median Age: 62years, IQR:46–69<br>M = 67.9%;<br>Diabetes 17 (32.1)<br>Congestive heart failure 9 (17.1)<br>Coronary Artery Disease 13 (24.5)<br>Hypertension 14 (26.4)<br>Cirrhosis 4 (7.5)<br>Chronic kidney disease 12 (22.6)<br>Thrombocytopenia 4 (7.5)<br>Malignancy 8 (15.1)<br>Lung Transplant 7 (13.2)<br>Chronic obstructive lung disease 7 (13.2) | Total BAL=53<br>BAL in NP negative=53   | BAL positive = 1   | NA                         | NA   | NA                | 1 March 2020 and 31 July 2020      |

**Table 1** (Continued)

| S. No | Study/place                     | Study Settings                 | Patient number;<br>Age; Males;<br>Comorbidities   | Intervention                               | Outcome          | BAL morphological<br>findings | Other<br>Microorganisms in<br>BAL | Clinical Outcomes | Time                                  |
|-------|---------------------------------|--------------------------------|---|--|------------------|-------------------------------|-----------------------------------|-------------------|---------------------------------------|
|       | Oberg et al., <sup>12</sup> USA | Multicentre, prospective study | N = 189;<br>Average Age:<br>60.8 years,<br>M = 58%;<br>Comorbid conditions 119 (63)<br>Hypertension 46 (24.3)<br>Diabetes mellitus II 33 (17.5)<br>Malignancy, not lung 31 (16.4) | Total BAL=189<br>BAL in NP<br>negative=189 | BAL positive = 0 | NA                            | NA                                | NA                | March 15, 2020, and November 9, 2020, |

FOB - Fiberoptic Bronchoscopy; BAL - Bronchoalveolar Lavage; SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2; M - Male; IQR- Inter Quartile Range; NA - Not Available.

## Results

911 records were identified at initial database extraction, of which nineteen articles were included in our systematic review,<sup>2,3,13–21,4–6,8–12</sup> after which two articles where BAL was done in only ten or less patients were excluded. In total, 17 articles were therefore included in the final meta-analysis (Fig. 1).

The pooled estimate of SARS-CoV-2 positivity in BAL was 11% (95%CI: 0.01–0.24) (Fig. 2). The robustness of this estimate was indicated by minor asymmetry in the Doi plot (Fig. 3). There was high heterogeneity in the estimate of the pooled proportion ( $I^2 = 96\%$ ). Further investigation using sensitivity analysis found that the exclusion of none of the studies significantly affected the pooled estimate (Fig. 4). Also, there appeared to be minimal risk of bias amongst the

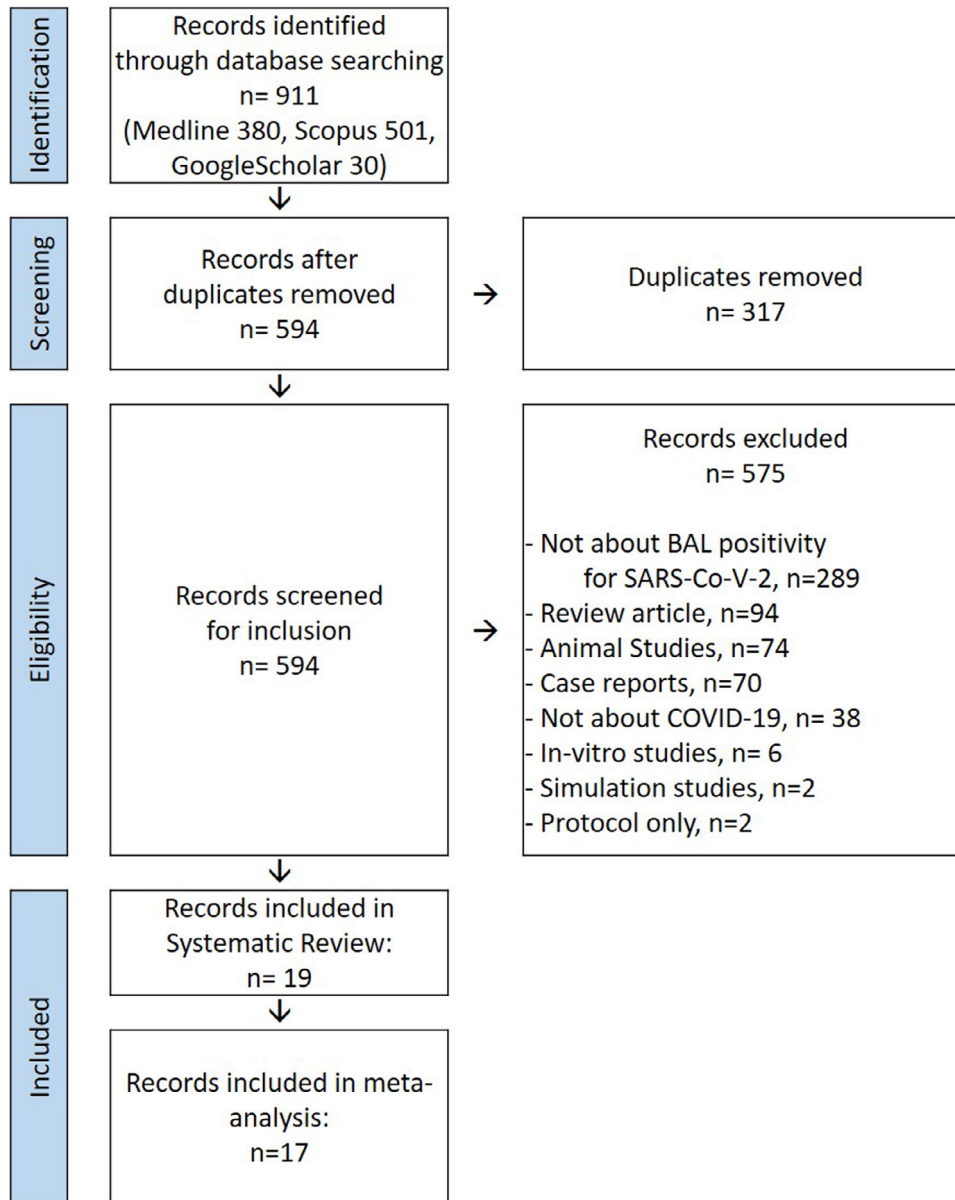


Fig. 1. PRISMA flow diagram depicting the flow of information through different phases of systematic review.



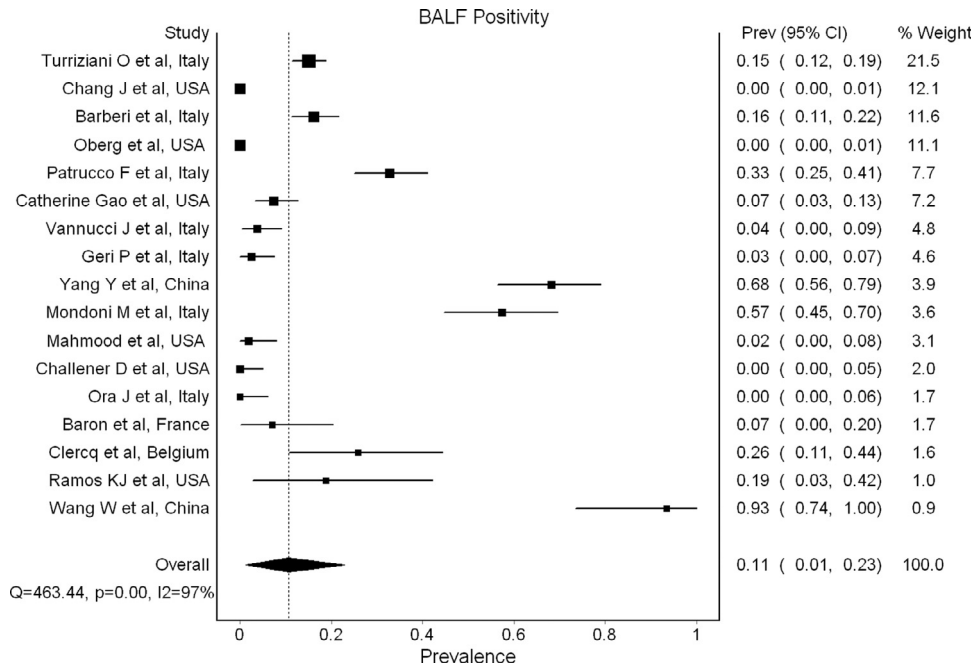


Fig. 2. Forest plot representing the pooled estimate of SARS-CoV2 positivity in BAL.

studies, particularly regarding the description of non-responders and few regarding sample size justification (Fig. 5).

**Discussion**

This meta-analysis attempts to assess the outcomes of BAL in detecting SARS-CoV-2 in patients with negative NP and or OP swabs by RT-PCR. We included a total of 19 studies in the systematic review, and 17 were included in the metanalysis. There was minimal risk of bias amongst the studies. A sensitivity analysis also showed that the results appear to be robust and not dependent on any individual study results.

BAL is an excellent method for the microbiological diagnosis of lung infections, especially in immunocompromised patients.<sup>22</sup>

Studies have shown the detection rate of various microorganisms in BAL fluid to range between 50 and 73%.<sup>22-24</sup> The microbiologic and molecular diagnostic testing of BAL samples widely available for etiology (bacterial, viral and, fungal) of pneumonia. Notably, diffuse alveolar hemorrhage (DAH), foamy alveolar macrophages and, a gamut of BAL cellular findings (eosinophilic, lymphocytic, or neutrophilic predominance) may be diagnostic or relatively so for pulmonary infections.<sup>25</sup> BAL diagnostic utility is reportedly 34–59%; etiologies include undiagnosed causes of acute hypoxemic respiratory failure, ventilator-associated pneumonia, and secondary infections. The latter is vital in terms of restricting superfluous antibiotic usage.<sup>26</sup> The drawback of BAL is the lack of ability to differentiate between colonizers and active infection by the recovered pathogenic microorganisms in the absence of clinical disease.<sup>27</sup>

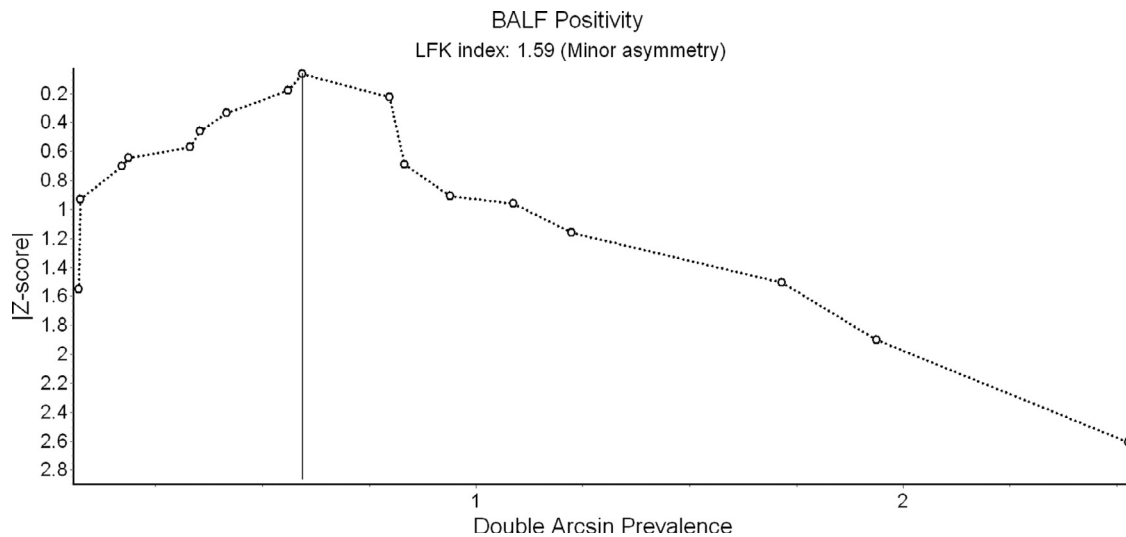
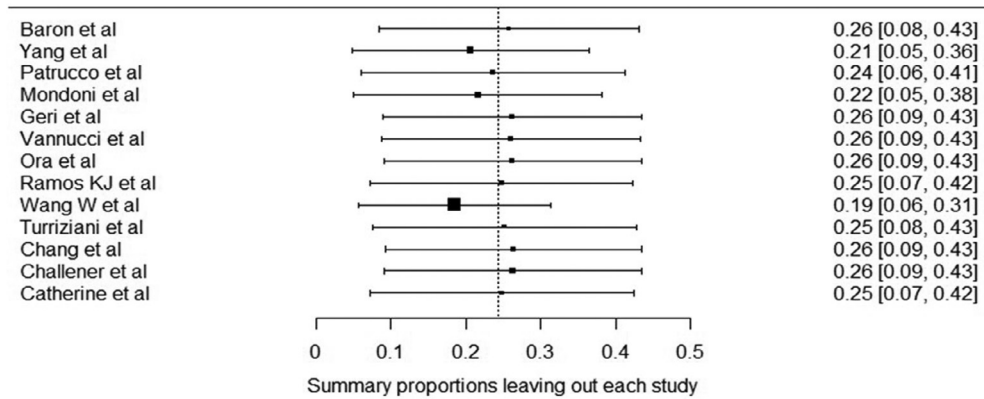


Fig. 3. DOI plot representing the robustness of estimate.

**Figure 4: Influential Analysis**

Each box represents a summary proportion estimated leaving out a study. The reference line indicates where the original summary proportion lies. From the graph, we can deduce that the further a box deviates from the reference line (e.g. study by Wang W et al.), the more pronounced the impact of the corresponding missing study will be on the original summary proportion

**Fig. 4.** Influential analysis.

We have tried to analyze BAL's role in diagnosing SARS CoV-2 infection when nasopharyngeal swabs are negative. The basis for the hypothesis that the virus may be detected in such cases is that the angiotensin-converting enzyme 2 (ACE2) binding affinity of the S protein is an important determinant of SARS-CoV-2 infectivity and disease severity.<sup>28</sup> Studies have shown the predominance of these receptors in the lower respiratory tract and SARS CoV-2 having higher receptor tropism in the lower respiratory tract.<sup>16,28</sup> Although studies have a wide range of positivity, a pooled estimate of 11% suggests that BAL may be used to confirm SARS CoV-2 infection where nasopharyngeal specimens are negative, and there is high clinical or radiological suspicion.

There are multiple studies of BAL performed in COVID-19 patients for microbiological sampling. The BAL specimen served two purposes: for patients with negative nasopharyngeal swabs for SARS-CoV-2, it provided an additional source for microbiological confirmation and diagnosing superadded infections. Studies also showed a predominance of neutrophils in these patients, which may be due to superadded bacterial or viral infections or simply a supplementary finding in severe COVID-19 acute respiratory distress syndrome (ARDS) patients.<sup>13</sup> Gelarden et al. compared the results of BAL cytopathology with clinical outcomes. In this study, longer hospital stay ( $p < 0.05$ ) and longer requirement for mechanical ventilation ( $p < 0.05$ ) was associated with BAL lymphocytosis, and the median atypical (activated) lymphocyte count was associated with shorter hospital stay ( $p < 0.05$ ), shorter time on mechanical ventilation ( $p < 0.05$ ) and improved survival.<sup>29</sup> Dentone et al. compared the analysis of BAL cellularity with clinical outcomes in patients on invasive mechanical ventilation. The majority of cells in their BAL analysis were neutrophils (70%, IQR 37.5–90.5) and macrophages (27%, IQR

7–49), while a minority were lymphocytes, 1%, TCD3+92% (IQR 82–95). Their ICU mortality was 32.8%. The non-survivors were of the older age group ( $p = 0.033$ ), and their peripheral lymphocytes ( $p = 0.012$ ) were lower than the survivors. The multivariate analysis showed that the percentage of macrophages in the BAL also correlated with poor outcome (OR 1.336, CI95% 1.014–1.759,  $p = 0.039$ ).<sup>30</sup>

Earlier in the pandemic, consensus statements suggested limiting bronchoscopy to urgent indications, and COVID-19 positivity was listed as a relative contraindication.<sup>31</sup> The purpose was to limit the risk of transmission of the virus amongst healthcare workers as bronchoscopy is an aerosol-generating procedure. Some guidelines suggested bronchoscopy could be performed in these patients with appropriate precautions.<sup>32</sup> Studies also demonstrated that performing BAL had a significant role in decision-making, especially in severe ARDS patients.<sup>13</sup> Yang et al. observed that the yield in severe cases was greater at 8–14 days and >15 days compared to mild cases. Also, severe cases were more commonly seen in higher age groups and male gender.<sup>33</sup> A few studies assessed for superadded infections and found associated viral, fungal, and bacterial organisms.<sup>13–15</sup>

Although specific CT scan of thorax features such as bilateral ground-glass opacities mixed with consolidation, mainly peripheral, suggestive of SARS CoV-2 infection, CT scan has low specificity (25%).<sup>24</sup> Thus, microbiological confirmation may be necessary when an alternative diagnosis is suspected. Studies to correlate the CT scan features with BAL findings have shown that patients with SARS-CoV-2 infection had more CT alterations than the SARS-CoV-2-negative patients,<sup>21,22</sup> suggesting CT scan may add substantial evidence in the diagnosis of this infection.

Risks to the patient of performing BAL are similar to that of flexible bronchoscopy, including hypoxemia, fever, bronchospasm, and

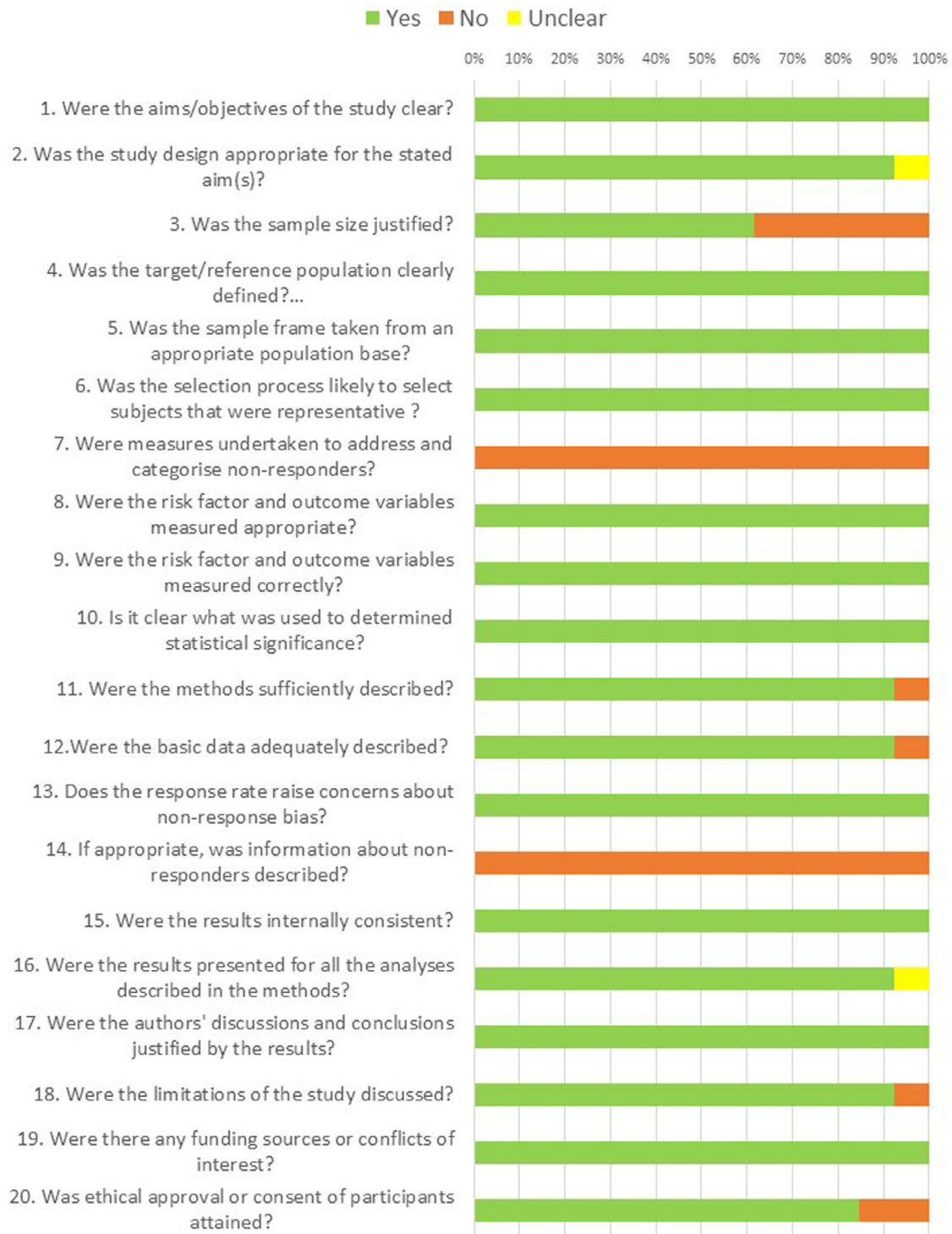


Fig. 5. Risk of bias.

more rarely, pneumothorax. In the setting of COVID-19, as for other infectious diseases, an additional risk is an infection of health care workers.<sup>34</sup>

One of the limitations of this review is the dynamicity of the current COVID-19 situation. The current evidence is still developing and is likely to demand revisions in the current estimates quickly. However, the prevalence estimates in the current study do provide an insight into the diagnostic utility of BAL in COVID-19.

## Conclusion

The current study demonstrates that BAL can be used to diagnose additional cases of primary disease and superadded infections in patients with severe COVID-19 lower respiratory tract infection when NP and or OP swabs are negative for RT-PCR SARS-CoV-2. Further, well-designed prospective studies are needed to substantiate these findings and inform guidelines for BAL in COVID-19 and other respiratory infections.

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