**Table S1.** PRISMA checklist [1].

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 3 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 4 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 5 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 5 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 5 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 5 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 5 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 5 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 5 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 6 |

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 5-6 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 5-6 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 5-6 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 5 |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 7 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 7 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 9 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 7-8 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 7-8 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | - |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 7-9 |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 10 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 11 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 12 |
| **FUNDING** | | | |

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 2 |

**Table S2.** Classification of COVID-19 severity [2].

| Severity | Definition |
|---|---|
| Mild | The clinical symptoms are mild with no abnormal radiological findings. |
| Moderate | Fever, cough, and other symptoms are presented with pneumonia on chest computed tomography. |
| Severe | One of the following conditions is met: (1) Respiratory distress, respiratory rate ≥ 30 per min; (2) Oxygen saturation on room air at rest ≤ 93%; (3) Partial pressure of oxygen in arterial blood / fraction of inspired oxygen ≤ 300 mmHg. |
| Critical | One of the following conditions has to be met: (1) Respiratory failure occurs and mechanical ventilation is required; (2) Shock occurs; (3) Patients with other organ dysfunction needing intensive care unit monitoring. |

**Table S3.** Data quality of the analyzed cohort

| Parameter | | Total | Data | % |
|---|---|---|---|---|
| Country | | 123 | 123 | 100.00% |
| Gender | | 123 | 122 | 99.19% |
| Age | | 123 | 120 | 97.56% |
| Comorbidities | | | | |
| | Hypertension | 123 | 82 | 66.67% |
| | Chronic heart disease | 123 | 84 | 68.29% |
| | Arrhythmia | 123 | 84 | 68.29% |
| | Type 2 diabetes mellitus | 123 | 82 | 66.67% |
| | Chronic obstructive lung disease | 123 | 82 | 66.67% |
| | Chronic kidney disease | 123 | 82 | 66.67% |
| | Chronic liver disease | 123 | 82 | 66.67% |
| | Immunosuppression | 123 | 82 | 66.67% |
| | Cancer | 123 | 84 | 68.29% |
| | Other | 123 | 78 | 63.41% |
| Chronic treatment | | 123 | 22 | 17.89% |
| Smoking status | | 123 | 16 | 13.01% |
| Current alcohol consumption | | 123 | 14 | 11.38% |
| Body mass index | | 123 | 7 | 5.69% |
| First episode characteristics | | | | |
| | Symptoms start date | 123 | 97 | 78.86% |
| | Symptoms end date | 123 | 52 | 42.28% |
| | First positive PCR date | 123 | 123 | 100.00% |
| | First negative PCR date | 123 | 97 | 78.86% |
| | Severity | 123 | 109 | 88.62% |
| | Fever | 123 | 108 | 87.80% |
| | Cough | 123 | 108 | 87.80% |
| | Dyspnea | 123 | 105 | 85.37% |
| | O2 saturation | 123 | 23 | 18.70% |
| | Arthromyalgia | 123 | 108 | 87.80% |
| | Headache | 123 | 108 | 87.80% |

| | | | | |
|---|---|---|---|---|
| | General cold symptoms | 123 | 108 | 87.80% |
| | Asthenia | 123 | 109 | 88.62% |
| | Gastrointestinal symptoms | 123 | 109 | 88.62% |
| | Other | 123 | 110 | 89.43% |
| | Hospitalization | 123 | 119 | 96.75% |
| | Department | 123 | 45 | 36.59% |
| | Days of hospitalization | 123 | 97 | 78.86% |
| | COVID-19 Treatment | 123 | 99 | 80.49% |
| | Chest X-ray | 123 | 19 | 15.45% |
| | Chest computed tomography | 123 | 55 | 44.72% |
| | Pneumonia | 123 | 62 | 50.41% |
| | Abdominal imaging | 123 | 10 | 8.13% |
| | Any laboratory measurement | 123 | 66 | 53.66% |
| | White blood cell count | 123 | 38 | 30.89% |
| | Lymphocyte count | 123 | 47 | 38.21% |
| | Lactate dehydrogenase | 123 | 27 | 21.95% |
| | C-reactive protein | 123 | 45 | 36.59% |
| | Procalcitonin | 123 | 30 | 24.39% |
| | Thrombocyte | 123 | 28 | 22.76% |
| | IgM status | 123 | 21 | 17.07% |
| | IgG status | 123 | 36 | 29.27% |
| Second episode characteristics | | | | |
| | Symptoms start date | 123 | 92 | 74.80% |
| | Symptoms end date | 123 | 67 | 54.47% |
| | First positive PCR date | 123 | 121 | 98.37% |
| | First negative PCR date | 123 | 59 | 47.97% |
| | Severity | 123 | 97 | 78.86% |
| | Fever | 123 | 100 | 81.30% |
| | Cough | 123 | 97 | 78.86% |
| | Dyspnea | 123 | 100 | 81.30% |
| | O2 saturation | 123 | 16 | 13.01% |
| | Arthromyalgia | 123 | 99 | 80.49% |
| | Headache | 123 | 100 | 81.30% |
| | General cold symptoms | 123 | 100 | 81.30% |
| | Asthenia | 123 | 100 | 81.30% |
| | Gastrointestinal symptoms | 123 | 100 | 81.30% |
| | Other | 123 | 101 | 82.11% |
| | Hospitalization | 123 | 111 | 90.24% |
| | Department | 123 | 47 | 38.21% |
| | Days of hospitalization | 123 | 66 | 53.66% |
| | COVID-19 Treatment | 123 | 67 | 54.47% |
| | Chest X-ray | 123 | 14 | 11.38% |
| | Chest computed tomography | 123 | 55 | 44.72% |
| | Pneumonia | 123 | 61 | 49.59% |
| | Abdominal imaging | 123 | 0 | 0.00% |
| | Any laboratory measurement | 123 | 49 | 39.84% |

| | | | | |
|---|---|---|---|---|
| | White blood cell count | 123 | 23 | 18.70% |
| | Lymphocyte count | 123 | 39 | 31.71% |
| | Lactate dehydrogenase | 123 | 11 | 8.94% |
| | C-reactive protein | 123 | 32 | 26.02% |
| | Procalcitonin | 123 | 7 | 5.69% |
| | Thrombocyte | 123 | 8 | 6.50% |
| | IgM status | 123 | 25 | 20.33% |
| | IgG status | 123 | 52 | 42.28% |

**Table S4.** Basic characteristics of included case reports

| Author | Country | Sex | Age | Repeated positivity length |
|---|---|---|---|---|
| Alfano G et al., 2020 [3] | Italy | Male | 72 | 35 |
| AlFehaidi A et al., 2020 [4] | Qatar | Female | 46 | 80 |
| Alonso FOM et al., 2021 [5] | Brazil | Male | 26 | 46 |
| Bentivegna E et al., 2021 [6] | Italy | Female | 62 | 46 |
| Bongiovani M et al., 2020 [7] | Italy | F/F/F | 81/ 85/ 48 | 32/ 28/ 117 |
| Bonifacio LP et al., 2020[8] | Brazil | Female | 24 | 140 |
| Chen D et al., 2020 [9] | China | Female | 46 | 18 |
| Colson P et al., 2020 [10] | France | Male | 70 | 119 |
| Coppola A et al., 2020 [11] | Italy | Male | 68 | 36 |
| de Brito CAA et al., 2020 [12] | Brazil | Male/ Female | 40/ 44 | 44/ 25 |
| Dou C et al., 2020 [13] | China | Male | 34 | 34 |
| Duggan NM et al., 2021 [14] | USA | Male | 82 | 48 |
| Fehdi AM et al., 2020 [15] | Morocco | Male | 69 | 18 |
| Fu W et al., 2020 [16] | China | Female/ Male /Female | 36/ 74/ 34 | 35/ 36/ 28 |
| Geling T et al., 2020 [17] | China | Male | 24 | 20 |
| Goldman DJ et al., 2020 [18] | USA | ND | 65 | 140 |
| Gupta V et al., 2020 [19] | India | M/F | 25/ 28 | 108/ 111 |
| He F et al., 2020 [20] | China | Female | 39 | 51 |
| Jiang M et al., 2020 [21] | China | Female/ Female | 35/ 56 | 27/ 28 |
| Lafaie L et al., 2020 [22] | France | Female/ Male /Female | 84/ 90/ 84 | 40/ 36/ 20 |
| Larson D et al., 2020 [23] | USA | Male | 42 | 65 |
| Leipe J et al., 2020 [24] | Germany | Male | 63 | 14 |
| Li J et al., 2020 [25] | China | Male | 50 | 34 |
| Liu F et al., 2020 [26] | China | Female | 57 | 24 |
| Liu F et al., 2020 [27] | China | Male | 35 | 30 |
| Loconsole D et al., 2020 [28] | Italy | Male | 48 | 43 |
| Luo A et al., 2020 [29] | China | Female | 58 | 36 |
| Ma BM et al., 2020 [30] | Japan | Female | 31 | 20 |
| Marchev S et al., 2020 [31] | Bulgaria | Male | 25 | 92 |
| Mardani M et al., 2020 [32] | Iran | Female | 64 | 35 |
| Mendoza JM et al., 2020 [33] | USA | Male | 51 | 60 |

| | | | | |
|---|---|---|---|---|
| Mulder M et al., 2020 [34] | Netherlands | Female | 89 | 59 |
| Nachmias V et al., 2020 [35] | Israel | Female | 20 | 111 |
| Nazir N et al., 2020 [36] | India | Male | 26 | 110 |
| Ogawa Y et al., 2020 [37] | Japan | Female | 81 | 44 |
| Qiao X et al., 2020 [38] | China | Female | 30 | 29 |
| Ravioli S et al., 2020 [39] | Switzerland | Female/ Female | 81/ 77 | 36/ 30 |
| Thomas SV et al., 2020 [40] | United Arab Emirates | Male | 39 | 43 |
| Tillett RL et al., 2021 [41] | USA | Male | 25 | 48 |
| To KKW et al., 2020 [42] | China | Male | 33 | 142 |
| van Elslande J et al., 2020 [43] | Belgium | Female | 51 | 93 |
| Wang P et al., 2021 [44] | China | Male | 33 | 84 |
| Wei L et al., 2020 [45] | China | Male | 61 | 61 |
| Yoo SY et al., 2020 [46] | China | Male | 8 | 35 |
| Yuan B et al., 2020 [47] | China | Male | 8 | 30 |
| Zanardini C et al., 2020 [48] | Italy | Female/ Female | 33/ 27 | 119/ 91 |
| Zhou X et al., 2020 [49] | China | Male | 40 | 25 |

**Table S5.** Basic characteristics of the included case series

| **Author.** | **Country** | **Nr of patients (female %)** | **Mean age (SD)** | **Mean repeated positivity length (SD)** |
|---|---|---|---|---|
| Chen Y et al., 2020 [50] | China | 4 (50) | 32 (15.6) | 21 (7.1) |
| Fernandes VTC et al., 2020 [51] | Brazil | 6 (16.7) | 46.2 (16) | 56.8 (9.7) |
| Gidari A et al., 2020 [52] | Italy | 9 (33.3) | 54.7 (17.7) | 60.9 (23.3) |
| Goussef M et al., 2020 [53] | France | 11 (45.5) | 58.3 (24.5) | 35.2 (8.8) |
| Li Y et al., 2020 [54] | China | 4 (50) | 62.3 (17.5) | 32.3 (20.8) |
| Peng J et al., 2020 [55] | China | 6 (50) | 41.3 (22.2) | 30.2 (9.3) |
| Tao W et al., 2020 [56] | China | 12 (41.7) | 48.2 (14) | 39.5 (26.1) |
| Tomassini S et al., 2020 [57] | UK | 6 (50) | 75.8 (16.7) | 66 (19.1) |
| Zhang B et al., 2020 [58] | China | 7 (14.3) | 22.4 (13.3) | 23.4 (4.8) |

**Table S6.** Difference of intervals organized by disease severity

| **Intervals (n/total)** | **Mild** **Mean (SD), Median (Q1-Q3)** | **Moderate** **Mean (SD), Median (Q1-Q3)** | **Severe** **Mean (SD), Median (Q1-Q3)** | **Critical** **Mean (SD), Median (Q1-Q3)** | **p-value** |
|---|---|---|---|---|---|
| **1st episode severity** | | | | | |
| **RSP** (123/123) | 51.35 (32.87)<br>37 (27-65) | 54.03 (34.70)<br>42.5 (28.5-70.5) | 41.06 (20.57)<br>34.5 (27-52.5) | 34.43 (11.46)<br>36 (20-44) | 0.537 |
| **NTP** (94/123) | 32.85 (32.23)<br>17 (11.5-46) | 33.06 (31.47)<br>20 (11-46) | 17.85 (11.40)<br>14 (10-21) | 17.17 (9.09)<br>19 (9-24) | 0.616 |
| **STS** (50/123) | 48.50 (27.16)<br>43 (25-73) | 63.35 (29.27)<br>58 (46-70) | 44.00 (23.11)<br>32.5 (28.5-55) | 36.83 (14.73)<br>40.5 (20-48) | 0.091 |
| **NSTS** (33/123) | 28.20 (24.99)<br>37 (2-43) | 35.89 (23.88)<br>32 (18-52) | 22.80 (23.61)<br>10 (8-36) | 18.67 (9.07)<br>20 (9-27) | 0.736 |
| **NSTP** (46/123) | 40.29 (22.57) | 27.79 (18.02) | 21.50 (21.35) | 19.00 (9.54) | 0.291 |

| | | | | | |
|---|---|---|---|---|---|
| | 43 (23-60) | 29 (11-40) | 12.5 (8-36) | 20 (9-28) | |
| | | | **2nd episode severity** | | |
| **RSP** (123/123) | 55.12 (37.82)<br>36 (26-84) | 48.55 (18.73)<br>43.5 (36-59) | 47.86 (13.13)<br>54 (35-59) | 33.89 (11.40)<br>36 (23-44) | 0.377 |
| **NTP** (94/123) | 34.17 (33.98)<br>17 (10.5-52.5) | 31.29 (17.70)<br>25.5 (20-45) | 24.00 (11.69)<br>24 (15.5-32.5) | 15.80 (9.44)<br>18 (9-20) | 0.486 |
| **STS** (50/123) | 61.17 (37.81)<br>49 (29.5-91) | 51.75 (22.46)<br>48 (41-62.5) | 49.83 (15.14)<br>56.5 (35-60) | 35.56 (12.89)<br>40 (27-45) | 0.188 |
| **NSTS** (33/123) | 27.50 (26.27)<br>25.5 (2-52) | 31.36 (23.24)<br>32 (15-40) | 31.67 (22.01)<br>31 (10-54) | 12.00 (9.32)<br>7.5 (6-20) | 0.412 |
| **NSTP** (46/123) | 26.58 (21.48)<br>15 (8-43) | 32.73 (16.68)<br>32 (23-42) | 34.33 (22.37)<br>39 (10-54) | 12.17 (9.97)<br>9.5 (4-20) | 0.120 |

NSTP: no-symptom to positive PCR interval; NSTS: no-symptom to symptom interval; NTP: negative to positive PCR interval; PCR: polymerase chain reaction; PTN: positive to negative PCR interval; Q1-Q3: 25 and 75% percentiles; RSP: repeatedly SARS-CoV-2 positivity; SD: standard deviation; STS: symptom to symptom interval

**Table S7.** Repeated SARS-CoV-2 positive intervals based on symptomatic cases

| | **Mean (SD) interval** | **Median (Q1-Q3) interval** |
|---|---|---|
| All included patients | 47.9 (30.1) days | 36 (28-49) days |
| Asymptomatic 1st episode | 75.3 (39.7) days | 84 (43-110) days |
| Asymptomatic 2nd episode | 58.7 (35.7) days | 43 (28-84) days |
| Both episode asymptomatic | 78.4 (43.6) days | 108 (31-110) days |

Q1-Q3: 25 and 75% percentiles; SD: standard deviation

**Table S8.** Risk of bias assessment using the CARE tool [59] for case reports

| Author | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| Alfano G et al., 2020 [3] | | | | | | | | |
| AlFehaidi A et al., 2020 [4] | | | | | | | | |
| Alonso FOM et al., 2021 [5] | | | | | | | | |
| Bentivegna E et al., 2021 [6] | | | | | | | | |
| Bongiovani M et al., 2020 [7] | | | | | | | | |
| Bonifacio LP et al., 2020[8] | | | | | | | | |
| Chen D et al., 2020 [9] | | | | | | | | |
| Colson P et al., 2020 [10] | | | | | | | | |
| Coppola A et al., 2020 [11] | | | | | | | | |
| de Brito CAA et al., 2020 [12] | | | | | | | | |
| Dou C et al., 2020 [13] | | | | | | | | |
| Duggan NM et al., 2021 [14] | | | | | | | | |
| Fehdi AM et al., 2020 [15] | | | | | | | | |
| Fu W et al., 2020 [16] | | | | | | | | |
| Geling T et al., 2020 [17] | | | | | | | | |
| Goldman DJ et al., 2020 [18] | | | | | | | | |
| Gupta V et al., 2020 [19] | | | | | | | | |
| He F et al., 2020 [20] | | | | | | | | |
| Jiang M et al., 2020 [21] | | | | | | | | |
| Lafaie L et al., 2020 [22] | | | | | | | | |
| Larson D et al., 2020 [23] | | | | | | | | |
| Leipe J et al., 2020 [24] | | | | | | | | |
| Li J et al., 2020 [25] | | | | | | | | |
| Liu F et al., 2020 [26] | | | | | | | | |
| Liu F et al., 2020 [27] | | | | | | | | |
| Loconsole D et al., 2020 [28] | | | | | | | | |
| Luo A et al., 2020 [29] | | | | | | | | |
| Ma BM et al., 2020 [30] | | | | | | | | |
| Marchev S et al., 2020 [31] | | | | | | | | |
| Mardani M et al., 2020 [32] | | | | | | | | |
| Mendoza JM et al., 2020 [33] | | | | | | | | |
| Mulder M et al., 2020 [34] | | | | | | | | |
| Nachmias V et al., 2020 [35] | | | | | | | | |
| Nazir N et al., 2020 [36] | | | | | | | | |
| Ogawa Y et al., 2020 [37] | | | | | | | | |
| Qiao X et al., 2020 [38] | | | | | | | | |
| Ravioli S et al., 2020 [39] | | | | | | | | |
| Thomas SV et al., 2020 [40] | | | | | | | | |
| Tillett RL et al., 2021 [41] | | | | | | | | |
| To KKW et al., 2020 [42] | | | | | | | | |
| van Elslande J et al., 2020 [43] | | | | | | | | |
| Wang P et al., 2021 [44] | | | | | | | | |
| Wei L et al., 2020 [45] | | | | | | | | |

| | |
|---|---|
| Yoo SY et al., 2020 [46] | |
| Yuan B et al., 2020 [47] | |
| Zanardini C et al., 2020 [48] | |
| Zhou X et al., 2020 [49] | |

**When assessing risk of bias in case reports, the following questions were answered:**

1. Were patient's demographic characteristics clearly described? 2. Was the patient's history clearly described and presented as a timeline? 3. Was the current clinical condition of the patient on presentation clearly described? 4. Were diagnostic tests or methods and the results clearly described? 5. Was the intervention(s) or treatment procedure(s) clearly described? 6. Was the post-intervention clinical condition clearly described? 7. Were adverse events (harms) or unanticipated events identified and described? 8. Does the case report provide takeaway lessons?

Based on the CARE guideline [59], each domain was assessed as low (green), unclear (yellow) or high (red) risk of bias based on the available descriptions in each included study.

**Table S9.** Risk of bias assessment using the CARE tool [59] for case series

| Author | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Chen Y et al., 2020 [50] | | | | | | | | | | N/A |
| Fernandes VTC et al., 2020 [51] | | | | | | | | | | N/A |
| Gidari A et al., 2020 [52] | | | | | | | | | | N/A |
| Goussef M et al., 2020 [53] | | | | | | | | | | N/A |
| Li Y et al., 2020 [54] | | | | | | | | | | N/A |
| Peng J et al., 2020 [55] | | | | | | | | | | N/A |
| Tao W et al., 2020 [56] | | | | | | | | | | N/A |
| Tomassini S et al., 2020 [57] | | | | | | | | | | N/A |
| Zhang B et al., 2020 [58] | | | | | | | | | | N/A |

**When assessing risk of bias in case series, the following questions were answered:**

1. Were there clear criteria for inclusion in the case series? 2. Was the condition measured in a standard, reliable way for all participants included in the case series? 3. Were valid methods used for identification of the condition for all participants included in the case series? 4. Did the case series have consecutive inclusion of participants? 5. Did the case series have complete inclusion of participants? 6. Was there clear reporting of the demographics of the participants in the study? 7. Was there clear reporting of clinical information of the participants? 8. Were the outcomes or follow up results of cases clearly reported? 9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information? 10. Was statistical analysis appropriate?

Based on the CARE guideline [59], each domain was assessed as low (green), unclear (yellow) or high (red) risk of bias based on the available descriptions in each included study. The last question was not assessed since statistical analysis was not relevant for the included case series.

**Table S10.** Summary of reported SARS-CoV-2 strains

| | Case number | 1st episode strain | 2nd episode strain |
|---|---|---|---|
| Goldman DJ et al [18] | Reinf_26 | clade 19B | clade 20A<br>A23403G mutation, which confers the D614G amino acid change in spike protein |
| Gupta V et al [19] | Reinf_27<br>Reinf_28 | both the genomes revealed 9 and 10 unique variant differences between the virus isolates from the 2 episodes of infection | |
| Colson P et al [10] | Reinf_33 | Nextrain clade 20A | Marseille 4 lineage<br>11 mutations that are hallmarks of the Marseille 4 lineage (C4543U, G5629U, G9526U, C11497U, G13993U, G15766U, A16889G, G17019U, G22992A, G28975C, G29399A) were absent from the genome obtained from the first sample. In contrast, 2 mutations (C2416U, G8371U) that are hallmarks of the genotype identified in the first sample were absent in the second genome. |
| Tillett RL et al [41] | Reinf_47 | Both strains were members of clade 20C. Specimen A had five further SNVs compared with the reference genome. Specimen B showed six additional SNVs and a mutation at position 14 407, adjacent to the SNV 14408C→T and recorded as a dinucleotide multinucleotide variant (MNV) at positions 14 407 and 14 408 of the genome. Six SNVs were shared between specimen A and specimen B (table 2). Specimen A had four additional SNVs not seen in specimen B, whereas specimen B had seven SNVs that were absent in specimen A. | |
| To KKW et al [42] | Reinf_48 | lineage B.2 | lineage B.1.79 |
| van Elslande J et al [43] | Reinf_49 | lineage B.1.1 | lineage A |
| Larson D et al [23] | Reinf_95 | lineage B.1.26 and the genome encoded the D614G variation in the spike protein | several potential variations |
| Mulder M et al [34] | Reinf_109 | The two strains differed at ten nucleotide positions in the ORF1a (4), ORF (2), Spike (2), ORF3a (1) and M (1) genes | |

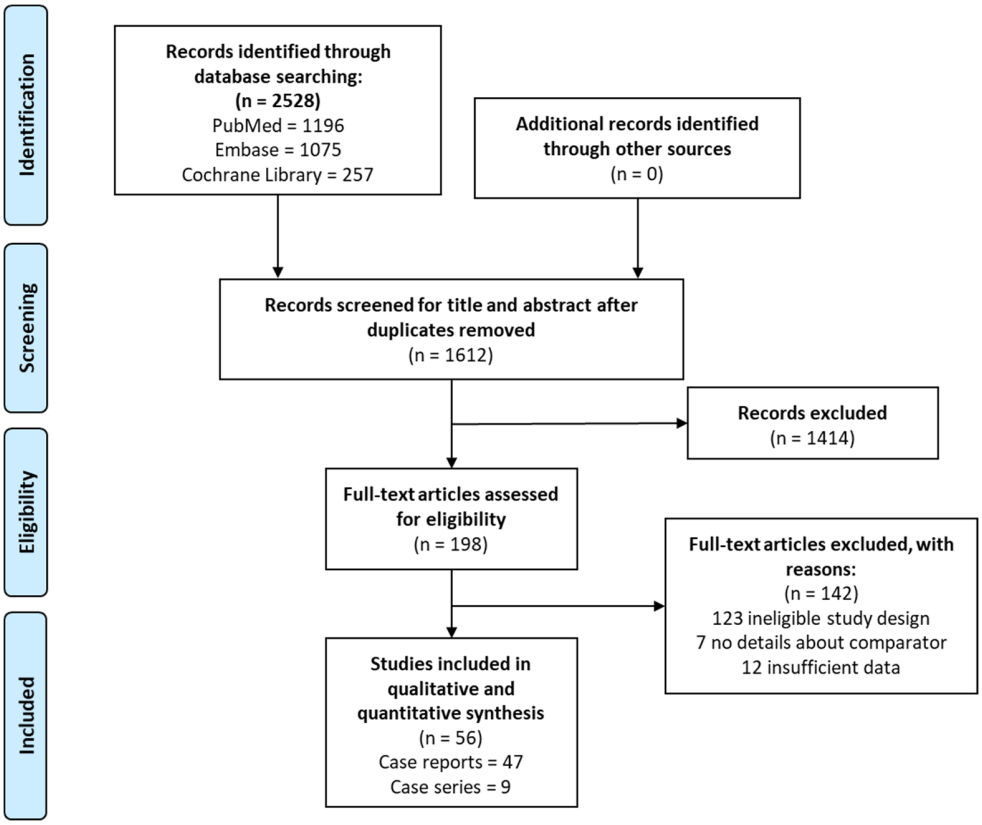


**Figure S1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist

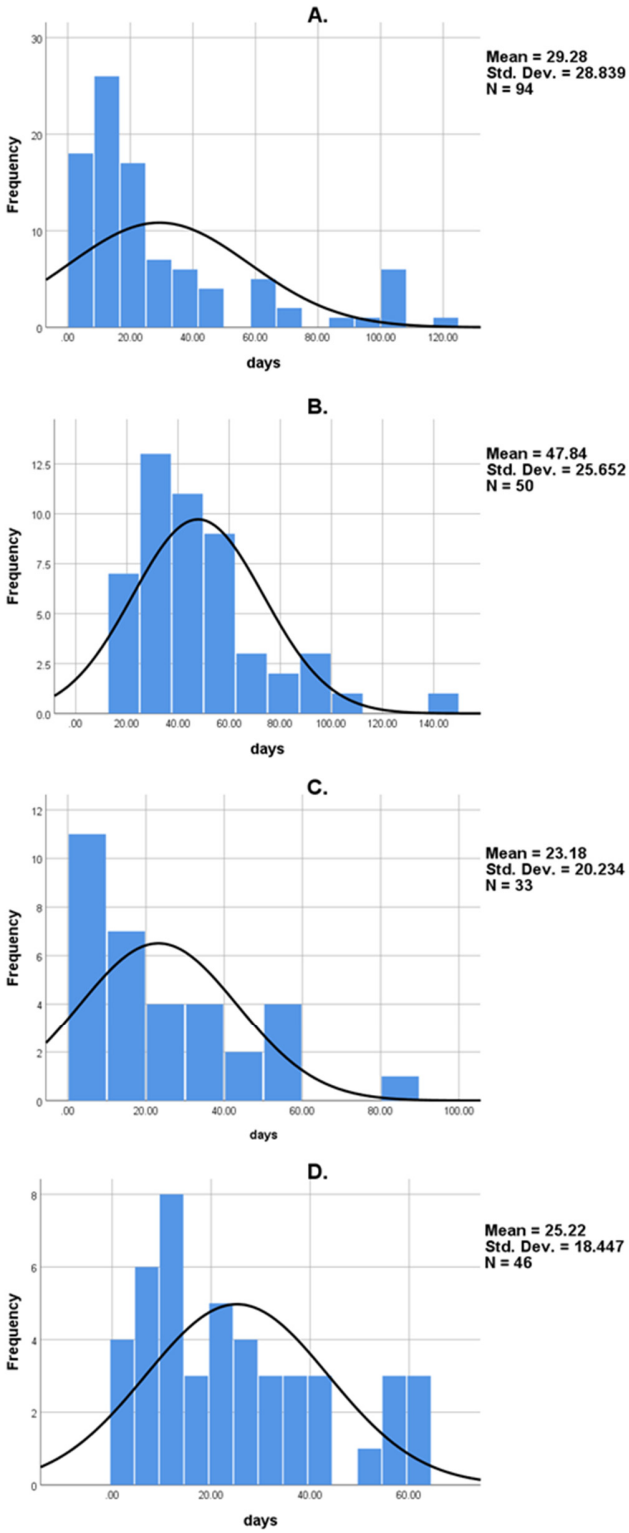


**Figure S2**. Histogram of analyzed intervals. (A) negative to positive polymerase chain reaction interval, (B) symptom to symptom interval, (C) no symptom to symptom, (D) no symptom to positive polymerase chain reaction interval

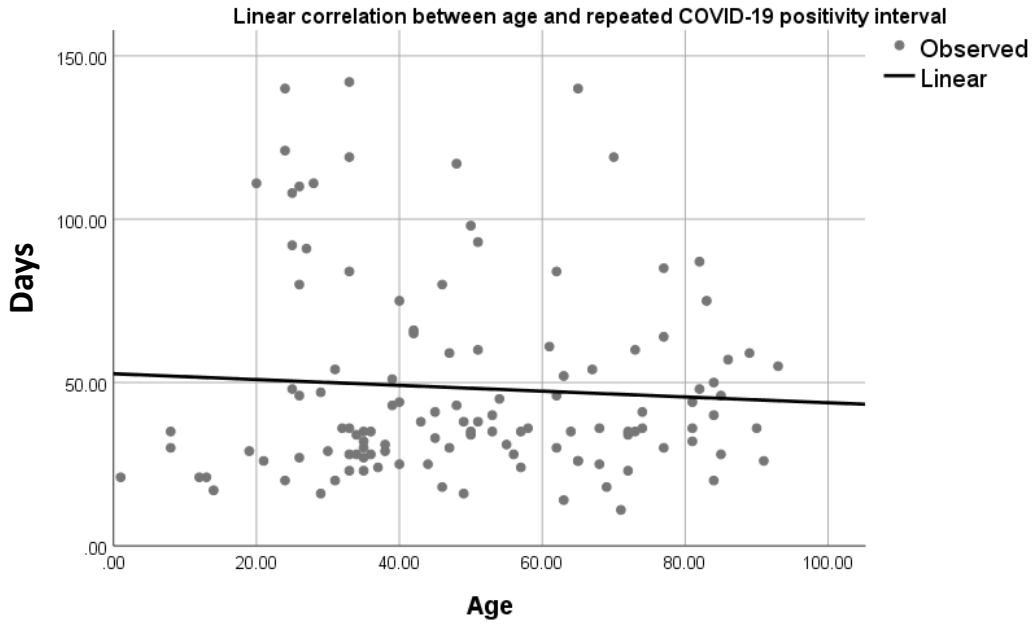


**Figure S3.** Correlation analysis between age (years) and repeated positivity length (days)

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