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Publishing in pandemic times: a bibliometric analysis of early medical publications on Kawasaki-like disease (MIS-C, PIMS-TS) related to SARS-CoV-2

Short title: Bibliometric analysis of early medical publications on Kawasaki-like disease related to SARS-CoV-2

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Abstract

Introduction: At the end of April 2020, three European pediatric societies published an alert on a new hyperinflammatory disorder linked to SARS-CoV-2. This disease has alternatively been called Kawasaki-like disease, pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 infection (PIMS-TS), and multisystem inflammatory syndrome in children (MIS-C).

These alerts provide a clear starting point from which to study the early response of the medical and scientific community to a new disease in terms of scientific publications, and to compare the timeline of this response with levels of general public interest. To this aim, we conducted a bibliometric analysis of articles on this disease published between 1 April and 5 July 2020.

Method: A literature search was performed using PubMed and in three preprint repositories. For each article, the name used for the disease in the title, the number of authors, the number of patients, the citations according to Google Scholar, the journal impact factor, and the Altmetric score were retrieved. Google search trends for the terms “Kawasaki” and “COVID,” “COVID-19,” and “coronavirus” were also retrieved, as was the number of Reuters news articles published on the topic. These data were compared longitudinally on a weekly basis. The quality of the reporting of the study was evaluated using the STROBE guidelines for observational studies with more than three patients and using the CARE guidelines for case reports of three or fewer patients.

Results: Eighty-six articles were included, among which ten were preprints (three of which were subsequently published) and 49 were clinical articles (57%). A total of 857 patients were described. The median number of authors per article was five (range, 1–45), the median number of patients was four (1–186), the median number of citations was one (0–170), the median Altmetric score was 12 (0–7242), and the median journal impact factor was 3.7 (1–74.7). For the clinical articles, the median percentage of STROBE or CARE checklist items satisfied was 70% (IQR, 56.75–79.25; range, 40–90). Guideline adherence was significantly higher for observational studies than for case reports (median percentage of checklist items satisfied, 78.5% vs 61.5%; $p<0.001$); however, guideline adherence did not differ significantly between peer-reviewed and preprint articles (median percentage of checklist items satisfied, 57% vs 72%; $p=0.205$). The only statistically significant difference between

clinical articles and other types of articles was the number of authors (median, 7 vs 2; $p=2.53E-9$). Fifty-seven of the 86 articles were authored by researchers from just three countries (the USA, 31; France, 14; and the UK, 12). The names most frequently used in the title were Kawasaki-like disease ($n=37$), followed by MIS-C ($n=27$), PIM-TS ($n=14$), and other names involving the term “inflammatory” ($n=12$). Google searches for related terms peaked between weeks 18 and 21, following the initial alerts and decreased rapidly thereafter. The number of Reuters articles on the subject was correlated with Google search trends ($\rho: 0.86$, 95% CI [0.59; 0.96]; $p=0.00016$), but the number of medical articles published was not ($\rho: -0.54$, 95% CI [-0.87; 0.14]; $p=0.11$). The first small case series was published less than 2 weeks after the initial alert; however, if all articles had been deposited as preprints when they were submitted to journals, the cumulative number of reported cases would have been 300% higher in week 18 (3 vs 1), 400% higher in week 19 (44 vs 11), 70% higher in week 20 (124 vs 73), and 54% higher in week 21 (129 vs 84).

Conclusion: In a period of 9 weeks after the initial alerts from European pediatric societies, 85 medical articles were published, involving 856 patients (one case report was published before the alerts), allowing rapid dissemination of research information. However, general public interest followed the news cycle rather than scientific releases. The quality of the reporting, as assessed by adherence to STROBE or CARE guidelines, was adequate with more than two-thirds of checklist items satisfied. Learned societies play an important role in the early dissemination of up-to-date peer-reviewed information. Preprint deposition should be encouraged to accelerate the dissemination of research information.

Keywords: COVID-19, SARS-CoV-2, Kawasaki-like, pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 infection (PIMS-TS), bibliometric, preprint, multisystem inflammatory syndrome in children (MIS-C)

1: Introduction

At the end of April 2020, three European pediatric societies each published an alert about critically ill children with inflammatory Kawasaki-like disease potentially linked to COVID-19: the SIP (Società Italiana di Pediatria, on 24 April), the PICS (Paediatric Intensive Care Society, on 27 April), and the SOFREMIP (SOciété Francophone de Rhumatologie Et des Maladies Inflammatoires Pédiatriques, on 29 April) [1–3]. This disease has since been named pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 infection (PIMS-TS) [4] and multisystem inflammatory syndrome in children (MIS-C) [5,6]. Early publications from China described Covid-19 in children as less severe with better outcomes than in adults, features that have subsequently been confirmed [7]. Several authors have pointed out that the possibility of postinfectious inflammatory presentations should have been foreseen in light of knowledge on classical Kawasaki disease [8,9]. Initial publications insisted on the low absolute number of cases and the urgent need for more information [10] while at the same time and following the alerts, public interest in Kawasaki-like disease and COVID-19 rose sharply, as reflected in Google Trends Data [11], suggesting that there was a public need for information. Bibliometric analysis has shown that between January and May 2020, more than 10,000 articles were published on COVID-19 [12], this massive output being associated with short submission to publication times [13] and the use of preprint servers [14], demonstrating the medical and scientific community's ability to react rapidly in a crisis. Using the alerts about Kawasaki-like disease as a clear starting point, the aim of this study was to assess the early response of the medical community in comparison with levels of interest in the general public.

We therefore conducted a bibliometric analysis of early publications on Kawasaki-like COVID-19-related disease (referred to in the following as KawaCOVID/PIMS-TS/MIS-C), in terms of the number of publications and patients described, and the quality of the reporting of published articles, and comparing these data with levels of lay interest in this topic.

2: Method

A search was conducted in MEDLINE (<https://pubmed.ncbi.nlm.nih.gov/>) between 3 and 12 July 2020 using the following terms: “PIMS-TS,” “pediatric inflammatory multisystemic syndrome covid-19,” “Multi-System Inflammatory Syndrome covid-19,” “kawasaki covid-19,” “Multisystem Inflammatory Syndrome in Children (MIS-C),” “Hyper-inflammatory Syndrome COVID-19 children,” “hyperinflammatory covid-19 children,” “Inflammatory syndrome children covid 19,” and “kawasaki coronavirus.” An additional search was performed on three preprint servers: medRxiv (<https://www.medrxiv.org/>), Research Square (<https://www.researchsquare.com/>), and Preprints (<https://www.preprints.org/>). Articles were included if they were specifically about KawaCOVID/PIMS-TS/MIS-C; general reviews about COVID-19 were not included. For each article we retrieved the submission date, the acceptance date and the publication date, the number of authors, the type of article (clinical, editorial/comments, reviews, others), and the name used in the title (Kawasaki, Pediatric Multisystem Inflammatory Syndrome, Multisystem inflammatory syndrome in children, or other names with the term “inflammatory”). Articles were counted by week of the year in terms of their publication date. A Google Trends search was performed on 16 July 2020 using

the terms “kawasaki covid,” “kawasaki COVID 19,” and “kawasaki coronavirus” among searches conducted since 1 January 2020 in all countries. For each article, the Altmetric attention score (<https://www.altmetric.com/>) was retrieved on 12 July 2020, and the citations counted by Google Scholar between 7 and 12 July 2020. A search was also conducted for news articles about Kawacovid/PIMS-TS/MIS-C published by Reuters (an international news organization; <https://www.reuters.com/news/archive/globalNewsJournal>). The quality of the reporting of the clinical studies was assessed using the STROBE (for articles with more than three patients; <https://www.equator-network.org/reporting-guidelines/strobe/>) and CARE (for articles with one to three patients; <https://www.equator-network.org/reporting-guidelines/care/>) guidelines. For each article we evaluated the number of adequately reported items in the corresponding checklist. The total number of items on the STROBE and CARE checklists were scored. Items that were not applicable to the study design were not counted and results were expressed as the percentage of checklist items satisfied. For the number of patients parameter, the authors that were published preprint were counted only once.

Results were compared using nonparametric tests and the software R, as implemented in BiostaTGV (<http://biostatgv.sentiweb.fr/>).

3: Results

The PubMed search returned 177 articles (358 hits including duplicates) among which 80 were on the subject of KawaCOVID/PIMS-TS/MIS-C. Ten preprints were also found (two in Preprints, four in ResearchSquare, and four in medRxiv). One of the articles published on medRxiv was also indexed in PubMed (**Figure 1**). Three preprints were published in a journal during the study period. The 79 peer-reviewed articles were published in 47 journals. Thirty journals published a single article, seven published two articles, eight published three articles, one published five articles, and one six articles. A total of 86 articles were therefore included

in the analysis, 49 of which were clinical articles (57%), 30 were editorial/comments (34.9%), and the remaining three were an epidemiological study, a statement of a medical hypothesis, and an analysis of Google Trends. Eight hundred and fifty-seven patients were described. The median number of authors per article was five (IQR, 3–9; range, 1–45), the median number of patients per article was four (IQR, 1–17; range, 1–186), the median number of citations per article was one (IQR, 0–3; range, 0–170), the median Altmetric score of each article was 12 (IQR, 1.25–84.75; range, 0–7242), and the median journal impact factor of each article was 3.7 (IQR, 1.911–22.9055; range, 1–74.699). There was a statistically significant association between the number of patients reported and the number of authors (ρ : 0.64, 95% CI [0.43; 0.78], $p=8.67E-7$).

Clinical research articles had significantly more authors than did the other types of papers (median, 7 vs 2; $p=2.53E-9$), but article type was not significantly associated with the number of citations (median, 1 vs 1; $p=0.15$), Altmetric score (median, 23.5 vs 6.5; $p=0.07$), or impact factor (median, 3.7 vs 3.7, $p=0.74$). Ten articles were multinational collaborations while 76 were written by authors working in a single country, mostly the USA (31 articles, including one preprint), France (14, including two unpublished preprints and one published preprint), and the UK (12 articles). The 19 remaining articles were published by authors working in 13 different countries (India, four; Italy, three; Switzerland, two; Canada, China, Iran, Israel, Korea, Poland, Singapore, Spain, Taiwan, and Turkey, one article each). For the 31 articles (17 clinical studies and 14 other types of article, excluding preprints) whose dates of submission and of online publication were available, the mean publication delay was 12.84 days (SD, 10; range, 0–43) with no difference between clinical studies (14.29, SD, 11.55; $n=17$) and others (11.07, SD, 7.89; $n=14$) $p=0.63$. The name used most frequently in the title was Kawasaki-like ($n=37$), followed by MIS-C ($n=27$), PIMS-TS ($n=14$), and other names including the term “inflammatory” ($n=12$). Six articles used two names in the title. The

characteristics of the articles from the USA, France, and the UK are listed in **Table 1**. There were no statistically significant differences between the three countries for any of the items. For 52 clinical articles (49 journal articles and three preprints), the median percentage of STROBE or CARE checklist items satisfied was 70% (IQR, 56.75–79.25%; range, 40–90%). Guideline adherence was significantly higher for observational studies (STROBE guidelines) than for case reports (CARE guidelines; median percentage of checklist items satisfied, 78.5% vs 61.5%; $p < 0.001$), but the corresponding difference between preprint and peer-reviewed articles was not statistically significant (median percentage of checklist items satisfied, 57% vs 72%; $p = 0.205$), either for observational studies (median percentage of STROBE checklist items satisfied, 69.5% vs 78.5%; $p = 0.86$) or for case control studies (median percentage of CARE checklist items satisfied, 57% vs 63%; $p = 0.67$). The percentage of checklist items satisfied was weakly and of borderline significance correlated with impact factor ($\rho: 0.2723$, 95% CI [-0.0473; 0.5413]; $p = 0.094$), but not with Altmetric score ($\rho: 0.2724$, 95% CI [-0.0472; 0.5414]; $p = 0.093$) and week of publication ($\rho: 0.1113$, 95% CI [-0.1694; 0.3754]; $p = 0.44$). For the three preprints that were subsequently published, there was no associated variation in the percentage of satisfied checklist items (mean: 66 vs 67%; $p = 0.58$).

The analysis of the weekly number of publications is shown in **Table 2**. The first article, a case report, was published in week 15 and no other article was published until week 18 (the pediatric societies' alerts were in weeks 17–18). The number of articles and the number of patients described increased rapidly to around ten articles per week by week 21 and more than 50 patients had already been described by week 20. Google searches peaked between weeks 18 and 21 and decreased rapidly thereafter. Limiting the analysis to after week 18 (when the initial alerts were released), the Google searches correlated with the number of Reuters articles on the topic ($\rho: 0.84$, 95% CI [0.44–0.96]; $p = 0.0026$) but not with the number of medical articles ($\rho: -0.54$, 95% CI [-0.87; 0.14]; $p = 0.11$) and the number of Reuters and

medical articles were negatively correlated (ρ : -0.72 , 95% CI $[-0.93; -0.16]$; $p=0.019$). The number of citations was correlated with the week of publication (ρ : -0.43 , 95% CI $[-0.59; -0.23]$; $p=5.19E-5$), but the latter was of borderline significance correlated with Altmetric score (ρ : -0.2 , 95% CI $[-0.41; 0.02]$; $p=0.07$) but not with journal impact factor (ρ : -0.2 , 95% CI $[-0.26; 0.2]$; $p=0.85$).

For the 17 clinical articles whose submission and publication dates were available, we estimated that had they also been deposited as preprints when they were submitted, this would have increased the cumulative number of patients described from one to three in week 18 (300% increase), from 11 to 44 in week 19 (400% increase), from 73 to 124 in week 20 (69% increase), and from 84 to 129 in week 21 (54% increase).

4: Discussion

This bibliometric analysis of KawaCOVID/PIMS-TS/MIS-C articles reveals a publication trend that has features in common with those of general COVID-19-related articles, namely a rapid growth in the number of publications and a short submission-to-publication time [13,14]. However, while preprints accounted for 40.9% of all general COVID-19-related articles, only 11.2% of all the articles on KawaCOVID at the time of survey were preprints [14].

Most articles were published by groups from a single country, indicating that in spite of the international scope of the pandemic, most research was conducted within national borders. The countries whose authors contributed the greatest number of articles (the USA, France, and the UK) had many cases of the disease, but while some of the first reports came from Italy, and Spain had 22 cases reported as of 15 May 2020 [4], these two countries are nearly

completely absent from the publication list. This suggests that rapid publication depends on factors other than the absolute number of cases.

The importance of semantics for this new syndrome (ranging from Kawasaki-like to new acronyms) has been highlighted [15]; however, it seems that in articles published during this period, one of three main terms was almost always used, with “Kawasaki-like” predominating. It is unclear whether this usage should be accepted (e.g., KawaCOVID) or if more general terms like MIS-C should be used. Analysis of Google search trends is useful in this context since Google is used for three-quarters of internet searches worldwide [11] and thus reveals the level of general public interest in the disease. Given that the terms “Kawasaki” and “COVID” are used in most European languages, Google trends are probably a reliable indicator of searches in these countries. Dey and Zhao have shown that the first queries appeared in early February, possibly reflecting earlier unreported cases of hyperinflammatory Kawasaki-like syndrome, and that the observed increase at the end of April/early May was linked to news coverage [11]. As a proxy for news coverage, we used the number of articles published by Reuters, an international news organization. There was a strong correlation in our data between the number of Reuters publications and Google search trends, but the number of scientific publications was not correlated with Google trends.

We evaluated the quality of the reporting using the CARE and STROBE guidelines. The median percentage of satisfied checklist items was 70% (78.5% for observational studies and 61.5% for case reports), which is in line with the value (70.6%) reported for articles published in high-impact medical journals [16], and there was no statistically significant difference in this regard between preprint and peer-reviewed articles. Thus, in spite of the accelerated publication process, the overall quality of the reporting seems to have been adequate.

Although the publication of these articles was accelerated, it is noteworthy that only one case report was published before the pediatric societies' initial alerts and then nearly 2 weeks went by before the first cohort was published [17]. There was consequently a 2-week period with heightened public interest but almost no scientific data available. The CDC, ECDC, and WHO statements on the topic were released nearly 3 weeks after the initial alerts [4–6]. This highlights the importance of early communication from learned societies along with the provision of clear information and regular updates of data published in citable and indexed journals. The question also arises of how general practitioners or pediatricians not affiliated with learned societies are informed other than through the media. Surprisingly, preprints seem to be used only rarely, notwithstanding their usefulness for early dissemination [18]. In the case of KawaCOVID/PIMS-TS/MIS-C, making preprint deposition mandatory would have increased the number of patients reported by nearly 70% in week 20.

The main limitations of this study are that we only surveyed the MEDLINE database and three preprint repositories. As for the number of cases, the presence of duplicates cannot be excluded.

5: Conclusion

We have conducted a bibliometric analysis of articles related to KawaCOVID/PIMS-TS/MIS-C. We found that the medical community responded rapidly to outline the main features of the syndrome but that general public interest followed the news cycle rather than the flow of scientific information. Medical societies play an important role in the early stages of an emerging disease and should probably be more proactive in publishing information as soon as it is available. Generalizing preprint deposition would facilitate the rapid dissemination of research information.

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Table 1: Bibliometric analysis

| | USA | France | UK | Total |
|------------------------------------|------------------------------------|--------------------------------------|--|-------------------------------|
| Articles | 31 | 14 (+1) | 12 | 86 (+3) |
| Preprints | 1 | 3 | 0 | 10 |
| Clinical | 19 | 9 (+1) | 8 | 49 (+3) |
| Others | 12 | 5 | 4 | 37 |
| Patients reported* | 470 | 231 | 132 | 857 |
| Patients per article* | 4 (1–28.5, 1–186) | 16 (10–21, 2–108) | 8 (3.75–20, 1–58) | 4 (1–17, 1–186) |
| Authors per article** | 4.5 (2.25–8.5, 1–45) | 11 (4–17.75, 1–34) | 6 (2–9.25, 1–21) | 5 (3–9, 1–45) |
| Citations per article | 1 (0–2.75, 0–94) | 2 (1–3.5, 0–35) | 1 (0–14.5, 0–170) | 1 (0–3, 0–170) |
| Altmetric score per article | 17.5 (3.25–69.75, 0–1895) | 55 (18–165, 0–1163) | 144 (4.5–816.5, 0–2297) | 12 (1.25–84.75, 0–7242) |
| Journal impact factor | 2,341 (1.911–38.244, 1.186–74.699) | 8,24 (5.9455–16.49425, 2.747–30.223) | 21,92 (3.77825–41.71075, 1.564–62.392) | 3.7 (1.911–22.9055, 1–74.699) |
| Kawasaki-like \$ | 11 | 7(+1) | 3 | 37(+3) |
| PIMS-TS \$ | 3 | 2 | 4 | 14 |
| MIS-C \$ | 15 | 5 | 2 | 27 |
| Other inflammatory \$ | 3 | 2 | 2 | 12 |

Footnotes: Results are reported as number (of articles or patients) or median (interquartile and range). The numbers in parentheses indicate subsequently published preprints; \$, name used in the title of the article, *, patients from published preprints are only counted once; **, authors from published preprints are only counted once

PIMS-TS, pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 infection; MIS-C, multisystem inflammatory syndrome in children

Table 2: Weekly totals of Google searches, Reuters articles, and scientific articles related to KawaCOVID/PIMS-TS/MIS-C

| <i>Week (2020)</i> | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | NA | Total |
|--|---------------|---------------|---------------|--------------------|-------------------|---------------|--------------------|---------------------|--------------------|--------------------|--------------|---------------------|---------------------|---------------------|----------------|
| <i>Google search trends \$</i> | 1.57 (1.3) | 2.24 (1.5) | 1.67 (1.2) | 32.52 (24.6) | 40.86 (28.3) | 55.9 (25.4) | 21.57 (15.7) | 8.43 (4.9) | 4.67 (2.7) | 4.33 (2.3) | 3.95 (2.2) | 3.62 (2.4) | 3.05 (2.1) | | |
| <i>Reuters articles</i> | 0 | 0 | 0 | 9 | 5 | 6 | 2 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 25 |
| <i>Total articles</i> | 1 | 0 | 0 | 2 | 4 | 8 | 10 | 10 | 11 | 14 | 5 | 10 | 11 | 3 | 89 |
| <i>Peer-reviewed articles</i> | 1 | 0 | 0 | 2 | 3 | 7 | 8* | 9* | 10* | 11 | 5 | 10 | 10 | 3 | 79 |
| <i>Preprints</i> | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 1 | 1 | 3 | 0 | 0 | 1 | 0 | 10 |
| <i>Clinical</i> | 1 | 0 | 0 | 0 | 3 | 3 | 8 | 4 | 7 | 10 | 2 | 8 | 5 | 1 | 52 |
| <i>Others</i> | 0 | 0 | 0 | 2 | 1 | 5 | 2 | 6 | 4 | 4 | 3 | 2 | 6 | 2 | 37 |
| <i>Patients reported</i> | 1 | 0 | 0 | 0 | 10 | 62 | 11 | 32 | 186 | 180 | 2 | 341 | 31 | 1 | 857 |
| <i>Cumulative number of patients reported</i> | 1 | 1 | 1 | 1 | 11 | 73 | 84 | 116 | 302 | 482 | 484 | 825 | 856 | 857 | 857 |
| Metrics | | | | | | | | | | | | | | | |
| <i>Median citations per article (range)</i> | 94 | 0 | 0 | 18.5 (16–21) | 8.5 (3–170) | 8.5 (0–154) | 1 (0–11) | 1 (0–16) | 1 (0–21) | 1.5 (0–14) | 0 (0–2) | 0 (0–2) | 0 (0–2) | 0 (0–6) | 1 (0–170) |
| <i>Median Altmetric per article (range) €€</i> | 1006 | 0 | 0 | 128.5 (44–213) | 1158 (19–2297) | 835 (7–7242) | 9.5 (2–188) | 8 (0–109) | 19 (0–835) | 24.5 (0–284) | 3 (0–292) | 0 (0–1895) | 6 (0–794) | 0 (0–1) | 12 (0–7242) |
| <i>Impact factor</i> | - | | | 16.96 (3.7–30.223) | 1.19 (1.19–62.39) | 25 (1–61.392) | 2.28 (1.186–5.359) | 2.17 (1.508–41.185) | 5.29 (1.552–45.54) | 7.93 (1.375–46.54) | 2 (1–40.358) | 2.91 (1.298–74.699) | 8.54 (1.508–74.699) | 1.67 (0.1506–1.838) | 3.7 (1–74.699) |
| Names | | | | | | | | | | | | | | | |
| <i>Kawasaki-like</i> | 1 | 0 | 0 | 2 | 2 | 6 | 6 | 7 | 2 | 4 | 3 | 3 | 3 | 1 | 40 |
| <i>PIMS-TS</i> | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 3 | 5 | 0 | 2 | 2 | 1 | 14 |
| <i>MIS-C</i> | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 3 | 4 | 7 | 1 | 6 | 3 | 1 | 27 |
| <i>Other inflammatory</i> | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 1 | 4 | 1 | 0 | 1 | 1 | 0 | 12 |

Footnotes: Results are reported as number (of articles or patients), mean (SD) or median (range)\$ “kawasaki covid,” “kawasaki covid 19,” and “kawasaki coronavirus”; €, Altmetric on 12 July 2020; €€, Google Scholar citations as of 7–12 July 2020; * including published preprints

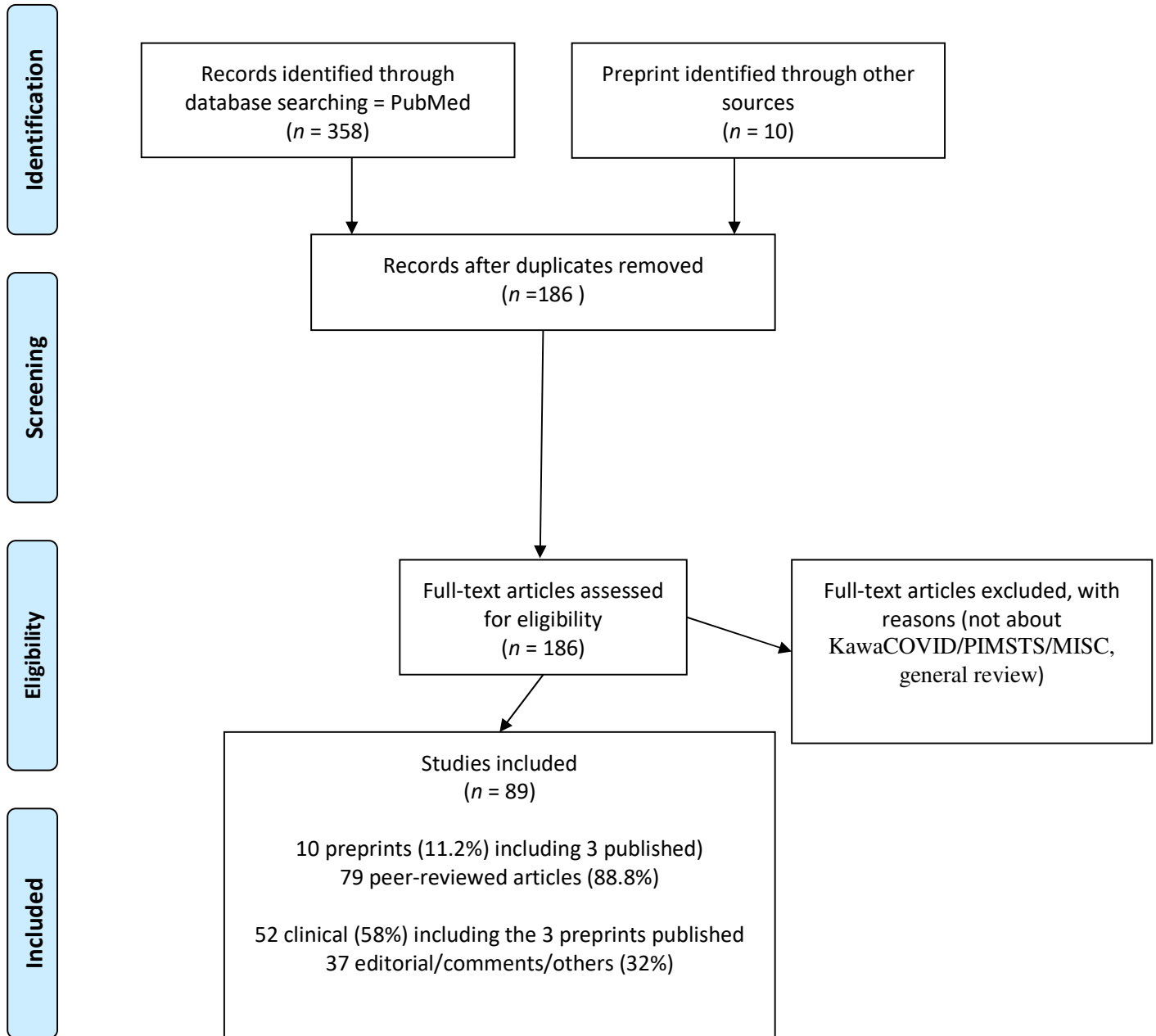
(patients from published preprints are only counted once); PIMS-TS, pediatric inflammatory multisystem syndrome , temporally associated with SARS-CoV-2 infection; MIS-C multisystem inflammatory syndrome in children; NA, week of publication not available

Figure 1: PRISMA Flow Diagram

PIMS-TS, pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 infection; MIS-C, multisystem inflammatory syndrome in children



PRISMA Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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