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Associated Data

Data supplied by the author:

Raw data are available in the Supplemental Files. PRISMA checklist S1 File. COVID-19 or SARS-CoV-2 publications with at least one researcher with Latin American affiliation. S2 File. Genome sequences from Latin American SARS-CoV-2 strains collected in the GISAID database.

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Contributions of Latin American researchers in the understanding the novel coronavirus outbreak: A literature review

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This paper aimed to give the visibility of Latin American researchers' contributions to the comprehension of COVID-19; our method was a literature review. Currently, the world is facing a health and socioeconomic crisis caused by the novel coronavirus, SARS-CoV-2, and its disease COVID-19. Therefore, in less than four months, researchers have published a significant number of articles related to this novel virus. For instance, a search focused on the Scopus database on April 10, 2020, showed 1224 documents published by authors with 1797 affiliations from 80 countries. 25.4%, 24.0%, and 12.6% of these national affiliations were from China, Europe, and the USA, respectively, making these regions leaders in COVID-19 research. In the case of Latin America, on April 10, 2020, we searched different databases, such as Scopus, PubMed, and Web of Science, finding that the contribution of this region was $2.7 \pm 0.6\%$ of the total publications found. In other words, we found 153 publications related to COVID-19 with at least one Latin American researcher. We summarized and processed the information from these 153 publications, finding active participation in topics like medical, social, and environmental considerations, bioinformatics, and epidemiology.

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4

5

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16 **Abstract**

17 This paper aimed to give the visibility of Latin American researchers' contributions to the
18 comprehension of COVID-19; our method was a literature review. Currently, the world is facing
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28 American researcher. We summarized and processed the information from these 153
29 publications, finding active participation in topics like medical, social, and environmental
30 considerations, bioinformatics, and epidemiology.

31

32 **1. Introduction**

33 Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel virus that mainly
34 affects the respiratory system through the new coronavirus disease 2019 (COVID-19) (Ciotti *et*
35 *al.*, 2020). COVID-19 has spread quickly; thus, on March 11, 2020, the World Health
36 Organization (WHO) declared it as a pandemic (Hussain *et al.*, 2020). Since the first cases
37 reported in Wuhan, China, in December 2019, until April 20, 2020, SARS-CoV-2 has affected

38 most countries in the world, with nearly 2.5 million people infected and 170,000 deaths (Johns
39 Hopkins University, 2020). Latin America is no stranger to this reality, totaling approximately
40 100,000 cases and 5,500 deaths, as shown in Table 1 (Johns Hopkins University, 2020).
41 However, these data may be lower than actual numbers because the number of tests per million
42 inhabitants remains low, which is caused by factors such as the limited availability of tests and
43 the difficulty of monitoring people without facilities like indigenous populations, vulnerable
44 groups, and Venezuelan refugees (Oliveira *et al.*, 2020; Torres & Sacoto, 2020).
45 SARS-CoV-2, as SARS and MERS, belongs to the family *Coronaviridae*, has a zoonotic origin,
46 and can remain on some surfaces for considerable periods (Ciotti *et al.*, 2020; van Doremalen *et*
47 *al.*, 2020). Additionally, COVID-19 is a new disease with no yet vaccines or targeted drugs,
48 making the containment of the outbreak difficult (Carnero Contentti & Correa, 2020). Therefore,
49 the recommendation is the self-isolation to reduce COVID-19 spreading, especially in more
50 susceptible people as older adults or patients with comorbidities (Diaz-Quijano *et al.*, 2020).
51 More general aspects of the current outbreak have been published in review articles according to
52 available information in the moment of publication. These reviews include other zoonotic
53 diseases (such as SARS and MERS), outbreak chronology, virus characteristics, zoonotic links,
54 transmission, diagnosis, disease characteristics, therapeutics & treatments, prevention,
55 epidemiological surveillance, and control (Ciotti *et al.*, 2020; Cupertino *et al.*, 2020; Huang *et*
56 *al.*, 2020; Millán-Oñate *et al.*, 2020; Palacios Cruz *et al.*, 2020; Rodriguez-Morales *et al.*, 2020a;
57 Sifuentes-Rodriguez & Palacios-Reyes, 2020; Siordia, 2020; Wu *et al.*, 2020; Zhu *et al.*, 2020).
58 In the past, during SARS and MERS outbreaks, research focused on coronaviruses increased
59 significantly, which was led by researchers from China and the USA (Bonilla-Aldana *et al.*,
60 2020b). This new outbreak is not an exception because thousands of articles have been published

61 in less than four months, where China, Europe, and the USA are leaders in the number of
62 publications. In the case of Latin America, it is a region with an increasingly high contribution to
63 science; thus, our question was, what are the contributions of Latin American researchers in
64 understanding this novel coronavirus outbreak? Therefore, our purpose in this review was to
65 highlight the contributions of this region in the comprehension of SARS-CoV-2 and COVID-19.
66 The literature survey consisted of revising and summarizing publications with Latin American
67 researchers. Keeping in mind that several researchers from this region work together with
68 researchers from other continents, we included publications submitted by these types of
69 international research groups. Hence, the relevance of this review focused on finding the
70 research interests of Latin American researchers according to global and regional priorities.

71

72 **2. Survey methodology**

73 **2.1. Search strategy**

74 We performed the present review following the PRISMA guidelines. The search was done on
75 April 10, 2020, using Scopus, Web of Science, PubMed, ScienceDirect, Wiley, Sage, LILACS,
76 and SciELO databases because they are the main academic literature collections globally and
77 regionally. Other databases like Springer Link were excluded because they do not allow to
78 filtrate by affiliation. The search equation used had ("COVID 19" OR "COVID-19" OR "SARS-
79 CoV-2" OR "SARS CoV 2" OR "SARS-CoV 2" OR "2019-nCoV" OR "2019 nCoV" OR
80 "nCoV-2019" OR "nCoV 2019" OR "hCoV-19" OR "hCoV 19") in all fields and (Argentina OR
81 Bolivia OR Brasil OR Brazil OR Chile OR Colombia OR Cuba OR Ecuador OR Salvador OR
82 Guatemala OR Haiti OR Honduras OR Mexico OR Nicaragua OR Panama OR Paraguay OR

83 Peru OR Dominicana OR Uruguay OR Venezuela) in affiliation field. We did not consider
84 preprints during the search stage. No interfaces were used in the present literature review.

85

86 **2.2. Article selection and data extraction**

87 After the search stage, both reviewers (KYFS and LMSB) removed all duplicated publications,
88 which included a manual revision because some publications were simultaneously in English,
89 Spanish, or Portuguese. Later, we performed a second manual revision to verify that all
90 publications had at least one researcher with a Latin American affiliation. After these two
91 manual revisions, we did not exclude more publications, and final publications were included in
92 the qualitative synthesis. Before the qualitative synthesis, we collected the following
93 information, which was used in the bibliometric analysis: title, authors, journal, DOI, type of
94 publication, national affiliation of Latin American researchers, and topic of publication.

95

96 **2.3. Data analysis**

97 We summarized information from the collected publications according to the type of publication,
98 the topic of publication, and the national affiliation in the “Bibliometric analysis” section. The
99 first purpose of this section was to quantify contributions of the region in the global context, and
100 the contribution by country in the regional context. The second purpose was to classify the
101 publications by topic and type, which allowed us to organize the next sections of this literature
102 review. In the following two sections, “Phylogenetic and molecular understanding” and “medical
103 contributions”, we compiled information from research articles and reviews. The last section,
104 called “Additional concerns”, was included to highlight contributions not covered in the two

105 main topics, but discussed in the remaining publications (commentaries, letters to the editor,
106 editorials, communications, perspectives, points of view, and contributions).

107

108 **3. Bibliometric analysis**

109 Following the PRISMA guidelines shown in Figure 1, we found 301 publications in the
110 considered databases; this number decreased to 161 after excluding duplicates. Later, we
111 manually excluded eight additional publications due to affiliations from New Mexico (1) and
112 Pennsylvania (7) were confused with Mexico and Panama, respectively. Therefore, this
113 qualitative analysis included 153 publications, which contained at least one researcher with Latin
114 American affiliation (see Supplementary S1 file for complete information of publications). We
115 highlight that several publications were not exclusively submitted by Latin American
116 researchers, some of which are part of research groups together with North American, European,
117 or Asian researchers. Figure 2 presents the classification of publications by type, where most of
118 them were letters to the editor or commentaries, editorials, and research articles.

119

120 Regardless of the number of authors from the same country but different institutions, among all
121 publications, we highlight that 15 of them were submitted by groups in which there were
122 researchers from at least two Latin American countries. Therefore, these publications were
123 counted for each nation involved; thus, these 15 publications have 56 national affiliations. Most
124 of these publications were due to the Latin American Network of Coronavirus Disease 2019-
125 COVID-19 Research (LANCOVID-19), which was created to integrate the region around this
126 new outbreak (Rodriguez-Morales *et al.*, 2020d). The remaining 138 publications were submitted
127 by groups in which there were researchers from a single Latin American country. Therefore,

128 these publications were counted once for the country, disregarding whether they were submitted
129 by one or more researchers with the same national affiliation; in other words, these 138
130 publications have 138 national affiliations. In summary, the 153 publications accounted for 194
131 national affiliations. Figure 3 shows publications by national affiliation, where Brazil had the
132 highest contribution with 80 publications, followed by Colombia, Mexico, and Argentina, with
133 36, 18, and 14 publications, respectively. Conversely, the following Latin American countries
134 had no publications: Cuba, Costa Rica, Dominican Republic, El Salvador, Guatemala, Haiti, and
135 Nicaragua.

136 We did the same search without the affiliation field restriction. We found 1224, 615, 3538, 1841,
137 665, 48, 2627, and 34 publications in Scopus, Web of Science, PubMed, ScienceDirect, Wiley,
138 Sage, LILACS, and SciELO databases, respectively. Hence, publications with Latin American
139 researchers in these databases, Figure 1, represent 2.9%, 3.1%, 2.8%, 3.3%, 2.9%, 2.1%, 1.6%,
140 and 76.5% of all publications, respectively. Excluding Scielo, which is a Latin American
141 database, the contribution of the region was $2.7 \pm 0.6\%$. This low value could be associated with
142 the science gap (gap in science funding, technology, facilities) between the region and the
143 developed countries. However, other possibilities are the late coronavirus appearance in the
144 region (between February and March), as opposed to the initial outbreak (December 2019) and
145 the number of Latin American cases (nearly 4% world total), as shown in Table 1.

146 Finally, Figure 4 shows the classification of publications by topic, which were medical
147 considerations (surgery recommendations, diagnosis, comorbidities, medical guidelines,
148 dentistry considerations, among others), social and environmental considerations, general aspects
149 (zoonotic links, spreading, origin, disease, surveillance, among others), epidemiological
150 analyses, bioinformatics (molecular and phylogenetic analyses, molecular simulations, genetic

151 annotations, among others), mental health considerations, search for potential treatments, and
152 meta-analyses. Excluding the general aspects, the remaining topics are shown in the following
153 sections.

154

155 **4. Phylogenetic and molecular understanding**

156 The researcher with the highest number of research articles was Ph.D. Marta Giovanetti, who has
157 contributed to SARS-CoV-2 understanding through bioinformatic analyses (Angeletti *et al.*,
158 2020; Benvenuto *et al.*, 2020a; Benvenuto *et al.*, 2020b; Benvenuto *et al.*, 2020c; Benvenuto *et*
159 *al.*, 2020d; Cleemput *et al.*, 2020; Giovanetti *et al.*, 2020a; Giovanetti *et al.*, 2020b). Her first
160 research focused on a phylogenetic analysis of SARS-CoV-2, finding that among the viruses
161 compared, this virus is closely related to bat-SL-CoVZXC21 (GenBank ID MG772934.1), while
162 the least related is MERS (Benvenuto *et al.*, 2020b). However, Cardenas-Conejo *et al.* (2020)
163 proposed that SARS-CoV-2 has a closer relation to bat-SL-CoV-RaTG13 (GenBank ID
164 MN996532.1), then, authors suggested first that SARS-CoV-2 is unlikely to come directly from
165 pangolin viruses, and second, that if SARS-CoV-2 has a recombinant origin, this recombination
166 did not happen in ORF1ab. Nevertheless, both Benvenuto *et al.* (2020b) and Cardenas-Conejo *et*
167 *al.* (2020) concluded that the novel virus could come from a bat SARS-like coronavirus isolate,
168 which is in agreement with reports from the GISAID database (Hadfield *et al.*, 2018; Sagulenko
169 *et al.*, 2018).

170 Subsequent studies of the Giovanetti group found differences in the superficial spike protein S of
171 SARS-CoV-2 through structural analyses, which could give a higher ability to infect humans
172 when compared to other coronaviruses (Benvenuto *et al.*, 2020b). This ability could be attributed
173 to two mutations found in the non-structural protein 2 (nsp2) and nsp3, both originating from a

174 possible positive pressure (Angeletti *et al.*, 2020). Similarly, evaluating *in silico* molecular
175 interactions between the human angiotensin-converting enzyme 2 (ACE2) receptor and the spike
176 protein of some coronaviruses, Ortega *et al.* (2020a) found that SARS-CoV-2 has some modified
177 residues. Such residues could improve the recognition and interaction with the ACE2 receptor,
178 providing SARS-CoV-2 with a higher infectiousness, which is in agreement with another study
179 published simultaneously (Andersen *et al.*, 2020). Likewise, performing *in silico* molecular
180 interactions, Ortega *et al.* (2020b) evaluated the interaction between the protease of SARS-CoV-
181 2 and some protease inhibitors as a strategy to control COVID-19 infection. The most energetic
182 interactions predicted were using Saquinavir, Lopinavir, and Tipranavir, which are treatments for
183 HIV patients; however, experimentation is required to validate these simulations.

184 In a later study, the Giovanetti group analyzed SARS-CoV-2 mutations through time, finding
185 two variations located in nsp6 and ORF10, which could be caused by a positive selective
186 pressure, leading to a lower protein structure stability and possibly (awaiting for evidence) a
187 higher virulence (Benvenuto *et al.*, 2020a). Cardenas-Conejo *et al.* (2020) similarly detected
188 variations in nsp6 and eight deleted amino acids in nsp1 from some Japanese virus strains.

189 Although these *in silico* studies are a first approach and require experimental validation
190 (Ciccozzi *et al.*, 2020), they could also be a first step to aid in identifying treatments or vaccines.

191 Lastly, Giovanetti simultaneously contributed to another research group to develop and validate
192 an open-access tool, called the Genome Detective Coronavirus Typing Tool, which analyzes
193 SARS-CoV-2 genomes to generate new knowledge of COVID-19 outbreak (Cleemput *et al.*,
194 2020).

195 Concerning the sequencing of SARS-CoV-2 genomes to understand this novel coronavirus, some
196 Latin American researchers have contributed to the publication of sequences of isolated strains

197 from countries such as Chile (Castillo *et al.*, 2020) or Nepal (Sah *et al.*, 2020). Researchers from
198 other countries have also sequenced the genomes of strains from Argentina, Brazil, Chile,
199 Colombia, Ecuador, Mexico, Panama, Peru, and Uruguay, totaling 98 genome sequences until
200 April 20, 2020 (see Supplementary S2 file for detailed information of all sequences). The
201 GISAID database has these 98 sequences collected along with 10,380 others, meaning that Latin
202 American contribution is near 0.94% (Hadfield *et al.*, 2018; Sagulenko *et al.*, 2018). Table 2
203 summarizes this information by country, showing that Brazil and Mexico have the highest
204 number of sequenced genomes, 52 and 17, respectively. Figure 5 presents some of the Latin
205 American SARS-CoV-2 strains in the phylogenetic tree, evidencing the high heterogeneity
206 among them because they belong to different clades.

207

208 **5. Medical contributions**

209 **5.1. Epidemiological analyses**

210 Studies to track first cases in different countries have been performed, such as the case of tracing
211 the first cases of COVID-19 in countries like Italy (Giovanetti *et al.*, 2020b) and Chile (Castillo
212 *et al.*, 2020) using phylogenetic analyses. Both studies found that the first cases came from China
213 and Europe since S and G variants of SARS-CoV-2 were detected. In the case of Italy, a reentry
214 from Germany was detected (Giovanetti *et al.*, 2020a). Tracing of imported cases to other Latin
215 American countries has also been performed using strategies such as data recovery of
216 international flights from the most affected countries to Brazil (Candido *et al.*, 2020), or
217 recompilation of epidemiological data from hospitals in Bolivia (Escalera-Antezana *et al.*, 2020).
218 Both studies concluded that the first imported cases came from Europe, specifically from Italy
219 and Spain. Moreover, other bioinformatics tools have been used to contribute to epidemiological

220 understanding. For example, a Bayesian phylogeographic reconstruction suggested that Wuhan
221 was effectively the outbreak epicenter on November 25, 2019, spreading later to other Chinese
222 regions (Benvenuto *et al.*, 2020c).
223 Additionally, the geo-positioning of some cases and the heterogeneity of the outbreak progress
224 among countries, with demographic similarities, have been reported (de Figueiredo *et al.*, 2020;
225 Xu *et al.*, 2020). Other epidemiological studies have been done to predict the COVID-19
226 spreading (Benvenuto *et al.*, 2020d; Córdova-Lepe *et al.*, 2020; González-Jaramillo *et al.*, 2020;
227 Manrique-Abril *et al.*, 2020), which concluded that containment strategies are required to avoid
228 overspreading in countries like Chile and Colombia. Similarly, Kraemer *et al.* (2020) analyzed
229 the effect of mobility in China before and after the sanitary containment of Wuhan in the
230 COVID-19 spreading in this country; they demonstrated that decreasing mobility favors the
231 reduction of COVID-19 spreading.

232

233 **5.2. Meta-analyses performed**

234 Latin American researchers have also published meta-analyses of clinical, laboratory, and image
235 data from reported COVID-19 cases (Borges do Nascimento *et al.*, 2020; Rodriguez-Morales *et*
236 *al.*, 2020b). On the one hand, the meta-analysis submitted by Rodriguez-Morales *et al.* (2020b)
237 on February 29, 2020, used 19 articles with 2,874 patients for quantitative analyses. On the other
238 hand, the meta-analysis of Borges do Nascimento *et al.* (2020), submitted six days later,
239 employed 61 studies with 59,254 patients. Both revisions included the most common symptoms
240 as well as typical abnormalities observed in chest radiographs and computed tomographies,
241 which were like other respiratory illnesses and viral pneumonia, making it difficult to distinguish
242 from them (Borges do Nascimento *et al.*, 2020). Oxygen support in critical patients was also

243 analyzed, where Borges do Nascimento *et al.* (2020) suggested that excluding the non-invasive
244 ventilation usage since no evidence supports its benefits.
245 Regarding lethality, the most affected population (81%) was the older group (60 years or more),
246 but additional information is required to understand the COVID-19 impact on other continents
247 because most of the data used in these meta-analyses came from China. Therefore, meta-analyses
248 using Latin American cases would also be ideal for determining how COVID-19 could affect this
249 region, which has some differences, such as lower average age or higher exposure to respiratory
250 infections than other regions like Europe (Amariles *et al.*, 2020a). A third meta-analysis was
251 found, which suggested that it could be possible to predict if a patient with COVID-19 can
252 present complications. Lagunas-Rangel (2020) hypothesized that complications are related to
253 high levels of neutrophil-to-lymphocyte ratio (NLR) and low levels of lymphocyte-to-C-reactive
254 protein ratio (LCR).

255

256 **5.3. Search for potential treatments**

257 Concerning treatments to respiratory issues, Khoury *et al.* (2020) revised respiratory therapies
258 for COVID-19 patients using cell-based treatments such as mesenchymal stem cells (MSCs),
259 derivatives, or other cells, which have shown positive results in pre-clinical models of influenza.
260 Conversely, they argued that there were few coronavirus studies, such as the case of seven
261 COVID-19 patients in Beijing treated with MSCs, who showed apparent improvements up to 4
262 days after treatment, but lacked detailed information (Leng *et al.*, 2020). Therefore, after a
263 systematic search in databases, Khoury *et al.* (2020) found 27 ongoing treatments with 1,287
264 patients. The authors also highlighted the importance of following ethical protocols for these
265 types of treatments.

266 Besides the previously mentioned review, since currently there are no approved treatments or
267 vaccines for COVID-19, other revisions have summarized the development of clinical trials for
268 COVID-19 treatments. This is the case of the search made by Rosa & Santos (2020), who looked
269 for ongoing clinical trials in Clinicaltrials.gov. The authors used some constraints in their search,
270 such as low cost, reduced time to reach markets, existing pharmaceutical supplies, or the
271 possibility to combine with other drugs. In total, 24 clinical trials were found, most of them in
272 clinical phases 2, 3, or 4, with a scheduled end in 2020. These ongoing clinical trials are using
273 chloroquine, hydroxychloroquine, human immunoglobulin, remdesivir, arbidol, lopinavir,
274 ritonavir, oseltamivir, darunavir, cobicistat, interferons, carrimycin, danoprevir, xiyanning,
275 favipiravir, thalidomide, vitamin C, methylprednisolone, pirfenidone, bromhexie, bevacizumab,
276 fingolimod, and traditional Chinese medicines (TCM).

277 Similarly, Serafin *et al.* (2020) searched for new treatments for coronaviruses like SARS-CoV,
278 SARS-CoV-2, and HCoV-OC43 in PubMed, SCOPUS, and Web of Science databases. The
279 drugs found as SARS-CoV-2 treatments are captopril, chloroquine, clomipramine, disulfiram,
280 enalapril, hydroxychloroquine, mefloquine, metformin, nitazoxanide, remdesivir, and
281 teicoplanin. This review highlighted positive results using chloroquine, hydroxychloroquine,
282 teicoplanin, and hydroxychloroquine in conjunction with azithromycin. Finally, Rosales-
283 Mendoza (2020) suggested that a potential treatment with biotechnological origin could be
284 produced using plant species as hosts.

285

286 **5.4. Medical considerations**

287 Most medical articles studied populations at risk and comorbidities, also provided
288 recommendations and guidelines for medical personnel. Rascado Sedes *et al.* (2020) developed a

289 contingency plan that allows an optimal response of the intensive care units (ICU) to the
290 pandemic. The plan considers possible scenarios, the need for human and technical resources,
291 communication and information, optimized use of resources, and personal protective equipment
292 (PPE).

293 Healthcare workers, emergency room physicians, anesthesiologists, dentists, ophthalmologists,
294 head and neck surgeons, maxillofacial surgeons, and otolaryngologists are among the most
295 vulnerable ones because they perform procedures that can aerosolize secretions (Kowalski *et al.*,
296 2020). According to several studies, articles, and protocols, Boccalatte *et al.* (2020) summarized
297 recommendations related to PPE, mandatory use of protective suits, head covers, eye protection,
298 mask, gloves, and N95, FFP2, or PAPR masks, personnel training, and techniques or
299 manoeuvres for different medical practices.

300 Concerning surgeries, although there is no information about to translate risks to the operating
301 room team during such procedures to COVID-19 patients, the recommendation is to postpone
302 them (Cohen *et al.*, 2020; Ducournau *et al.*, 2020). The situations in which a delay in the surgical
303 procedure may affect the patient, such as some oncologic or organ transplant surgeries, surgery
304 must be performed following strict preventive measures. In the case of unpostponable abdominal
305 surgeries, a laparotomic operation with regional anesthesia should be preferred (Carneiro *et al.*,
306 2020; Cohen *et al.*, 2020; Correia *et al.*, 2020; Quintão *et al.*, 2020). Other articles summarized
307 protocols and recommendations for hand (Ducournau *et al.*, 2020), head and neck (Kowalski *et*
308 *al.*, 2020), and urologic surgeries (Puliatti *et al.*, 2020).

309 Researchers have also performed literature reviews concerning populations with higher risk due
310 to comorbidities. First, Hussain *et al.* (2020) focused on patients with diabetes mellitus and
311 COVID-19. They summarized the different determinants that associate this pathology with

312 greater severity and death, as well as the importance of multidisciplinary medical management.

313 The authors mentioned that COVID-19 could cause pancreatic damage, which could affect

314 patients with diabetes. Likewise, the positive effects of hydroxychloroquine and chloroquine on

315 diabetic patients were mentioned, such as reducing insulin degradation tending to normalize

316 glucose levels. Therefore, in case hydroxychloroquine or chloroquine is administered,

317 antidiabetic drug doses should be readjusted to avoid hypoglycemic events. The authors also

318 mentioned the necessity to continue studying in these patients the chronic inflammation, immune

319 response, coagulation activity, and vascular permeability, as well as whether hyperglycemia or

320 hypoglycemia can alter the virulence of SARS-CoV-2, or whether the virus itself interferes with

321 insulin secretion or glycemic control. All this information will be needed to propose adequate

322 clinical treatments.

323 Likewise, Puliatti *et al.* (2020) considered the effect of SARS-CoV-2 in different organs of the

324 urinary tract. They highlighted that ACE2-positive cells (target of SARS-CoV-2 spike proteins)

325 have been found in these organs, which could have a high risk of affectation, even leading to

326 death, which explains the kidney damage experimented in some COVID-19 patients. Similarly,

327 chronic hemodialysis patients are also at particular risk due to their immunosuppression status,

328 advanced age, and comorbidities coexistence. Vega-Vega *et al.* (2020) summarized the

329 recommendations for these patients proposed by three international organizations: Center for

330 Disease Control and Prevention (CDC), the Spanish Society of Nephrology, and the Latin

331 American Society of Nephrology and Hypertension, to which were added suggestions of some

332 experts. Some recommendations are the proper definition of cases, guidelines for patients and

333 family, scrutiny of suspicious COVID-19 cases and their management within hemodialysis units,

334 PPE employment, and sanitation of surfaces and devices.

335 Another group at risk mentioned by researchers is related to critical COVID-19 patients who
336 need assisted ventilation. Some authors recommend taking into account some considerations
337 before using high-flow nasal oxygen therapy, non-invasive ventilation, or extracorporeal
338 membrane oxygenation (ECMO), the latter being a treatment that no all medical centers can
339 afford. First, if the medical center has adequate protection levels for health workers from exhaled
340 air dispersed, and second, the impact of treatment on acute respiratory distress syndrome
341 (ARDS) (Bartlett *et al.*, 2020; Ñamendys-Silva, 2020a; Ñamendys-Silva, 2020b). Similarly,
342 Chica-Meza *et al.* (2020) summarized conventional and non-conventional respiratory therapies
343 in critical COVID-19 patients, including recommendations and considerations. Finally, surveys
344 have been performed to identify COVID-19 impacts in patients at risk, such as pediatric patients
345 with cancer (Hrusak *et al.*, 2020), but the information is still limited; however, the
346 recommendation is to follow the same medical practices described previously.

347

348 **5.5. Mental health considerations**

349 Mental health care must be considered, given that quarantine can cause boredom, loneliness,
350 anger, anxiety, depression, and stress. Patients and health workers should have mental health
351 services (Carvalho *et al.*, 2020b; Lima *et al.*, 2020). In especial when more people can be
352 affected by mental issues during the outbreak than by the outbreak itself (Ornell *et al.*, 2020),
353 and previous outbreaks have caused post-traumatic stress disorder (PTSD) in health workers
354 (Torales *et al.*, 2020).

355 Concerning performed studies on mental issues, first, Fonseca *et al.* (2020) established
356 recommendations for patients with schizophrenia. Among recommendations are an adequate
357 identification of COVID-19 symptoms, prevention of worsening of psychiatric symptoms,

358 relapses due to the closed environment, fear of disease and isolation, use of telemedicine,
359 promoting adherence to antipsychotic medication regimens, reducing emotional distress, hygiene
360 practices, and family support. Finally, Carvalho *et al.* (2020a), using questionnaires to Brazilians,
361 investigated whether extroverted and conscientious people are engaged with the containment
362 measures implemented during the COVID-19 pandemic. They found that extroverted people
363 seem to lack commitment to containment measures, while people with conscientiousness
364 personality tend to follow recommendations. Therefore, at least in Brazil, strategies for
365 extroverted people should be proposed to avoid they become transmission vectors. However, the
366 idiosyncrasy is similar throughout Latin America; thus, these strategies should be required in the
367 entire region.

368

369 **6. Additional Concerns**

370 **6.1. Social and environmental concerns**

- 371 • Telemedicine should be considered as an alternative to patient attention to avoid COVID-19
372 spreading. However, this strategy is limited because of the scarce existence of telemedicine
373 systems; thus, social media could be used (Assis Machado *et al.*, 2020; Quintão *et al.*, 2020).
- 374 • Elachola *et al.* (2020) highlighted that there are no prevalence and effectiveness studies on
375 using facemasks related to the COVID-19 outbreak. This information could be useful in
376 providing recommendations about their usage. However, based on past outbreaks, the
377 evidence did not show positive or negative effects when the population used facemasks
378 (Stern *et al.*, 2020).
- 379 • Since the first COVID-19 cases reported in Latin America, fake news and misinformation
380 have increased, where even treatments with potential health affectations have been proposed,

- 381 as in the case of using chloroform or ether as alleged COVID-19 treatments (Lana *et al.*,
382 2020; Martins & Santos, 2020). Additionally, information should be verified, avoiding panic
383 spreading, which has caused panic buying of supplies and medications (Cuan-Baltazar *et al.*,
384 2020).
- 385 • The quick COVID-19 spreading in different regions and countries could cause that health
386 workers to become overwhelmed, therefore training new personal, although challenging, is a
387 necessity that could help to attend the current outbreak. Additionally, the pharmacy
388 workforce should be prepared as they are the first ones to attend possible cases of infection
389 (Amariles *et al.*, 2020b; Aruru *et al.*, 2020; Haines *et al.*, 2020).
 - 390 • Countries with low or middle incomes, such as Latin American countries, may have already
391 saturated their health systems. Hence, the COVID-19 outbreak could oversaturate them
392 (Carneiro *et al.*, 2020), which can be exacerbated by the lack of government preparation and
393 social policies, such as the Ecuadorian case (Hallo *et al.*, 2020).
 - 394 • Based on events that occurred with the “Diamond Princess” cruise, alternatives should be
395 proposed to quarantine people from other cruises and illegal immigrants entering a country
396 (Sawano *et al.*, 2020).
 - 397 • Due to the current outbreak, many activities have been interrupted, which joined the
398 socioeconomic limitations of vulnerable groups, could lead to food insecurity in these
399 populations, who even have no access to clean water (Oliveira *et al.*, 2020).
 - 400 • Knowing that COVID-19 has a zoonotic origin, One Health approach has taken relevance,
401 which seeks integrative studies where the health of humans, environment, and animals are
402 considered to understand the virus environment, allowing the prevention or mitigation of
403 future outbreaks (Bonilla-Aldana *et al.*, 2020a).

404

405 **6.2. Medical concerns**

- 406 • Initial reports of some pathologies such as rheumatic diseases or neuromyelitis optica
407 spectrum disorder (NMOSD) have shown that they do not increase the risk of complications
408 like other comorbidities. However, further studies are needed (Carnero Contentti & Correa,
409 2020; Figueroa-Parra *et al.*, 2020).
- 410 • Angiotensin II receptor blockers (ATII-RB) are hypertensive drugs that increase ACE2
411 expression; therefore, there is a possibility that they can favor the internalization of SARS-
412 CoV-2 within the cell; thus, further studies are required. However, suspending ATII-RB
413 therapy may cause even higher affectations than COVID-19 itself; the risk-benefit ratio
414 should be evaluated. In case doctors consider suspending it, there are other options like
415 thiazide diuretics drugs (Gracia-Ramos, 2020; Marin, 2020).
- 416 • As previously mentioned, chloroquine and hydroxychloroquine are *in vitro* inhibitors of
417 SARS-CoV-2 infection. However, concerns are focused on whether these medications could
418 decrease viral load or prevent infection, clinical disease, clinical severity, or even death.
419 Other factors, such as side effects, should also be considered (Kim *et al.*, 2020; Monteiro *et*
420 *al.*, 2020; Picot *et al.*, 2020).
- 421 • COVID-19 mainly affects the respiratory system, but it can also alter the central nervous
422 system. Hence, possible affectations in the respiratory center could exacerbate respiratory
423 distress caused by pulmonary affectation (Conde *et al.*, 2020).
- 424 • Tropical countries affected by dengue could face two outbreaks at the same time, dengue and
425 COVID-19, which could affect the population, even coinfecting some patients
426 simultaneously. Both outbreaks will require the intensive attention of health systems to avoid

427 a crossed affectation between them, which can be challenging and overwhelming for the
428 health systems (Lorenz *et al.*, 2020; Navarro *et al.*, 2020; Rodriguez-Morales *et al.*, 2020c;
429 Saavedra-Velasco *et al.*, 2020).

- 430 • As SARS-CoV-2 can remain in saliva, oral health professionals require research focused on
431 the influence of COVID-19 in their activities to take appropriate measures. However, the
432 recommendation is to stop dental treatments (Martelli-Júnior *et al.*, 2020; Napimoga &
433 Freitas, 2020; Sabino-Silva *et al.*, 2020).
- 434 • Strategies during intubation are not the only important ones to avoid COVID-19 spreading in
435 health workers during medical procedures; strategies for extubation are also required
436 (Trujillo, 2020).
- 437 • There is no evidence that immunosuppressant treatments (ITS) could decrease or increase the
438 risk of severe COVID-19 infection; therefore, further investigation is recommended. In case
439 treatments are suspended, factors such as potential issues on patients should be considered
440 (Carnero Contentti & Correa, 2020).
- 441 • There is limited evidence of COVID-19 effect on pregnant women; hence, cases of pregnant
442 women with COVID-19 should be studied to understand the clinical impact of the infection
443 (Zambrano *et al.*, 2020).

444

445 **Conclusions**

446 Although our purpose was to give visibility to the contribution of Latin American researchers in
447 the knowledge generation related to the COVID-19 outbreak, this review has two drawbacks.
448 The first is the continuous availability of new publications; therefore, an observation window
449 was employed. Second, several Latin American researchers are currently working on other

450 continents without a Latin American affiliation, making them impossible to track. However, after
451 this literature review, we were able to evidence the active participation of Latin American
452 researchers in different subjects, whether as members of national, regional (LANCOVID-19), or
453 even international research groups. Concerning our findings, the publications evidenced that
454 these research groups have advanced in molecular and medical subjects, mainly in genetic
455 understanding, epidemiological behaviors, meta-analyses, interaction between COVID-19 and
456 other pathologies, and recommendations to medical procedures. Finally, understanding that this
457 health crisis requires the commitment of as many researchers as possible, our wish is that the
458 contribution of Latin American researchers continues to grow. Some topics with regional and
459 global interest for future studies include *in silico* analyses of potential treatments and their
460 respective *in vitro* and *in vivo* validations, meta-analysis of Latin American patients, and
461 epidemiological surveillances. Regarding medical considerations, a deeper understanding of the
462 COVID-19 interaction with risk comorbidities is needed to propose adequate clinical treatments.
463 The same applies to unexplored/underexplored physical and mental pathologies, such as dengue.
464

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466 This review is in memory of all deceased by the COVID-19 outbreak.

467

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Figure 1

PRISMA Flow diagram of selection process of COVID-19 or SAR-CoV-2 publications containing researchers with Latin American affiliation.

Identification stage was performed on April 10, 2020.



PRISMA 2009 Flow Diagram

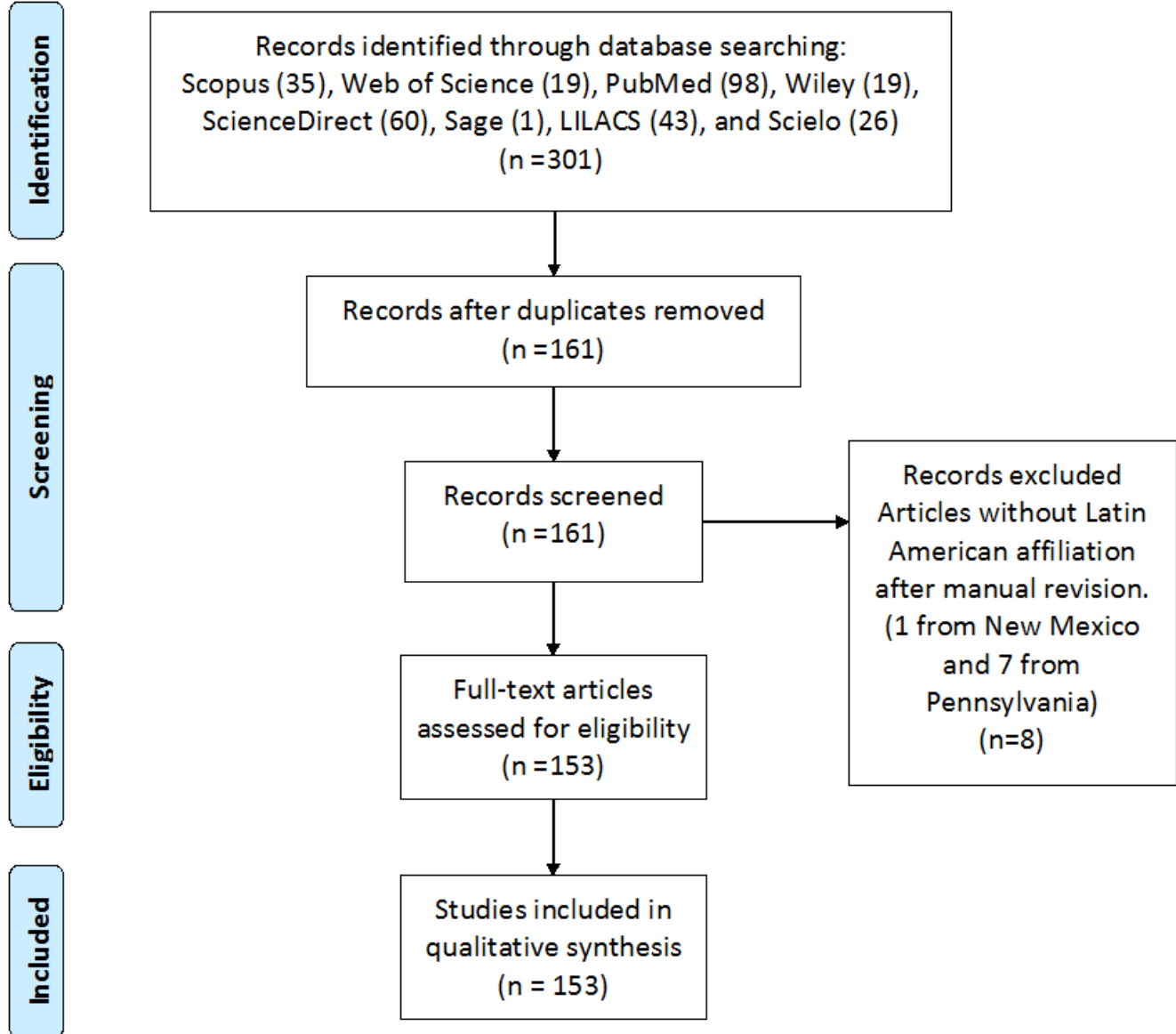


Figure 2

Classification of publications by category

Other publications refer to: Consensus statement, Contribution, and Technical note.

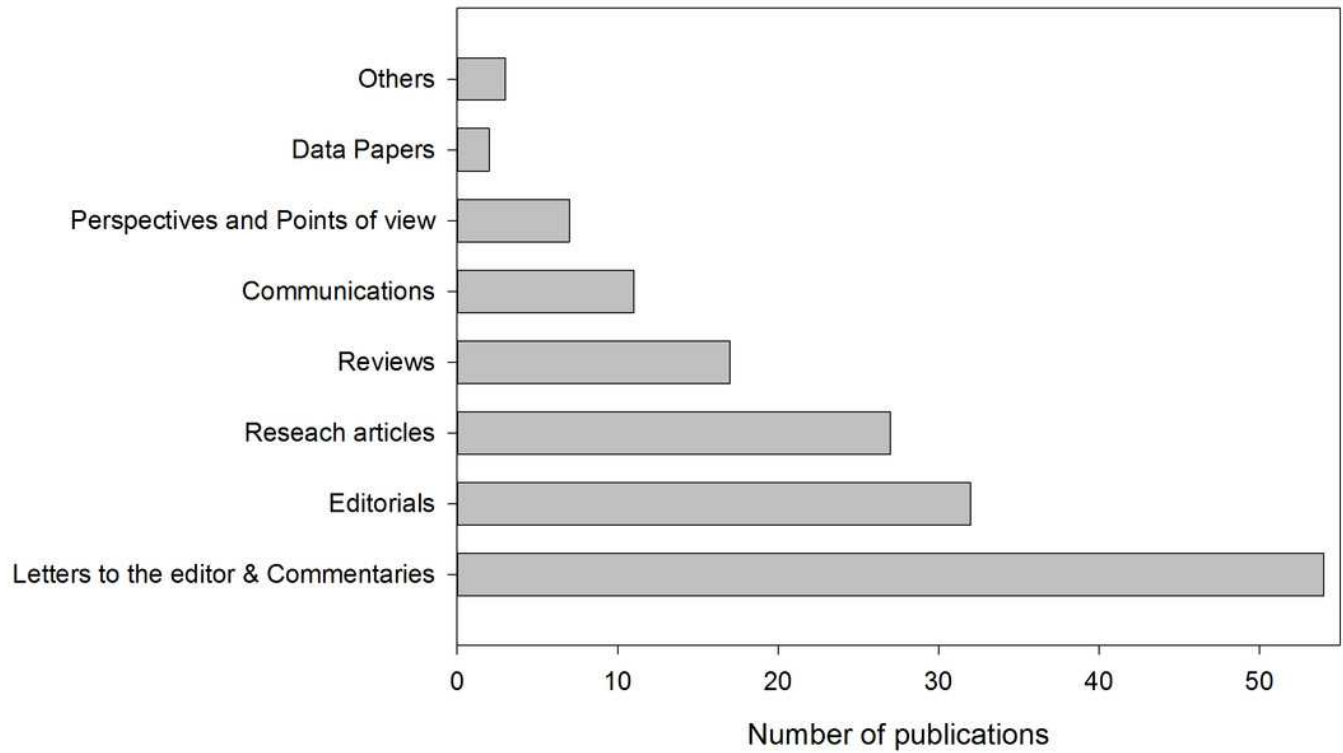


Figure 3

Classification of publications according to the national affiliation.

Several authors from the same country in a publication were counted as one contribution to the country. Publications with authors from different countries were counted as one for each country. Latin American countries not shown had no publications until April 10, 2020.

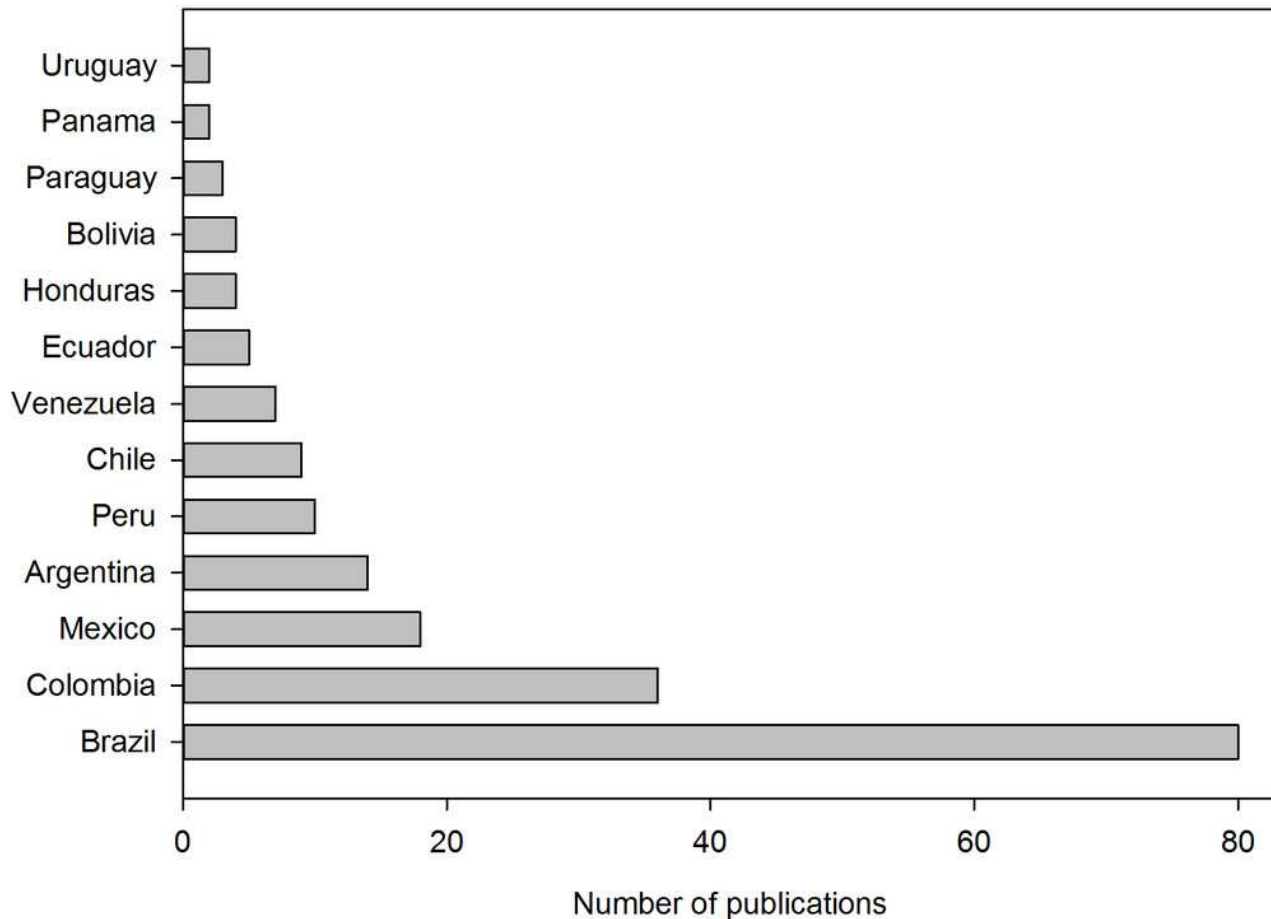


Figure 4

Classification of publications by topic.

Medical considerations refer to surgery recommendations, diagnosis, comorbidities, medical guidelines, dentistry considerations, among others. The general aspects include zoonotic links, spreading, origin, disease, surveillance, among others. Bioinformatics refers to molecular and phylogenetic analyses, molecular simulations, genetic annotations, among others.

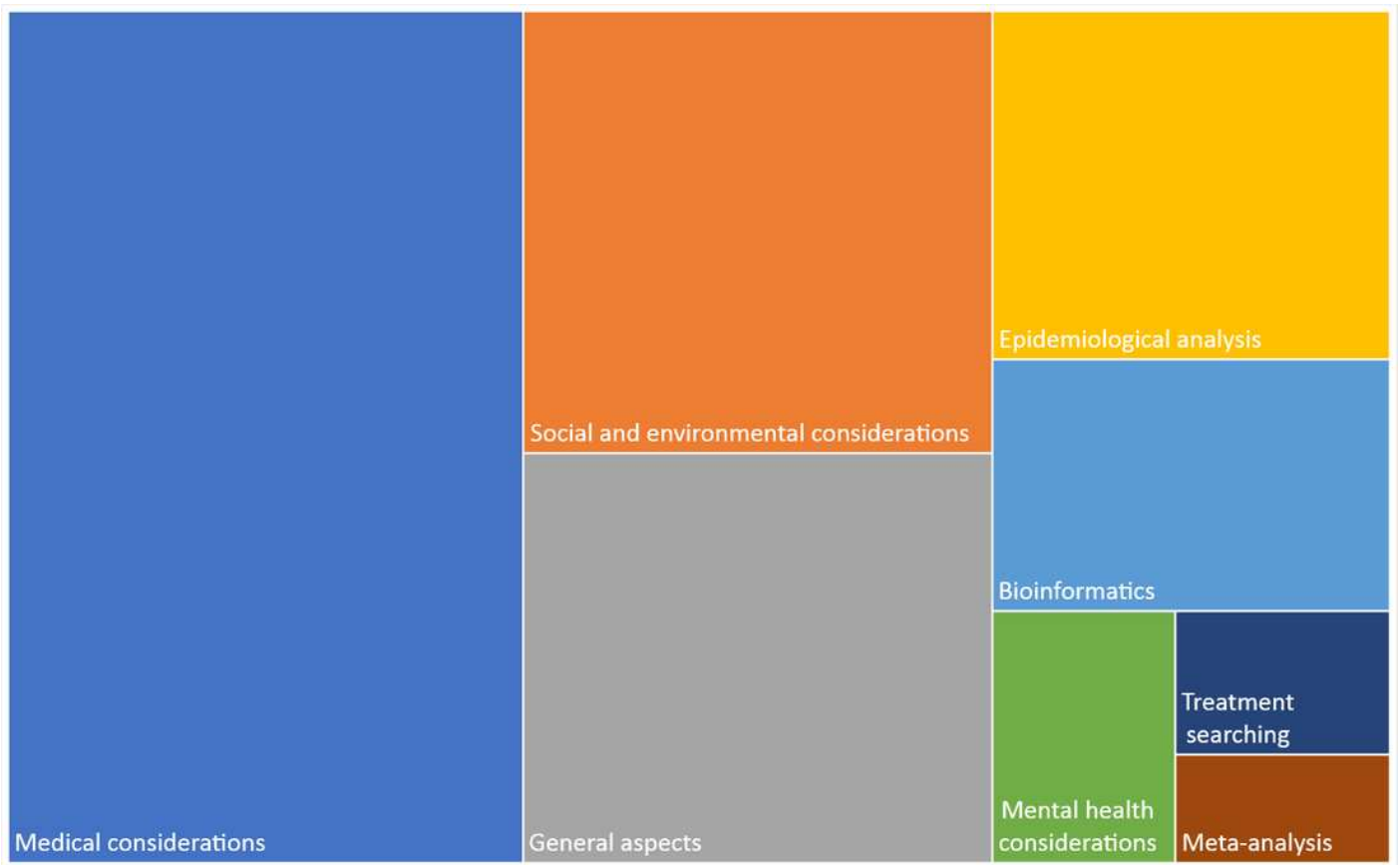


Figure 5

Phylogenetic location of genome sequences of some strains isolated in Latin America in the SARS-CoV-2 phylogenetic tree.

The phylogenetic tree was generated and adapted from the GISAID database (Hadfield *et al.*, 2018; Sagulenko *et al.*, 2018). The tree was retrieved on April 20, 2020.

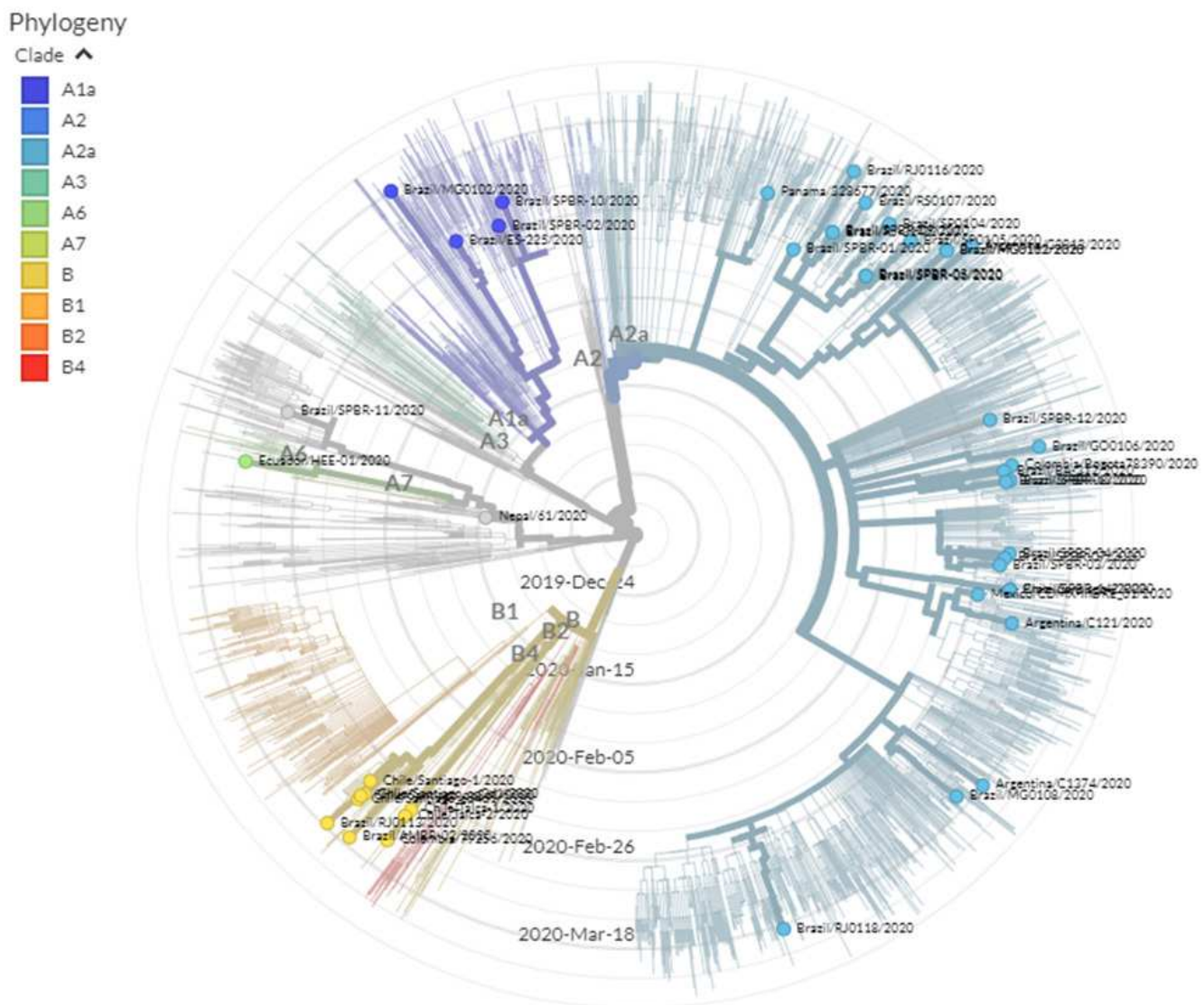


Table 1 (on next page)

Summary of the COVID-19 outbreak affectation in the Latin American countries.

Total cases and total deaths are reported until April 20, 2020 (Johns Hopkins University 2020).

Country	First case	Cases	Deaths
Argentina	Mar 3	2941	136
Bolivia	Mar 10	564	33
Brazil	Feb 25	40581	2845
Chile	Mar 3	10507	139
Colombia	Mar 6	3963	189
Costa Rica	Mar 6	662	6
Cuba	Mar 11	1087	36
Dominican Rep.	Mar 1	4964	235
Ecuador	Feb 14	10128	507
El Salvador	Mar 18	218	7
Guatemala	Mar 13	289	7
Haiti	Mar 2	47	3
Honduras	Mar 11	477	46
Mexico	Feb 27	8261	686
Nicaragua	Mar 18	10	2
Panama	Mar 8	4467	126
Paraguay	Mar 7	208	8
Peru	Mar 6	16325	445
Uruguay	Mar 13	528	10
Venezuela	Mar 13	256	9
	Total	106483	5475

Table 2 (on next page)

Summary of genome sequences of SARS-CoV-2 strains isolated in Latin America and collected in GISAID database.

Information updated on April 20, 2020 (Hadfield *et al.* 2018; Sagulenko *et al.* 2018).

Country	Submitting lab	Location	Total
Argentina	Instituto Nacional Enfermedades Infecciosas C.G.Malbran	Argentina	3
Brazil	Bioinformatics Laboratory - LNCC	Goiais	1
		Minas Gerais	5
		Rio de Janeiro	7
		Rio Grande do Sul	1
		São Paulo	4
	Instituto Adolfo Lutz, Interdisciplinary Procedures Center, Strategic Laboratory	Brasilia	1
		Sao Paulo	2
		Sao Paulo	11
	Instituto Oswaldo Cruz FIOCRUZ - Laboratory of Respiratory Viruses and Measles (LVRS)	Maceio	1
		Feira de Santana	2
		Brasilia	5
		Vila Velha	1
		Niteroi	1
		Rio de Janeiro	6
Florianopolis		1	
Laboratorio de Ecologia de Doencas Transmissiveis na Amazonia, Instituto Leonidas e Maria Deane - Fiocruz Amazonia	Manaus	1	
	Laboratory of Virology	Brasilia	1
Chile	Instituto de Salud Publica de Chile	Santiago	2
		Talca	2
	MSSH Pathogen Surveillance Program	Santiago	3
Colombia	Instituto Nacional de Salud Universidad Cooperativa de Colombia Instituto Alexander von Humboldt Imperial College-London London School of Hygiene & Tropical Medicine	Antioquia	1
		Bogota	1
Ecuador	Institute of Microbiology, Universidad San Francisco de Quito	Pichincha	3
		Quito	1
Mexico	Instituto de Diagnostico y Referencia Epidemiologicos (INDRE)	Chiapas	1
		Estado de Mexico	1
		Mexico City	2
		Puebla	1
		Queretaro	1
	Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran	Mexico City	5
	Instituto Nacional de Enfermedades Respiratorias	Mexico City	5
Laboratorio Central de Epidemiología-DLVIE / Laboratorio de Secuenciación-Centro de Instrumentos. Instituto Mexicano del Seguro Social	Chihuahua	1	
Nepal ^a	The University of Hong Kong	Kathmandu	1
Panama	Gorgas Memorial Institute for Health Studies	Panama City	1
Peru	Laboratorio de Referencia Nacional de Biotecnologia y Biologia Molecular. Instituto Nacional de Salud Peru	Lima	2
Uruguay	Microbial Genomics Laboratory, Institut Pasteur Montevideo	Montevideo	9
Total general			98

- 1 ^aNepal was included due to researchers with Colombian and Honduran affiliations contributed in
- 2 its genome sequencing (Sah *et al.* 2020).