

1 Reliability of citations of medRxiv preprints in articles published on COVID-19 in the world
2 leading medical journals.

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24 **Abstract**

25 **Background:** Preprints have been widely cited during the COVID-19 pandemics, even in the
26 major medical journals. However, since subsequent publication of preprint is not always
27 mentioned in preprint repositories, some may be inappropriately cited or quoted. Our objectives
28 were to assess the reliability of preprint citations in articles on COVID-19, to the rate of
29 publication of preprints cited in these articles and to compare, if relevant, the content of the
30 preprints to their published version.

31 **Methods:** Articles published on COVID in 2020 in the BMJ, The Lancet, the JAMA and the NEJM
32 were manually screened to identify all articles citing at least one preprint from medRxiv. We
33 searched PubMed, Google and Google Scholar to assess if the preprint had been published in a
34 peer-reviewed journal, and when. Published articles were screened to assess if the title, data or
35 conclusions were identical to the preprint version.

36 **Results:** Among the 205 research articles on COVID published by the four major medical
37 journals in 2020, 60 (29.3%) cited at least one medRxiv preprint. Among the 182 preprints cited,
38 124 were published in a peer-reviewed journal, with 51 (41.1%) before the citing article was
39 published online and 73 (58.9%) later. There were differences in the title, the data or the
40 conclusion between the preprint cited and the published version for nearly half of them.
41 MedRxiv did not mentioned the publication for 53 (42.7%) of preprints.

42 **Conclusions:** More than a quarter of preprints citations were inappropriate since preprints were in
43 fact already published at the time of publication of the citing article, often with a different
44 content. Authors and editors should check the accuracy of the citations and of the quotations of
45 preprints before publishing manuscripts that cite them.

46

47 **Keywords:** Quality of reporting, Preprints, Peer review, Publication, MedRxiv, Medical

48 journals.

49

50 Key points

- 51 • Major medical journals cite preprints in their articles on COVID
- 52 • 41% of the preprint cited were in fact already published when the citing article was
53 published online and the published version should have been cited instead
- 54 • 40% of them displayed difference in the data when comparing to the published version
55 and 10% in the conclusions
- 56 • Differences in content between the preprint and the published version are also common
57 for preprints published after the publication of the citing article

59 INTRODUCTION

60 The scientific community has reacted rapidly to the medical challenges generated by the
61 coronavirus disease 2019 (COVID-19) pandemic, with a steady increase of literature in peer-
62 reviewed journals but also in preprint repositories [1–3]. Yet, a steep increase in the number of
63 posted preprints was observed between January and December 2020, from 797 to 14 290, out of
64 which 8858 (62.0%) were COVID-19-related [4].

65 However, preprints posted on preprint platforms are not subject to peer-review, and therefore
66 critical appraisal, until they are submitted to peer-reviewed journals. Only a small proportion will
67 be converted to scientific publications and the share of converted preprints shows a declining
68 trend over time [4–7]. For those finally passing the peer-review process, peer-reviewers’
69 comments and critiques lead authors to revise their manuscripts, substantially at times [4,6,8]. In
70 that case, the preprint is not the latest version of the work anymore and identifying if it has been
71 published, and referring to the published version instead of the preprint is a major issue as it
72 provides readers with the latest version of a now certified work.

73 However, matching preprints to subsequent peer review publications is a challenge. Yet, once a
74 preprint is published in a peer-reviewed venue, the preprint server is supposed to update its web
75 page, adding a prominent hyperlink leading to the newly published work. Nevertheless, it has
76 been observed that the preprint server MedRxiv reports only 39.7% of all existing publication
77 links [9]. It is therefore probable that some studies are inadequately cited as preprints, although
78 the work cited has been already published, and sometimes with a different content.

79 The first objective of our study was to assess the reliability of preprint citations in articles on
80 COVID-19 published by the world leading medical journals. The second objective was to assess

81 the rate of publication of preprints cited in articles appearing in these journals and the last
82 objective was to compare, if relevant, the content of the preprints to their published version.
83

84 **METHODS**

85 All research articles published on COVID-19 between the 1st of January and the 1st of December
86 2020 in the British Medical Journal (BMJ), The Lancet, the Journal of the American Medical
87 Association (JAMA) and the New England Journal of Medicine (NEJM) were identified through
88 the journal websites. We then manually screened these articles to identify all articles citing at
89 least one preprint from MedRxiv, in the text as a footnote but also in the reference list since all
90 these journals allow citation of preprints in the reference list of articles they published.

91 In September 2021, we searched PubMed, Google and Google Scholar to assess if each preprint
92 had been published in a peer-reviewed journal, using the title and the first author in the search
93 string. For each of those which had been published, we compared preprint version and associated
94 journal article to identify changes in the title and two evidence components: study results (*e.g.*
95 numeric changes in sample size, hazard ratio, odds ratio, event rate, or change in p-value) and
96 abstract conclusions (staying positive, negative or neutral regarding the intervention effect, and
97 reporting uncertainty in the findings or not). When different versions of the preprint were
98 available, we used the version existing at the time the citing article was first published online.
99 The results were considered different when the sizes of the samples, the main quantitative results
100 or the level of significance were different. The conclusions were considered similar if the
101 conclusions in the abstract of the published version remained positive, neutral, or negative
102 regarding the effect of the intervention, or reported the same uncertainties. The conclusions were
103 considered different otherwise. We finally collected the date of first posting of the preprint in
104 MedRxiv, the date of publication of the article citing the preprint and the date of online
105 publication in a journal of the preprint, if relevant.
106 Data were included in an Excel spreadsheet (Microsoft®).

107 **RESULTS**

108 The four major medical journals published 205 research articles on COVID until the 1st of
109 December 2020, among which 60 (29.3%) cited at least one preprint from medRxiv (Table 1).

110 **Table 1** Research articles published on COVID up to the 1st of December 2020, and citation of
111 preprints.

	Number of articles published	Articles citing at least one preprint (%)	Total number of references in articles citing at least one preprint	Number of preprints among the references (%)
BMJ	35	20 (57.1%)	956	91 (9.5%)
JAMA	89	14 (15.7%)	402	26 (6.5%)
Lancet	37	16 (43.2%)	647	53 (8.2%)
NEJM	44	10 (22.7%)	282	12 (4.3%)
Total	205	60 (29.3%)	2287	182 (8%)

112
113 Overall, 182 preprints were cited, among which 124 (68.1%) have been published in a peer-
114 reviewed journal (Figure 1). None of the preprints cited were withdrawn from medRxiv server.

115 **Figure 1:** Flow chart of preprint citations and publications.

116
117 However, among those 124 “preprints”, 51 (41.1%) had already been published when the citing
118 article was published online, at least 2 months before for 33 of them, and were, in fact, not
119 preprints anymore at that time.

120 Among these 51 superseded preprints, differences between the preprint version that was cited
121 and the published version were observed in the data or the conclusions for 21 (40%) of them and
122 in the title for 23 (45%) of them (Table 2).

123 **Table 2:** differences between the preprint and its published version

	SP	P
Same data / same conclusion	30 (59%)	40 (55%)
Same data / different conclusion	0 (0%)	0 (0%)
Different data / same conclusion	16 (31%)	20 (27%)
Different data / different conclusion	5 (10%)	13 (18%)
Different title	23 (45%)	24 (33%)

124

125 SP: supersided preprints, preprint published before the publication of the citing article

126 P: preprint published after the publication of the citing article

127

128 For the 73 other preprints, *i.e.* the 73 (124-51) which were not already published when the citing
129 article was made available online, differences between the preprint version that was cited and the
130 published version were observed in the data or the conclusions for 33 (45%) of them and in the
131 title for 24 (33%) of them (Table 2).

132 The differences in the results were often linked to different sample sizes. For example, in the
133 study assessing factors associated with hospital admission and critical illness, the preprint
134 version included 4,103 participants whereas the article published in the BMJ included 5,279
135 participants [10,11]. This led to different conclusions, with an odds ratio for hospital admission
136 among people > 75 years shifting from 66.8% (95% confidence interval 44.7 to 102.6) in the
137 preprint to 37.9% (95% confidence interval 26.1 to 56.0) in the final article.

138 If we consider only the preprints that were not already published when the citing article was
139 available online, the rate of publication was 55.7% (73 out of 131), with a median publication
140 delay of 65 days (minimum 1 – maximum 486).

141 The fact that the preprint had been published in a peer-reviewed journal was not mentioned in
142 medRxiv for 20 (39.2%) of the 51 superseded preprints and 33 (45.2%) of the 73 other preprints
143 ($p=0.23$).

144 Overall, the median interval between the first posting of a preprint in MedRxiv and its
145 publication in a peer-reviewed journal was 94 days.

146

147 **DISCUSSION**

148 We found that preprint are frequently cited in research articles on COVID-19 published in the
149 world's leading medical journals. However, nearly half of the citations are inappropriate since
150 the preprint was already published when the citing article was published online. Furthermore,
151 many preprints cited will not be published in peer-reviewed journals, or will be but with different
152 data.

153
154 Articles on COVID have been published in many different journals but we chose to investigate
155 the BMJ, The Lancet, the JAMA and the NEJM because they are the medical journals that have
156 published much of the research on Covid-19 [12,13].

157 Many preprint platforms exist, the oldest coming from the early 1990th in the physical sciences.
158 We chose to use MedRxiv, which was launched in June 2019 to provide a dedicated platform
159 and processes for preprints in medicine and health related sciences, because it became
160 particularly popular during the pandemic and is the server that hosted the largest number of
161 preprints on COVID-19 [1,14].

162
163 More than 40 % of these citations were inappropriate since, at the time of online publication of
164 the citing article, the preprint was already published in a peer-reviewed journal.

165 The fact that a large proportion of preprints cited in articles published in peer-reviewed journals
166 were not preprint anymore at the time of publication of the citing article has not been reported in
167 the literature, to our knowledge. This would not be a problem if the contents of the preprint and
168 its published version were similar. However, we observed differences in the data and even a
169 different conclusion for nearly half and 10% of them, respectively. Therefore, searching for a

170 potential peer-reviewed article before citing a paper as a preprint would better reflect the latest
171 evidence available in many cases. However, identifying the subsequent publication of a preprint
172 can be difficult since we observed, that MedRxiv often does not mention the publication of the
173 preprints in a peer-reviewed journal, although it is supposed to display link to journal publication
174 within a month [14], which confirms previous studies [9,15]. Furthermore, in our study, nearly
175 half of the preprints have a different title than their published version and just a copy and paste in
176 PubMed or Google might not allow identifying the published version.

177
178 The interest and validity of preprints have been largely debated, with pros and cons, even before
179 the COVID-19 pandemics [16]. This debate has largely increased about COVID preprints,
180 balancing between the interests of early dissemination of knowledge and the risk of postulated
181 claims without evidence, which will be used by scientists, healthcare workers, and the general
182 public [4,17,18].

183 Preprints posted on platforms are not subject to peer-review and therefore critical appraisal, but
184 some preprint platforms perform screening check, usually related to scope of the article (*e.g.*
185 scientific content, not spam, relevant material, language), plagiarism and legal/ethical/societal
186 issues and compliance [14]. Among the 44 preprint platforms identified by Kirkham *et al.* as
187 having biomedical and medical scope, only three of them (Research Square, bioRxiv and
188 medRxiv) check whether the content contains unfounded medical claims [14].

189 Despite these checks, MedRxiv platform states that “preprints are preliminary reports of work
190 that have not been certified by peer review. They should not be relied on to guide clinical
191 practice or health-related behavior and should not be reported in news media as established
192 information »

193 However, preprints have been widely used during the COVID-19 pandemic where much of the
194 preliminary evidence has been made available through preprints at the time of WHO declaring
195 the epidemic a public health emergency. Only a fraction of these preprints is subsequently
196 published in peer-reviewed journals.

197 In our study, nearly half of the preprints which had not been published in a peer-reviewed journal
198 before being cited as a preprint, were not subsequently published in peer-reviewed journals.

199 Our study may have underestimated the real rate of publication of cited preprints. However,
200 among the preprints that were not finally published, all but one had been posted in MedRxiv
201 before mid-August 2020 and we searched for publication more than one year after the posting. A
202 subsequent publication is therefore improbable, considering the usual median delay of
203 publication reported in other studies, ranging from 28 to 110 days [5–7,19], with a mean of 68
204 days according to a large review [1]. In our study, all the preprints subsequently published were
205 published within 10 months following the publication of the citing article, but one.

206 The rate of subsequent publications of preprints cited in the four world-leading medical journals
207 is higher than the rate of publication of preprints reported in other studies, ranging from 6.9 to
208 21.1% [1,4,5,7,19–21]. However, the rates of publication reported in those studies are probably
209 underestimated since they relied on information about subsequent publication in MedRxiv,
210 which we observed to be largely inaccurate, confirming previous reports [9].

211 For the preprints which were finally published, the differences between the preprints and their
212 published version were frequent and close to those reported in another study on 139 preprints,
213 with changes in the study results or the abstract conclusions between the first preprint version to
214 journal article for 38% and 29% of preprints, respectively [6]. However, when studying 67

215 studies on Covid-19 prevention or treatment, Bero *et al.* found only 23 articles (34%) that had no
216 discrepancies in results reporting between preprints and journal publications [8].

217 The changes in the conclusions were less frequent than the changes in studies' result, mostly
218 because conclusions were usually broad, such as “among patients hospitalized with Covid-19,
219 those who received hydroxychloroquine did not have a lower incidence of death at 28 days than
220 those who received usual care” [22].

221 These changes can be the consequence of publishing preliminary results in a preprint and final
222 results in a peer-reviewed journal, of the fact that some preprints receive comments that allow
223 authors to improve their manuscript prior to submission to a journal, or of the improvement of
224 the quality of the report following the peer reviewed process.

225 Preprints on COVID-19 posted in preprint servers are shorter and contain less references than
226 non-COVID-19 preprints, which suggests that authors tend to publish preliminary results [1].

227 Concerning gradual quality improving, although preprint servers offer authors the opportunity to
228 post updated versions of a preprint, enabling them to incorporate feedback, correct mistakes, or
229 add additional data and analysis, the majority of preprints on COVID-19 in preprint servers exist
230 in fact as only a single version [1]. A study on bioRxiv preprints showed that less than 10% of
231 preprints received at least one comment, and one third were posted by the preprint's authors
232 themselves [23].

233 Although little empirical evidence is available to support the use of editorial peer review as a
234 mechanism to ensure quality of biomedical research [24], the peer review process is a still
235 considered a cornerstone to improve the quality of scientific publications [25].

236 In light of that, in our study, when combining the 58 preprints that were published and the 56 that
237 appeared finally in a peer-reviewed journal, but with different results or conclusions, we can
238 consider that 62.6% of the quotations of preprints may not be fully reliable.

239
240 Another interest of preprints is that they allow free access to research findings, while a large
241 proportion of journal articles often remain behind subscription paywalls. , in response to the
242 pandemic, a number of journal publishers began to alter their open-access policies in relation to
243 COVID-19 manuscripts and made COVID-19 literature temporarily open access [1].

244
245 Finally, the quality of research had to be, in response to the pandemic, put in balance with the
246 need to get rapidly new information to tackle this new threat. Communicating science through
247 preprints allow to share research at a faster rate and with greater transparency than allowed by
248 the current journal infrastructure. Nevertheless, according to the shortcoming of preprints, they
249 should not appear in the reference list of journals but could be cited in the text as such, or, at
250 least, the preprint status should be made clear in the text of a manuscript if citing the research
251 and not just in the reference list [25,26].

252 A promising alternative is the introduction of brief summaries of preprints with significant
253 potential to impact clinical practice in a specific section of biomedical journals [27,28]. Another
254 one is to replace the word “preprint”, which can be misleading, by 'Unrefereed manuscript',
255 "Manuscript awaiting peer review" or "Non-reviewed manuscript" [29].

256

257

258 **CONCLUSIONS**

259 More than 40% of preprints cited in the major medical journals were in fact already published at
260 the time of publication of the citing article. Therefore, authors should check the accuracy of the
261 citation and the quotations of preprints just before submitting the manuscript, and once again
262 when signing the proofs. They should not rely only on the information displayed on MedRxiv
263 website to identify subsequent publication. To overcome medRxiv weaknesses, authors should
264 manually search bibliographic databases to determine if a preprint has been subsequently peer-
265 reviewed and published, keeping in mind the nearly half of the preprints have a different title
266 than their published version. Publishers should also check the accuracy of the citations of
267 preprints before online publication of citing articles.

268 The debate on the interest of preprints has largely increased during the COVID preprints,
269 balancing between the interests of early dissemination of knowledge and the risk of postulated
270 claims without evidence. However, considering the significant number of changes in the content
271 or even the conclusions between the preprints and their published version, quotations of preprints
272 should be considered with caution, even in the articles published in the major medical journals.

273

274

275 **Declarations**

276 Ethics approval and consent to participate: not applicable

277 Consent for publication: not applicable

278 Availability of data and materials: The datasets used and/or analysed during the current study
279 are available at <https://doi.org/10.5281/zenodo.5985960>

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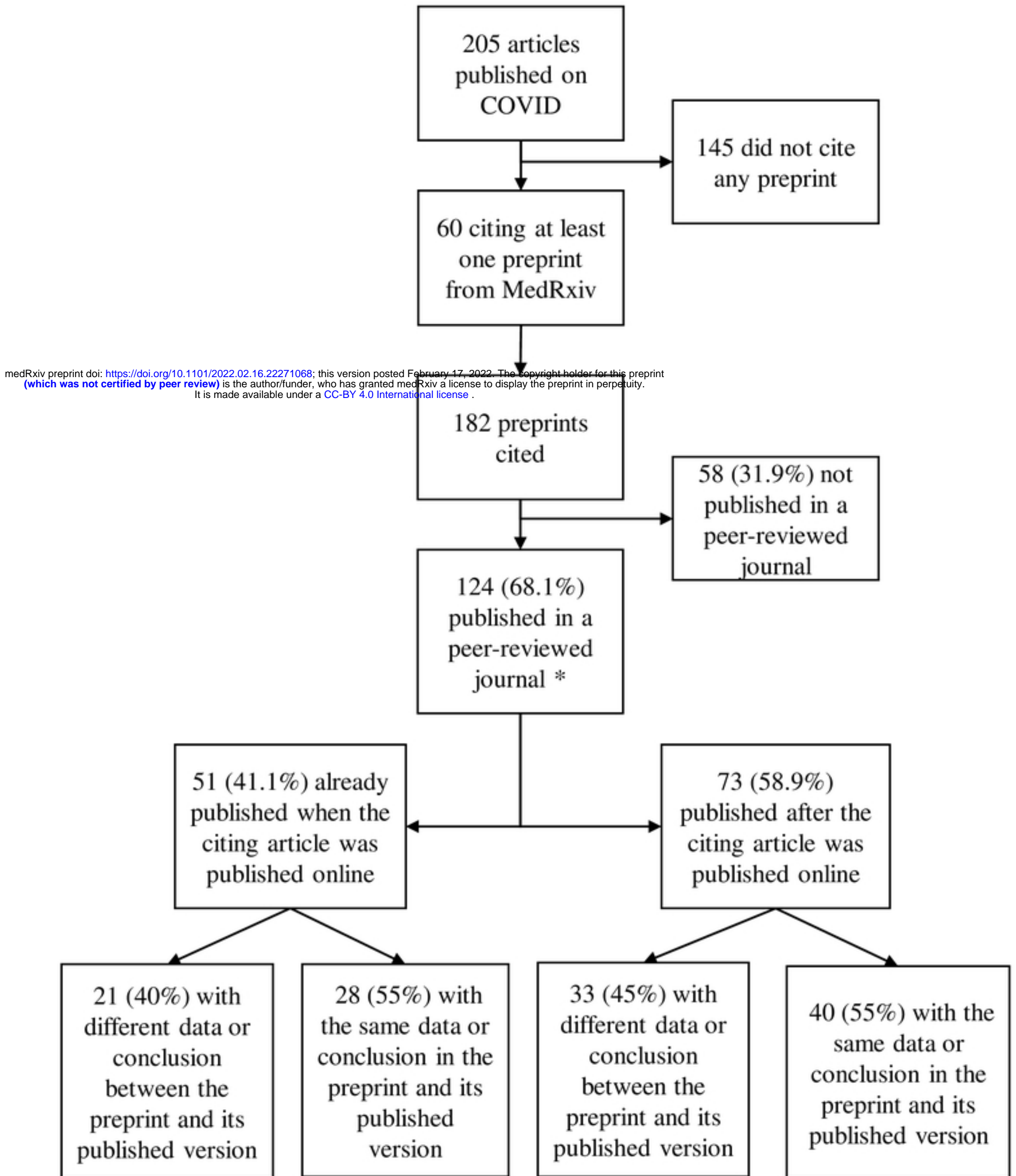
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Figure 1: Flowchart of preprint citations and publications



* : 53 (42.7%) of publication not mentioned in MedRxiv