Comparison of confirmed COVID-19 with SARS and MERS cases - Clinical characteristics, laboratory findings, radiographic signs and outcomes: A systematic review and meta-analysis

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Summary
Introduction: Within this large-scale study, we compared clinical symptoms, laboratory findings, radiographic signs, and outcomes of COVID-19, SARS, and MERS to find unique features.

Method: We searched all relevant literature published up to February 28, 2020. Depending on the heterogeneity test, we used either random or fixed-effect models to analyze the appropriateness of the pooled results. Study has been registered in the PROSPERO database (ID 176106).

Result: Overall 114 articles included in this study; 52 251 COVID-19 confirmed patients (20 studies), 10 037 SARS (51 studies), and 8139 MERS patients (43 studies) were included. The most common symptom was fever; COVID-19 (85.6%, P < .001), SARS (96%, P < .001), and MERS (74%, P < .001), respectively. Analysis showed that 84% of Covid-19 patients, 86% of SARS patients, and 74.7% of MERS patients had an abnormal chest X-ray. The mortality rate in COVID-19 (5.6%, P < .001) was lower than SARS (13%, P < .001) and MERS (35%, P < .001) between all confirmed patients.

Conclusions: At the time of submission, the mortality rate in COVID-19 confirmed cases is lower than in SARS- and MERS-infected patients. Clinical outcomes and findings would be biased by reporting only confirmed cases, and this should be considered when interpreting the data.

KeyWords
coronavirus, COVID-19, meta-analysis, Middle East respiratory syndrome coronavirus, SARS virus, severe acute respiratory syndrome

Abbreviations: ACE2, angiotensin-converting enzyme 2; ARDS, acute respiratory distress syndrome; CDC, Centre for Disease Controls; CI, confidence interval; COVID-19, coronavirus disease 2019; CRP, C-reaction protein; CT scan, computed tomography scan; ESR, erythrocyte sedimentation rate; GGO, ground-glass opacity; ICU, intensive care unit; IL, interleukin; IQR, interquartile range; MCP-1, monocyte chemotactic protein 1; MERS, Middle East respiratory syndrome; N, number; NA, not known; PRISMA, preferred reporting items for systematic reviews and meta-analyses statement; RT-PCR, real-time polymerase chain reaction; SARS, severe acute respiratory syndrome; SARS-Cov-2, severe acute respiratory syndrome coronavirus-2; TNF-α, tumor necrosis factor-α; WBCs, white blood cells; WHO, World Health Organization.
1 | INTRODUCTION

During the last two decades, coronaviruses have been recognized as one of the most critical human pathogenic viruses that affect global health and cause concern in the world health system.\(^1\) Coronavirus is classified into four genera: alpha, beta, delta, and gamma. Major human pathogenic viruses belong to the beta genus, including Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and the 2019 novel coronavirus (COVID-19).\(^2\)

Although coronaviruses are recognized as causes of the common cold, SARS was the first coronavirus to cause a life-threatening respiratory infection in humans. It was endemic in Guangzhou China in 2002-2003 and quickly spread to other countries in Asia, the Americas, Europe, and South Africa. A total of 8098 SARS infected cases and 774 deaths (about 10% mortality) were reported.\(^3\)

About a decade later, MERS caused respiratory infection in the Middle East. Most of these patients had a history of travel to the Arabian Peninsula, or they were in contact with infected people, of which some were camel shepherds. After the Middle East, the second outbreak of MERS occurred in 2014-2017 in South Korea, indicating the circulation of the virus and a more significant concern for the world health community. At that time, MERS was responsible for infecting 2458 people and 848 deaths (about 35% mortality).\(^4\)

In December 2019, a cluster of Covid-19 patients with symptoms of pneumonia complicated with acute respiratory distress syndrome (ARDS) was observed in Wuhan, China.\(^5,6\) In comparison to SARS and MERS, Covid-19 has a higher rate of spread and became a pandemic in about 4 months. The high power of this large-scale dissemination led to the quarantine of several cities in different countries.\(^7\) Based on the World Health Organization (WHO) 57th report on 17 March 2020; worldwide there have been 179,112 confirmed cases, with 7426 deaths (about 4% mortality).\(^8\) There is no vaccine or targeted treatment currently available for COVID-19 infection. Treatment is mostly supportive, although multiple experimental antiviral medications are being evaluated.\(^9,10\) Thus, prevention and rapid diagnosis of infected patients are crucial. The trigger for rapid screening and treatment of COVID-19 patients is based on clinical symptoms, laboratory, and radiographic findings that are similar to SARS and MERS infections.

In this study, we attempted to distinguish the clinical symptoms, laboratory findings, radiographic signs, and outcomes of confirmed COVID-19, SARS, and MERS patients. All findings are compared to determine unique features among each of them. These data could be helpful in the early diagnosis and prevention of infection as well as providing more reliable epidemiological data on a large-scale for health care policies and future studies.

2 | METHODS

2.1 | Search strategy

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement (PRISMA) guidelines, and it has been registered in the PROSPERO database (ID 176106).\(^{11}\) We searched all studies published up to 28 February 2020, from the following databases: Embase, Scopus, PubMed, Web of Science, and the Cochrane library. Search medical subject headings (MeSH) terms used were: “COVID-19,” “Coronavirus,” “Severe Acute Respiratory Syndrome,” “SARS Virus,” “severe acute respiratory syndrome coronavirus 2,” “Coronavirus Infections,” “Middle East Respiratory Syndrome Coronavirus,” and all their synonyms like "Wuhan Coronavirus," "SARS-CoV-2," and “COVID-19,” “2019-nCoV” and MERS. Moreover, we searched for unpublished and grey literature with Google scholar, Centre for Disease Controls (CDC) and WHO databases. We also examined references of included articles to find additional relevant studies. There was no language restriction, and all included studies were written in English or Chinese languages; the latter was translated by https://translate.google.com/. Additional search strategy details are provided in Table S1.

2.2 | Study selection

Duplicate studies were removed using EndNote X7 (Thomson Reuters, New York, NY, USA). Records were initially screened by title and abstract by independently four authors (AP, SG, AK, and RF). The full-text of potentially eligible records was retrieved and examined, and any discrepancies were resolved by consensus.

2.3 | Eligibility and inclusion criteria

Studies had to fulfill the following predetermined criteria to be eligible for inclusion in our meta-analysis. All case-control, cross-sectional, cohort studies, case reports, and case series peer-reviewed studies were included if they reported the number of confirmed cases of patients with demographic data, [AND] [OR] clinical data, [AND] [OR] laboratory data, [AND] [OR] risk factor data.

2.4 | Exclusion criteria

Studies were excluded if they did not report the number of confirmed cases. Letters to the editor, individual case reports, review articles, and news reports were also excluded. Duplicate information from the same patient was combined and counted as a single case when the data was reported twice.

2.5 | Data extraction

All COVID-19 included publications were published in 2020, and all patients were from China. The following items were extracted from each article: first author, center and study location in China, countries, sample collection time, patient follow-up time, the
reference standard for infection confirmation, number of confirmed cases, study type, and all demographic, clinical, laboratory data, and risk factor data. Three of our authors (SG, AK, and RF) independently extracted data, and all extracted data were checked randomly by another author (AP); differences were resolved by consensus.

### 2.6 Quality assessment

Quality assessments of studies were performed by two reviewers independently according to the Critical Appraisal Checklist recommended by the Joanna Briggs Institute, and disagreements were resolved by consensus. The checklist is composed of nine questions that reviewers addressed for each study. The “Yes” answer to each question received one point. Thus, the final scores for each study could range from zero to nine (Table S2).

### Data cleaning and preparation

Data cleaning and preparation were done in Microsoft Excel 2010 (Microsoft©, Redmond, WA, USA), and further analyses were carried out via Comprehensive Meta-Analysis Software Version 2.0 (Biostat, Englewood, NJ). Determination of heterogeneity among the studies was undertaken using the chi-squared test (Cochran’s Q) to assess the appropriateness of pooling data. Depending on the heterogeneity test, we used either random or fixed-effect models for pooled results. In the case of high heterogeneity (I² > 50%), a random effect model (M-H heterogeneity) was applied, while in low heterogeneity cases (I² < 50%), a fixed-effect model was used. Percentages and means ± SDs were calculated to describe the distributions of categorical and continuous variables, respectively. P values reflect study heterogeneity with <.05 being significant. We also used the funnel plot, Begg’s, and Egger’s tests based on the symmetry assumption to detect publication bias (Figure S1).
| First author     | Sampling center/Country             | Sample collection time               | Published year | Patient follow-up (d) | N Confirmed patients | Mean age in years (IQR) | N sex (male) | Reference standard | Study type |
|------------------|------------------------------------|-------------------------------------|----------------|-----------------------|----------------------|------------------------|--------------|-------------------|------------|
| Nanshan Chen 14 | Wuhan Jinyintan Hospital           | 1 Jan to 20 Jan 2020                | 2020          | 5-24                  | 99                   | 55.5 (21-82)           | 67           | RT-PCR            | Retrospective|
| Kaiyuan Sun 15   | Multicenter                        | 20 Jan-29, 2020                    | 2020          | 42                    | 288                  | 49 (2-89)              | 62.3         | CDC guideline     | Retrospective|
| Jie Li 16        | Dazhou Central Hospital            | 22 January-10 February 2020         | 2020          | 1-21                  | 17                   | 45.1 (32-65)           | 9            | RT-PCR            | Retrospective|
| Dawei Wang 17    | Zhongnan Hospital of Wuhan         | 1 January-28 January 2020           | 2020          | 6-34                  | 138                  | 56 (42-68)             | 75           | RT-PCR            | Retrospective|
| Chaolin Huang 18 | Jin Yintan Hospital (Wuhan)        | 31 Dec 2019-UN                      | 2020          | NA                    | 41                   | 49 (41-58)             | 30           | RT-PCR            | Retrospective|
| Weijie Guan 19   | Multicenter                        | NA                                  | 2020          | NA                    | 1099                 | 47 (35-58)             | 640          | RT-PCR            | Retrospective|
| Yang Yang 20     | NA                                 | 2020                                | 51 d          | 4021                  | 49                   | 2211                   | NA           | RT-PCR            | Retrospective|
| Lei Chen (Chinese)21 | Tongji hospital in Wuhan         | 14-29 January 2020                  | 2020          | 15 d                  | 29                   | 56 (26-79)             | 21           | RT-PCR            | Retrospective|
| Adam Bernheim 22 | Multicenter                        | 18 January-2 February 2020          | 2020          | 12 d                  | 121                  | 45 (18-80)             | 61           | RT-PCR & CT scan | Retrospective|
| Feng Pan 23      | Union Hospital                     | 12 Jan-6 Feb 2020                   | 2020          | NA                    | 21                   | 40 (25-63)             | 15           | RT-PCR            | Retrospective|
| Jin Zhang 24     | No.7 hospital of Wuhan             | 16th Jan to 3rd Feb 2020            | 2020          | NA                    | 140                  | 57 (25-87)             | 71           | RT-PCR            | Retrospective|
| Yichun Cheng 25  | Tongji hospital in Wuhan           | 28 January-11 February 2020         | 2020          | 10 (7-13)             | 710                  | 63 (51-71)             | 374          | RT-PCR            | Retrospective|
| Ming-Yen 26      | Hong Kong-Shenzhen Hospital        | NA                                  | 2020          | NA                    | 21                   | 56 (37-65)             | 13           | RT-PCR            | Retrospective|
| Sijia Tian 27    | Beijing Emergency Medical Service  | 20 Jan to 10 Feb 2020               | 2020          | Feb. 10 20           | 262                  | 47.5 (1-94)            | 127          | RT-PCR            | Retrospective|
| Qun Li 28        | NA                                 | NA                                  | 2020          | NA                    | 425                  | 15-89 (26-82)          | 240          | WHO guideline     | Retrospective|
| De Chang 29      | Three hospitals in Beijing         | 16 January-29 January 2020          | 2020          | 4 Feb. 2020          | 13                   | 34 (34-48)             | 10           | NA                | Retrospective|
| Xiao-Wei Xu 30   | Zhejiang province                  | 10 January-26 January 2020          | 2020          | 10 d                  | 62                   | 41 (32-52)             | 36           | WHO guideline     | Retrospective|
| Fengxiang Song 31 | Center for Disease Control, Shanghai | 20 January-27 January 2020         | 2020          | NA                    | 51                   | 49 (16-76)             | 25           | CT scan & nucleic acid test | Retrospective|
| Michael Chung 32 | Multicenter                        | 18-27 January 2020                  | 2020          | NA                    | 21                   | 51 (29-77)             | 13           | CT scan, NA      | Retrospective|
| Zunyou Wu (CDC) 33 | Multicenter                      | through 11 February 2020            | 2020          | 15 d                  | 44 672               | 30-79                  | 22 981       | nucleic acid test result | Retrospective|

**TABLE 1** Characterization of included studies
| First author              | Sampling center/Country | Sample collection time       | Published year | Patient follow-up (d) | N Confirmed patients | Mean age in years (IQR) | N sex (male) | Reference standard | Study type          |
|--------------------------|-------------------------|------------------------------|----------------|-----------------------|----------------------|-------------------------|-------------|--------------------|---------------------|
| All S. Omran 34          | Saudi Arabia            | 2013                         | 2013           | NA                    | 3                    | UN                      | UN          | RT-PCR             | Case series         |
| Owen Tak-Yin Tsang 35    | Hong Kong               | 26 January 2003-31 March 2003| 2003           | NA                    | 156                  | UN                      | 90          | RT-PCR             | Retrospective        |
| Li-Yang Hsu 36           | Singapore               | 2003                         | 2003           | NA                    | 20                   | (19-73)                 | 5           | RT-PCR             | Retrospective        |
| Christl A Donnelly 37    | Hong Kong               | 2003                         | 2003           | NA                    | 1425                 | UN                      | UN          | RT-PCR             | Prospective          |
| Christopher 38           | Canada                  | 2003                         | 2003           | NA                    | 144                  | (34-57)                 | NA          | RT-PCR             | Retrospective        |
| Monali Varia 39          | Canada                  | 2003                         | 2003           | NA                    | 128                  | 42 (21 m-68 y)          | 51          | RT-PCR             | Retrospective        |
| Robert A Fowler 40       | Canada                  | 2003                         | 2003           | NA                    | 38                   | (39-69.6)               | 23          | RT-PCR             | Retrospective        |
| J S M Peiris 41          | China                   | 2003                         | 2003           | NA                    | 50                   | (23-74)                 | NA          | RT-PCR             | Prospective          |
| J S M Peiris 42          | Hong Kong               | 2003                         | 2003           | NA                    | 75                   | UN                      | 36          | RT-PCR             | Prospective          |
| J W M Chan 43            | Hong Kong               | 2003                         | 2003           | NA                    | 115                  | UN                      | NA          | RT-PCR             | Retrospective        |
| Jann-Tay Wang 44         | Taiwan                  | 2003                         | 2003           | NA                    | 76                   | 46.5 (24-87)            | 34          | RT-PCR             | Retrospective        |
| K L E Hon 45             | China                   | 2003                         | 2003           | NA                    | 10                   | NA                      | 2           | RT-PCR             | Retrospective        |
| K. T. Wong 46            | Hong Kong               | 2003                         | 2003           | NA                    | 138                  | 39 (20-83)              | 66          | RT-PCR             | Retrospective        |
| Kamaljit Singh 47        | Singapore               | 2003                         | 2003           | NA                    | 14                   | 58 (21-84)              | 5           | CT scan and RT-PCR | Retrospective        |
| Kenneth W. Tsang 48      | China                   | 2003                         | 2003           | NA                    | 10                   | 52.5 ± 11               | 5           | RT-PCR             | Retrospective        |
| Marianna Ofner-Agostini 49 | Canada                | 2003                         | 2006           | NA                    | 17                   | 39.2 (27-58)            | 4           | RT-PCR             | Retrospective        |
| N S Zhong 50             | China                   | 2002                         | 2003           | NA                    | 50                   | 38.4                    | 28          | RT-PCR             | Retrospective        |
| Nelson Lee 51            | China                   | 2003                         | 2004           | NA                    | 17                   | 34 (22-57)              | 6           | RT-PCR             | Retrospective        |
| Nelson Lee 52            | China                   | 2003                         | 2003           | NA                    | 138                  | NA                      | NA          | RT-PCR             | Cohort               |
| P.L. Ho 53               | China                   | 2003                         | 2005           | NA                    | 44                   | 39.27 ± 11.26           | 22          | RT-PCR             | Retrospective        |
| Ping Tim Tsui 54         | China                   | 2003                         | 2003           | NA                    | 323                  | 41 ± 14 (18-83)         | NA          | RT-PCR             | Retrospective        |
| Raymond S M Wong 55      | China                   | 2003                         | 2003           | NA                    | 157                  | NA                      | 64          | RT-PCR             | Retrospective        |
| Thomas W 56              | Singapore               | 2003                         | 2003           | NA                    | 199                  | NA                      | 65          | RT-PCR             | Cohort               |
| Timothy H Rainer 57      | China                   | 2003                         | 2003           | NA                    | 97                   | 37.0 ± 15.4             | 37          | RT-PCR             | Prospective          |
| W.N. Wong 58             | Hong Kong               | 2003                         | 2003           | NA                    | 205                  | 35.9 ± 16.2             | 90          | RT-PCR             | Cohort               |
| Z. Zhao 59               | China                   | 2002                         | 2003           | NA                    | 190                  | NA                      | NA          | RT-PCR             | Prospective          |
| Susan M. Poutanen 60     | Canada                  | 2003                         | 2005           | NA                    | 10                   | NA                      | NA          | RT-PCR             | Retrospective        |
| I.F.N. Hung 61           | China                   | 2004                         | 2004           | NA                    | 154                  | 41.5 (20-80)            | 92          | RT-PCR             | Retrospective        |
| Hoang Thu Vu 62          | Vietnam                 | 2003                         | 2004           | NA                    | 62                   | NA                      | NA          | RT-PCR             | Retrospective        |
**TABLE 1**  (Continued)

**COVID-19 studies (Total of 20 studies, 52,251 patients)**

| First author         | Sampling center/Country | Sample collection time | Published year | Patient follow-up (d) | N Confirmed patients | Mean age in years (IQR) | N sex (male) | Reference standard | Study type |
|----------------------|-------------------------|------------------------|----------------|-----------------------|----------------------|------------------------|--------------|-------------------|------------|
| F. Chena63           | Hong Kong               | 2002                   | 2004           | NA                    | 10                   | NA                     | 5            | RT-PCR            | Retrospective |
| C.W. Leung64         | China                   | 2004                   | 2004           | NA                    | 64                   | 11.7                   | 29           | RT-PCR            | Retrospective |
| Monica Avendano65     | Canada                  | 2003                   | 2003           | NA                    | 14                   | 42 ± 9 (27-63)         | 3            | RT-PCR            | Retrospective |
| Padmini Srikantiah66  | Us                      | 2003                   | 2005           | NA                    | 8                    | NA                     | NA           | RT-PCR            | Retrospective |
| Kwok H. Chan67        | Hong Kong               | 2004                   | 2004           | NA                    | 322                  | NA                     | NA           | RT-PCR            | Cohort      |
| Wannian Liang68       | China                   | 2003                   | 2003           | NA                    | 2443                 | 33 (1.0-90)            | NA           | RT-PCR            | Prospective |
| Xinchun Chen69        | China                   | 2004                   | 2004           | NA                    | 36                   | 30.3 ± 12.15           | 20           | RT-PCR            | Retrospective |
| Chi-wai Leung70       | Hong Kong               | 2004                   | 2004           | NA                    | 44                   | 12 (17-50)             | 20           | RT-PCR            | Prospective |
| LCL Heung71           | Hong Kong               | 2006                   | 2006           | NA                    | 93                   | NA                     | 18           | IF                | Cross-sectional |
| Ming-Han Tsai72       | Taiwan                  | 2003                   | 2008           | NA                    | 124                  | NA                     | NA           | ELISA             | Retrospective |
| Hy A. Dwosh73         | Us                      | 2003                   | 2003           | NA                    | 16                   | (24-80)                | 4            | RT-PCR            | Retrospective |
| Ari Bitnun73          | Canada                  | 2003                   | 2003           | NA                    | 15                   | NA                     | 6            | RT-PCR            | Prospective |
| Alice S. Ho74         | Hong Kong               | 2003                   | 2003           | NA                    | 40                   | (24-50)                | 9            | RT-PCR            | Retrospective |
| Leonard Grinblat75     | Canada                  | 2003                   | 2003           | NA                    | 40                   | 42.7 ± 13.5 (17-73)    | 18           | RT-PCR            | Retrospective |
| Cheng-Kuo Fan76       | Taiwan                  | 2005                   | 2005           | NA                    | 43                   | 41.0 ± 17.1            | 22           | RT-PCR            | Descriptive |
| Kin Wing Choi77       | Hong Kong               | 2003                   | 2003           | NA                    | 227                  | 39 (18-96)             | 75           | RT-PCR            | Retrospective |
| GM Leung78            | Hong Kong               | 2003                   | 2003           | NA                    | 1755                 | NA                     | 777          | RT-PCR            | Retrospective |
| Chung-Ming Chu79      | China                   | 2005                   | 2005           | NA                    | 79                   | 39.4 ± 11.5 (20-72)    | 38           | RT-PCR            | Retrospective |
| Kwok Hong Chu80       | Hong Kong               | 2004                   | 2004           | NA                    | 536                  | NA                     | NA           | RT-PCR            | Retrospective |
| T.-N. Jang81          | Taiwan                  | 2003                   | 2004           | NA                    | 29                   | 42.9 (22-82)           | 9            | RT-PCR            | Retrospective |
| Tze-wai Wong82        | China                   | 2004                   | 2004           | NA                    | 16                   | 22.3                   | 8            | RT-PCR            | Retrospective |
| Wei-Kung Wang83       | Taiwan                  | 2003                   | 2004           | NA                    | 17                   | 21-54                  | 9            | RT-PCR            | Retrospective |

**MERS studies (Total 43 studies, 8,139 patients)**

| First author           | Sampling center/Country | Sample collection time | Published year | Patient follow-up (d) | N Confirmed patients | Mean age in years (IQR) (Q1-Q3) | N sex (male) | Reference standard | Study type |
|------------------------|-------------------------|------------------------|----------------|-----------------------|----------------------|---------------------------------|--------------|-------------------|------------|
| Asad S. Aburizaiza84   | Saudi Arabia            | 2012                   | 2012           | NA                    | 8                    | (16-62)                         | NA           | IFA               | Cross-sectional |
| Marcel A. Müller85     | Saudi Arabia            | 2012-2013              | 2015           | NA                    | 15                   | 37.13 ± 8.64 (15-62)            | NA           | ELISA, IFA        | Cross-sectional |
| Abdulkarim Alheetheel86 | Saudi Arabia            | 2016                   | 2017           | NA                    | 30                   | NA                             | NA           | RT-PCR            | Cross-sectional |
| Abdulaziz A. Bin Saeed87 | Saudi Arabia           | 2015                   | 2016           | NA                    | 384                  | (1-66)                          | 226          | NA                | Cross-sectional |
| First author | Sampling center/Country | Sample collection time | Published year | Patient follow-up (d) | N Confirmed patients | Mean age in years (IQR) | N sex (male) | Reference standard | Study type |
|--------------|-------------------------|------------------------|----------------|-----------------------|----------------------|------------------------|--------------|-------------------|------------|
| Boyeong Ryu  | South Korea             | 2015                   | 2015           | NA                    | 34                   | (34-56.7)              | 20           | RT-PCR            | Cross-sectional |
| Jamal Ahmazadeh | Iran                  | 2019                   | 2019           | NA                    | 107                  | 50 ± 17                | 80           | NA                | Cross-sectional |
| Kazhal Mobarakii | Iran                  | 2019                  | 2019           | NA                    | 229                  | NA                     | 171          | RT-PCR            | Epidemiological analysis |
| Abdullah Assiri | Saudi Arabia         | 2013                   | 2013           | NA                    | 47                   | 55                     | 36           | RT-PCR            | Retrospective |
| Korea Centers for Disease | South Korea | 2015 | 2015 | NA | 186 | 55 (42-66) | 111 | RT-PCR | Retrospective |
| Abdullah Assiri | Saudi Arabia         | 2013                   | 2013           | NA                    | 23                   | 56 (24-94)             | 17           | RT-PCR            | Retrospective |
| Abdullah Assiri | Saudi Arabia         | 2014                   | 2016           | NA                    | 38                   | 51 (17-84)             | 28           | RT-PCR            | Retrospective |
| Abdullah M. Assiri | Saudi Arabia       | 2015                   | 2016           | NA                    | 143                  | 58 (2.0-99)            | 91           | RT-PCR            | Retrospective |
| Ashraf Abdel Halim | Egypt                | 2015                   | 2016           | NA                    | 32                   | 43.99 ± 13.03          | 20           | RT-PCR            | Retrospective |
| Deborah L. Hastings | Saudi Arabia      | 2014                   | 2016           | NA                    | 78                   | 53                     | 59           | RT-PCR            | Retrospective |
| F S Alhamlan | Saudi Arabia         | 2012-2015              | 2016           | NA                    | 1275                 | 50 (0-109)             | 807/1246     | RT-PCR            | Retrospective |
| H.E. El Bushra | Saudi Arabia         | 2015                   | 2016           | NA                    | 52                   | NA                     | 31           | RT-PCR            | Retrospective |
| Hanan H. Balkhy | Saudi Arabia         | 2016                   | 2016           | NA                    | 130                  | 56.3                   | 66           | RT-PCR            | Retrospective |
| Ikwo K. Oboho | Saudi Arabia         | 2014                   | 2015           | NA                    | 255                  | 45 (30-59)             | 174          | RT-PCR            | Retrospective |
| Kyung Min Kim | South Korea          | 2015                   | 2015           | NA                    | 36                   | 51                     | 20/36        | RT-PCR            | Retrospective |
| Ziad A. Memish | Saudi Arabia         | 2013                   | 2013           | NA                    | 7                    | (29-59)                | 0            | RT-PCR            | Retrospective |
| Won Suk Choi | South Korea           | 2015                   | 2015           | NA                    | 186                  | 5 (16-86)              | 111          | RT-PCR            | Retrospective observational |
| Mohammad Mousa Al-Abdallat | Jordan  | 2012 | 2014 | NA | 9 | 40 (25-60) | 6 | RT-PCR | Retrospective |
| Mustafa Saad | Saudi Arabia         | 2012-2014              | 2014           | NA                    | 70                   | 62 (1-90)              | 46           | RT-PCR            | Retrospective |
| Yaseen M. Arab | Saudi Arabia         | 2012-2013              | 2014           | NA                    | 12                   | 59 (36-83)             | 8            | RT-PCR            | Case series |
| Maimuna S. Majumder | South Korea | 2015 | 2015 | NA | 159 | 55 ± 15.9 (16-87) | 94 | RT-PCR | Retrospective |
| Victor Virlogeux | South Korea         | 2015                   | 2016           | NA                    | 107                  | 54.6                   | 96           | NA                | Retrospective |
| Jaffar A. Al-Tawfiq | Saudi Arabia  | NA | 17 | 60.7 | 11 | RT-PCR | Case-control |
| Thamer H. Alenazi | Saudi Arabia       | 2015                   | 2017           | NA                    | 130                  | 56.5                   | 66           | RT-PCR            | Prospective |
| Abdullah J. Alsahafi | Saudi Arabia      | 2012-2015              | 2015           | NA                    | 939                  | NA                     | 624          | NA                | NA |
| Karuna M. Das | Saudi Arabia         | 2015                   | 2015           | NA                    | 55                   | 54 ± 16 (12 to 85)     | 16           | RT-PCR            | Retrospective |
| Anwar E. Ahmed | Saudi Arabia         | 2014-2016              | 2017           | NA                    | 660                  | 53.9 ±17.9 (2-109)     | 452          | NA                | Retrospective |
| Anwar E. Ahmed | WHO website          | 2015-2017              | 2017           | NA                    | 537                  | 55 ± 17.9 (2-109)      | 370          | NA                | Retrospective |

(Continues)
RESULTS

3.1 Characteristics of included studies

The process of study selection is displayed in Figure 1. A total of 36,115 reports were screened for the analysis of patients with COVID-19, 36,014 were excluded after the title, and abstract screening and the full text of 81 reports were reviewed in full text. We excluded studies that did not report sufficient data. Out of 114 included studies, 20 studies met the inclusion criteria for COVID-19, 51 for SARS, 43 for MERS. The characteristics of the selected articles are summarized in Table 1. Of the 20 COVID-19 studies that were included in the analysis, 19 studies were in English, and one was in Chinese.21 All COVID-19 studies were retrospective, published in 2020, and all patients were from China.

3.2 Quality assessment

Quality assessment of included studies was performed based on the Critical Appraisal Checklist, and the final quality scores of the included studies are represented in Table S2. In brief, studies by Chen et al,14 Wang et al,17 Huang et al,18 Guan et al,19 Zhang et al,24 Cheng et al,25 Li et al,28 Xu et al,30 and Song et al31 had the highest quality of the COVID-19 studies available in the purpose of this study.

3.3 Demographics, baseline characteristics, and clinical characterization

Overall, 52,251 confirmed patients with COVID-19 infection, 10,037 with SARS, and 8,139 with MERS were included in the meta-analysis, of which 53.7% (95% CI 50-56.8, P < .001) of COVID-19, 43% (95% CI 40-46.5, P < .001) of SARS, 66% (95% CI 63-69, P < .001), of MERS included patients were male. Funnel plots for included studies did not detect significant publication bias (Figure S1). Table 2 shows that most COVID-19 patients (85.6% (95% CI 73-93, P < .001), SARS 96% (95% CI 93-97.6, P < .001), and MERS 74% (95% CI 63.5-83.5, P < .001) had fever (Figure S2). Cough was the second most common symptom presenting in COVID-19 patients (63% (95% CI 59-67, P < .001), SARS 54.2% (95% CI 49-59, P < .001), and MERS 61% (95% CI 51-70, P < .001) of patients (Figure S3).

Shortness of breath was less common in Covid-19 patients (17% (95% CI 9-31.5, P < .001), in comparison to SARS 32% (95% CI 20-46, P < .001), and MERS 51% (95% CI 41-63, P < .001). Likewise, chills were less common in Covid-19 patients 17% (95% CI 6.5-38, P < .001), in comparison to SARS 57.5% (95% CI 50-64, P < .001), and MERS 41% (95% CI 16-72, P < .001).

A much smaller proportion of COVID-19 patients had sore throat (12.3% (95% CI 7.8-17, P < .06), headache 12.2% (95% CI 8.3-18, P < .001), diarrhea 7.3% (95% CI 4.6-11.4, P < .001), rhinorrhea 6% (95% CI 3-12, P < .43), nausea and vomiting 6%
|                  | COVID-19 (Total of 20 Studies, 52,251 Patients) | SARS (Total of 51 Studies, 10,037 Patients) | MERS (Total 43 Studies, 8,139 Patients) |
|------------------|-------------------------------------------------|---------------------------------------------|----------------------------------------|
|                  | Included studies number | Included patients number | Included studies number | Included patients number | Included studies number | Included patients number |
| **Clinical**     | **presentation**       | (CI 95%)                    | **presentation**       | (CI 95%)                    | **presentation**       | (CI 95%)                    |
| **Age, y**       | 49.5 (mean)           | (46-52.5)                   | 37.5 (34.5-40.5)                   | 52 (51-54.5)                   |
| **Sex (Male)**   | 53.7 (50-56.8)        | 20                           | 43 (%) (40-46.5)                    | 66 (63-69)                   |
| **Fever**        | 85.6 (73-93)          | 15                           | 96 (93-97.6)                      | 74 (63.5-83.5)                |
| **Cough**        | 63 (55.5-70)          | 15                           | 54.2 (49-59)                      | 61 (51-70)                   |
| **Fatigue**      | 40.3 (29-52.5)        | 11                           | -                               | 28 (21-35)                   |
| **Sputum**       | 28 (19-39)            | 7                            | 21 (16-27)                       | 31.5 (22-43)                 |
| **production/  **|                    |                              | **Expectoration**                | **Myalgia**                   |
| **Expectoration**|                    |                              | 26 (14-43)                       | 33.3 (26.5-41)                |
| **Dyspnea**      | 20 (12.6-32)          | 7                            | 32 (20.5-45.5)                   | 40 (23-57)                   |
| **Shortness of** | 17 (9-31.5)           | 3                            | 32 (20-46)                       | 51 (41-63)                   |
| **Chill**        | 17 (6.5-38)           | 2                            | 57.5 (50-64)                     | 41 (16-72)                   |
| **Sore throat**  | 12.3 (7.8-17)         | 6                            | 17 (14-21)                       | 16.5 (10-26)                 |
| **Headache**     | 12.2 (8.3-18)         | 10                           | 38 (30-46)                       | 15 (11-20)                   |
| **Diarrhea**     | 7.3 (4.6-11.4)        | 11                           | 24 (17.5-31.5)                   | 17.3 (14.5-20.5)             |
| **Rhinorrhea**   | 6 (3-12)              | 3                            | 13 (8.5-20)                      | 6 (1-20)                     |
| **Nausea and**   | 6 (2.7-13)            | 4                            | 18.5 (13-25)                     | 20 (16-25)                   |
| **vomiting**     |                      |                              |                                |                            |
| **Runny nose**   | 4 (1-14)              | 1                            | 18 (9-30)                        | 21 (4-61)                    |

**Comorbid conditions**

COVID-19 | SARS | MERS

(Continues)
| Table 2 (Continued) |
|---------------------|
| **COVID-19 (Total of 20 Studies, 52,251 Patients)** | **SARS (Total of 51 Studies, 10,037 Patients)** | **MERS (Total 43 Studies, 8,139 Patients)** |
| **Clinical presentation a** (CI 95%) | **Included studies number** | **Included patients number** | **Clinical presentation a** (CI 95%) | **Included studies number** | **Included patients number** | **Clinical Presentation a** (CI 95%) | **Included studies number** | **Included patients number** |
| Recent travel or contact with endemic people resident of Wuhan | 69.5 (54.5-81) | 7 | 45.443 (20-34) | 1 | 156 | - | - |
| Chronic diseases | 41.2 (20-66) | 3 | 1227 | - | - | - | - |
| Exposure to seafood market | 24.3 (9.6-49) | 5 | 732 | - | - | - | - |
| Sick contacts with respiratory illness | 15 (4.5-39.6) | 4 | 829 | - | - | - | - |
| Hypertension | 15 (8.5-24.6) | 10 | 46 270 | 14 (5.5-31) | 4 | 504 | 36 (28-45) | 10 | 677 |
| ARDS | 10.6 (4-26.7) | 5 | 1439 | 51 (6-94) | 2 | 204 | 29 (14-51) | 2 | 55 |
| Diabetes | 8 (4-15) | 8 | 46 232 | 9.9 (5-16.5) | 10 | 2304 | 46 (34.5-58) | 17 | 1086 |
| Current smoker | 7.7 (3.7-15) | 5 | 1348 | 7.5 (5-11) | 4 | 347 | 21.5 (14-32) | 9 | 144 |
| Chronic liver disease | 5.7 (3.8-8.4) | 8 | 499 | 13.5 (5-30) | 6 | 604 | 9 (4-21) | 5 | 53 |
| Digestive system disease | 3.5 (2.5-4.9) | 2 | 1198 | 10.5 (6-5-6) | 5 | 504 | 16.5 (10-25) | 11 | 152 |
| Health care worker | 3 (2-4.6) | 3 | 46 196 | 28.5 (18-43) | 12 | 2328 | 21 (17-25.5) | 20 | 1232 |
| Past smoker | 3 (1.1-7.5) | 2 | 1239 | - | - | - | - |
| Cardiovascular and cerebrovascular diseases | 2.3 (2.2-2.5) | 8 | 46 302 | 9.5 (5-22) | 8 | 1045 | 20.5 (15-27) | 15 | 407 |
| Chronic respiratory disease | 2.2 (0.6-8) | 4 | 45 911 | 30 (15-50) | 10 | 2224 | 9 (6.5-12) | 1 | 939 |
| Cancer | 1.7 (0.4-7.4) | 6 | 46 078 | 1.3 (0.2-10) | 3 | 504 | 12 (7-20) | 10 | 182 |
| Renal failure | 2.3 (1-4) | 7 | 2289 | 4 (2.5-7) | 8 | 1103 | 20.5 (14-24.5) | 15 | 366 |
| Clinical presentation | Included studies number | Included patients number | Clinical presentation | Included studies number | Included patients number | Clinical presentation | Included studies number | Included patients number |
|-----------------------|-------------------------|--------------------------|-----------------------|-------------------------|--------------------------|-----------------------|-------------------------|--------------------------|
| COVID-19              | 20                      | (12-31)                  | 3                     | 281                     | 17.7 (6-42)              | 4                     | 21                      |
| SARS                  | 3281                    | 17.7 (6-42)              | 20                    | (12-32)                 | 9                       | 657                   |
| MERS                  | 42                      | 14 (5-31)                | 9                     | 1657                    | 35                      | 6987                  |

Abbreviations: ARDS, acute respiratory distress syndrome; CI, confidence interval; CT scan, CT scan; ICU, intensive care unit.

*Age is an exception, presented in mean age in years.
More detail information about demographics and clinical characterization of COVID-19 (Table S3), SARS (Table S4), and MERS patients (Table S5) demonstrated in the supplementary material.

### 3.4 | Risk factors and clinical characteristics of patients infected with COVID-19

The greatest risk for COVID-19 patients 69.5% (95% CI 54.5-81, \( P < .001 \)) up to 28 February 2020, is a history of recent travel to Wuhan, contact with people from Wuhan, or were Wuhan residents, and 24.3% (95% CI 9.6-49, \( P < .001 \)) had exposure at the seafood market(s). The most common comorbid chronic condition for COVID-19 and SARS is hypertension, and for MERS diabetes, 46% (95% CI 34.5-58, \( P < .001 \)). Overall, 41.2% (95% CI 20-66, \( P < .001 \)) of COVID-19 patients had a history of chronic diseases. Acute respiratory syndrome (ARDS) occurred more frequently in SARS 51% (95% CI 6-94, \( P < .001 \)) compared to MERS 29% (95% CI 14-51, \( P < .001 \)) and COVID-19 10.6% (95% CI 4-26.7, \( P < .001 \)).

More detailed information about comorbid conditions of COVID-19 (Table S6), SARS (Table S7), and MERS (Table S8) patients is demonstrated in the supplementary material.

### 3.5 | Chest X-ray and CT scan findings in patients infected with COVID-19

Analysis showed that 84% (95% CI 78-8.5, \( P < .001 \)) of COVID-19 patients, 86% (95% CI 77-92, \( P < .001 \)) of SARS patients, and 74.7% (95% CI 6.5-26.7, \( P < .001 \)) of MERS patients had abnormal radiological findings on chest X-ray and CT scans. The radiological abnormalities in COVID-19 patients were bilateral involvement of chest X-ray 76.8% (95% CI 62-8.5, \( P < .001 \)), consolidation 75.5% (95% CI 50.5-91, \( P < .001 \)), and ground-glass opacity 71% (95% CI 40-90, \( P < .001 \)) (Table 2). More detailed information about chest X-ray and CT scan findings of COVID-19 (Table S9), SARS (Table S10), and MERS patients (Table S11) is demonstrated in the supplementary material.

### 3.6 | Outcome

Most COVID-19 confirmed patients required hospitalization 85.4% (95% CI 68-94, \( P < .001 \)) and 20.6% (95% CI 6.7-48, \( P < .001 \)) were deemed to be in critical condition. The mortality rate of COVID-19 confirmed cases was 5.6% (95% CI 2.5-12.5, \( P < .001 \)), SARS 13% (95% CI 9-17, \( P < .001 \)), and MERS 35% (95% CI 31-39, \( P < .001 \)) (Figure 2).

### 3.7 | Laboratory findings of patients infected with COVID-19

The laboratory findings showed that among a subset of patients 4.5% (261/52 251) where data were available, thrombocytosis in COVID-19 patients was 61% (95% CI 45-72, \( P < .001 \)) which is more than double that of SARS at 30% (95% CI 35-64, \( P < .001 \)) and MERS 30% (95% CI 22-58, \( P < .001 \)). The most SARS patients 71% (95% CI 62-78, \( P < .001 \)) had decreased lymphocytes, and the most of MERS patients had decrease platelets 62% (95% CI 52-74, \( P < .001 \)) in their laboratory findings (Table 3).
Prior to 2002, coronaviruses were associated with mild respiratory illness, but with the emergence of SARS in 2002, MERS in 2012, and now in late 2019, COVID-19, it is established that coronaviruses infections can be associated with severe respiratory disease. The virus is transmitted via respiratory droplets or infected inanimate objects, and with its rapid spread worldwide in just a few months, the WHO has officially declared the COVID 19 outbreak a pandemic.22,126

### TABLE 3
Laboratory features for confirmed patients with COVID-19

|                  | Normal range | Mean (CI 95%) | Total patient number | Number of studies | Mean (CI 95%) | Total patient number | Number of studies | Mean (CI 95%) | Total patient number | Number of studies |
|------------------|--------------|---------------|----------------------|------------------|---------------|----------------------|------------------|---------------|----------------------|------------------|
| **Leucocytes**   | 3.5-9.5      | 5.55 (×10⁹ per L) (5.1-5.9) | 2361               | 11               | 5.1 (×10⁹ per L) (3.3-7) | 367               | 8               | 7.4 (×10⁹ per L) (6.8-7.6) | 280               | 5               |
| Increased        | 13.3 (%)     | 28 (%)        |                      |                  | 30 (%)        |                      |                  |                |                      |                  |
| Decreased        | 26 (%)       | 41 (%)        |                      |                  |                |                      |                  |                |                      |                  |
| **Neutrophils**  | 1.8-6.3      | 3.6 (×10⁹ per L) (3.1-4.1) | 412               | 8               | 4.6 (4.6-7.1)     | 614               | 5               | 5.3 (5-5.5)     | 150               | 2               |
| Increased        | -            | 5 (%)         |                      |                  |                |                      |                  |                |                      |                  |
| Decreased        | -            | 17.5 (%)      |                      |                  |                |                      |                  |                |                      |                  |
| **Lymphocytes**  | 1.1-3.2      | 0.98 (×10⁹ per L) (0.9-1.06) | 2361               | 11               | 0.74 (×10⁹ per L) (0.66-0.816) | 825               | 10              | -              | 210               | 4               |
| Decreased        | 62.5 (%)     | 71 (%)        |                      |                  |                |                      |                  |                |                      |                  |
| **Platelets**    | 125-350      | 186.5 (×10⁹ per L) (167-205) | 2200              | 9               | 179 (×10⁹ per L) (159-199) | 1912              | 5               | -              | 178               | 3               |
| Decreased        | 13 (%)       | 0.2 (%)       |                      |                  |                |                      |                  |                |                      |                  |
| Increased        | 61 (%)       | 41.5 (%)      |                      |                  |                |                      |                  |                |                      |                  |
| **CRPa**         | 0-0.5        | 29.6 (mg/L) (16.7-42.5) | 290               | 5               | 22.8 (mg/L) (22-35) | 256               | 2               | -              | 156               | 3               |
| Increased        | 81 (%)       | 93 (%)        |                      |                  |                |                      |                  |                |                      |                  |
| **Hemoglobin**   | 130-175      | 119 (g/L) (106-132) | 2062              | 8               | -              |                      |                  |                |                      |                  |
| ESRb             | 0-15         | 42 (mm/h) (46-57) | 120               | 2               | -              |                      |                  |                |                      |                  |
| **Albumi**       | 40-55        | 36.8 (g/L) (24.5-46) | 120               | 2               | -              |                      |                  |                |                      |                  |
| Decreased        | 80%          | -             |                      |                  |                |                      |                  |                |                      |                  |
| **Interleukin-6**| 0.0-7        | 7.9 (mg/mL) (6.8-8.6) | 99                | 2               | -              |                      |                  |                |                      |                  |
| Increased        | 52%          | -             |                      |                  |                |                      |                  |                |                      |                  |
| **LDHc**         | 120-250      | 280 (268-294) | 1783              | 9               | -              |                      |                  |                |                      |                  |
| Increased        | 70.3 (%)     | -             |                      |                  |                |                      |                  |                |                      |                  |

Abbreviations: CRP, C reaction protein; ESR, erythrocyte sedimentation rate; WBCs, white blood cells.

*a*Increased or decreased refers to values above or below the normal range.

*b*Erythrocyte sedimentation rate.

*c*Lactate dehydrogenase.

### DISCUSSION

Our results show that fever and cough were the most common clinical symptoms in COVID-19, SARS, and MERS. Among 52 251 patients with COVID-19 infection, while fatigue, sputum production, and myalgia (muscle soreness) were the next most frequent clinical symptoms; diarrhea, rhinorrhea, nausea, and vomiting were less common. Within the 10 037 confirmed SARS patients, the next most frequent clinical manifestations were chills, myalgia, headache, and dyspnea. Moreover, 8139 MERS patients commonly exhibited shortness of breath, chills, and dyspnea.
Shortness of breath was less common in COVID-19 patients (17%), in comparison to SARS (32%) and MERS (51%). Likewise, chills were less common in COVID-19 patients (17%), in comparison to SARS (57.5%) and MERS (41%). Therefore, these clinical symptoms should help distinguish the various coronavirus infections from each other.

Our analysis indicated recent travel to Wuhan, contact with people from Wuhan or residency in Wuhan, exposure to persons with respiratory symptoms, and seafood market exposures were common risks among those contracting COVID-19. Furthermore, chronic respiratory disease and recent travel to SARS endemic areas were most common among those contracting SARS. In addition, 28% of SARS patients and 21% of MERS confirmed patients were health care workers, which is higher than COVID-19 cases (3%). This data indicate that in coronavirus outbreaks, isolating infected individuals is one of the most important ways of controlling transmission.

We find that most of the patients with COVID-19, SARS, and MERS had abnormal chest radiological findings. With ground-glass opacity and consolidation in COVID-19 patients being more frequent than in SARS and MERS patients. Other studies reported that significant similarity exists when comparing radiological findings of COVID-19 patients with those suffering from complicated viral pneumonia such as SARS and MERS. Therefore, there appear to be no distinguishing radiological findings when comparing human coronaviruses.

The mortality rate was 5.6%, 13%, and 35% among COVID-19-, SARS-, and MERS-infected patients, respectively. While the mortality rate among COVID-19 patients is lower than SARS and MERS, COVID-19 is proving to have a higher contagious potency, resulting in a higher number of deaths. It should be recognized that these numbers are biased due to the data set, including publications related to screening practices (eg, only those with symptoms being screened) increased the percentage value. The actual mortality rate from COVID-19 is almost certainly much lower than that found in this study. As more data emerges from screening asymptomatic or mildly symptomatic individuals in China and around the world, the exact mortality rate will be better understood.

Among COVID-19, SARS, and MERS patients, leukocytosis was found in 13.3%, 28%, and 30%, respectively, and leukopenia in 26%, 32%, and 41%, respectively.

Most of the patients with coronavirus had abnormal chest radiological findings. On the other hand, runny nose and rhinorrhea are less common symptoms in coronavirus-infected patients, which indicates the virus preferentially affects the lower respiratory tract. A study by Zhao et al showed that ACE2 is a COVID-19 virus receptor and that it is typically expressed on pulmonary alveolar epithelial cells. Another study reported that following COVID-19 infection deregulated cytokine/chemokine response and higher virus titer causes an inflammatory cytokine storm with lung immunopathological injury. Inflammation related to the cytokine storm in the lungs may then spread throughout the body via the circulation system. COVID-19 patients have been reported to have increased plasma concentration of inflammation-related cytokines, including interleukin (IL)-2,6,7,10, tumor necrosis factor-α (TNF-α), and monocyte chemoattractant protein I (MCP-I) especially in moribund patients. Our data collected here show that ARDS occurred in 10.6% of reported patients with COVID-19 infection. A previous study showed that ACE2 (main receptor of COVID-19) expression is higher in people with pulmonary ARDS and acute respiratory injury.

Several limitations of this study exist. Publication bias and study heterogeneity are unavoidable in this type of study. Therefore, it should be considered when interpreting the outcomes of the reports and our final data set. Furthermore, this study likely overestimates disease severity due to a lack of screening for asymptomatic or mildly symptomatic individuals and subsequent publication bias related to these factors. Likely, many infected persons have not been detected, thus falsely elevating the rates of hospitalization, critical condition, and mortality. The lower quality analysis and reporting in some of the included publications is another limitation of the study. To prevent language bias, we included reports in languages other than English. Additionally, we searched for a variety of sites and databases to prevent internet platform bias. Using Egger’s regression test, we did not find significant publication bias. Journal bias is an issue facing those who carry out a meta-analysis, yet it does not usually affect the general conclusions. However, we cannot reject the occurrence of other biases in this study, such as choice bias, since several journals are not indexed in Embase, Scopus, PubMed, Web of Science, and the Cochrane library and unpublished data from some regions of the world.

5 CONCLUSIONS

Fever and cough are the most common symptoms of COVID-19, SARS, and MERS-infected patients. The mortality rate in COVID-19 confirmed cases was lower than SARS- and MERS-infected patients. Clinical outcomes and findings may be biased by reporting only confirmed cases, and it should be considered when interpreting the data.

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CONFLICT OF INTEREST

The authors have declared that no conflict of interests.

AUTHOR CONTRIBUTIONS

Conceived and designed the study: A.P., S.G.
Comprehensive research: S.G., A.K., A.P., R.F.
Analyzed the data: A.P.
Wrote and revised the paper: A.P., S.G., A.K., R.F., B.B., D.T., R.T., N.B., J.P.I.
Participated in data analysis and manuscript editing: A.P., S.G., A.K., R.F., B.B., D.T., R.T., N.B., J.P.I.

ETHICAL STATEMENT

The manuscript is a systematic review, so the ethical approval was not required for the study.
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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of this article.

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