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Epidemiological characterization of asymptomatic carriers of COVID-19 in Colombia

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1 **Epidemiological characterization of asymptomatic carriers of COVID-19 in Colombia**

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15 **ABSTRACT (187 words)**

16 **Introduction:** Asymptomatic carriers (AC) of the new Severe Acute Respiratory Syndrome
17 Coronavirus 2 (SARS-CoV-2) represent an important source of spread for Coronavirus
18 Disease 2019 (COVID-19). Early diagnosis of these cases is a powerful tool to control the
19 pandemic. Our objective was to characterize patients with AC status and identify associated
20 sociodemographic factors.

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21 **Methods:** Using a cross-sectional design and the national database of daily occurrence of
22 COVID-19, we characterized both socially and demographically all ACs. Additional
23 Correspondence Analysis and Logistic Regression Model were performed to identify
24 characteristics associated with AC state (OR, 95% CI).

25 **Results:** 2338 ACs (11.8%; 95% CI, 11.3-12.2%) were identified, mainly in epidemiological
26 week 18 [EW] (3.98; 3.24-4.90). Age ≤ 39 years (1.56; 1.42-1.72). Male sex (1.39; 1.26-
27 1.53), cases imported from Argentina, Spain, Peru, Brazil, Costa Rica or Mexico (3.37; 1.47-
28 7.71) and autochthonous cases (4.35 ; 2.12-8.93) increased the risk of identifying AC. We
29 also identified groups of departments with moderate (3.68; 3.13-4.33) and strong (8.31; 6.10-
30 7.46) association with AC.

31 **Conclusion:** Sociodemographic characteristics strongly associated with AC were identified,
32 which may explain its epidemiological relevance and usefulness to optimize mass screening
33 strategies and prevent person-to-person transmission.

34 **Key words:** COVID-19; Asymptomatic; Carrier States; Risk factors, Novel Coronavirus.

35 Article summary' section consisting of the heading: 'Strengths and limitations of this study',
36 and containing up to five bullet points that relate specifically to the study reported. This
37 should be placed after the abstract.

38 **Article summary**

- 39 • Asymptomatic carriers (AC) represent a silent source of spread for Coronavirus
40 Disease 2019 (COVID-19).
- 41 • ACs have been included in epidemiological predictive models to estimate the second
42 and third pandemic wave of COVID-19.

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- 43 • Epidemiological reports of ACs are frequently biased given the inclusion of pre-
44 symptomatic patients or the merge of ACs with patients with non-critical symptoms.
- 45 • Massive screening could improve current understanding of AC phenotype and thus
46 provide useful information for predictive mathematical models.
- 47 • Recognizing the silent movement of COVID-19 through ACs could result in more
48 effective public health strategies of containment and prevention.

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62 **TEXT (2481 words)**

63 **INTRODUCTION**

64 In March 2nd, 2020, Colombia reported the first case of Coronavirus Disease 2019 (COVID-
65 19), and as of May 23rd, more than 20,000 cases have been confirmed nationwide ¹.

66 Asymptomatic carriers (AC) may be associated with the accelerated growth of cases in the
67 initial phases of the pandemic, inadvertently spreading the infection to close contacts. In this
68 case, transmission can only be limited until a diagnosis of SARS-CoV-2 infection is rendered
69 after (i) isolation due to symptom onset, (ii) contact tracing or (iii) identification during
70 massive screening strategies ^{2,3}.

71 AC and pre-symptomatic cases are epidemiologically relevant since they represent a silent
72 source of spread in various public settings (e.g. public transportation, emergency rooms,
73 supermarkets, shelters) ⁴⁻⁶. The proportion of ACs has been estimated at 15-25%, but
74 seroprevalence studies have reported values of up to 43.2% (95% CI, 32.2-54.7%).
75 Nonetheless, many pre-symptomatic patients are wrongfully classified as ACs during the
76 incubation phase; to later become pauci-symptomatic or develop respiratory manifestations
77 ranging from pneumonia to respiratory failure, or exhibit any other clinical symptoms within
78 the COVID-19 spectrum ⁴⁻⁸.

79 Epidemiological predictive models have been developed and updated to incorporate silent
80 mobility through AC phenotype in anticipation for the second and third epidemic waves of
81 COVID-19. Such is the case for the SEIR model (Susceptible, Exposed, Infected and
82 Recovered), recently updated to SEAIR (Susceptible, Exposed, Asymptomatic, Infected and
83 Recovered) ⁹. In China, estimates indicate that 60-65% of ACs remained undetected.

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84 Therefore, under the SEIR model and applying machine-learning-based transmission
85 simulators (MLSim), including the number of undetected AC within its parameters and
86 assuming 15 close contacts per day, estimates suggest that as of April 15th, 2020, the United
87 States---the country contributing the majority of cases imported to Colombia---, could have
88 presented 277,641-to-495,128 latent cases of COVID-19, potentially increasing the spread
89 of the virus ¹⁰.

90 The assessment of ACs and the identification of sociodemographic characteristics associated
91 with this subpopulation could be useful to estimate sample calculations in massive screening
92 studies, as well as adjust control and mitigation measures---especially the intensity of
93 isolation. Therefore, the objective of our study was to characterize ACs demographically and
94 socially, as well as to identify individual characteristics in interaction models associated with
95 ACs.

96 **METHODOLOGY**

97 **Design and data selection.**

98 We performed a cross-sectional study with information from the National Institute of Health
99 (INS) database on COVID-19 cases updated until May 23, 2020. By INS protocol, suspected
100 AC cases remained in quarantine for 7 days while monitoring the appearance of symptoms
101 on a daily basis; on the eighth day, a nasal swab sample was collected to identify or rule out
102 AC state. Records without health status information (symptomatic, asymptomatic) were
103 excluded. The database is public, with de-identified patient data and IRB approval was thus
104 exempt.

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106 Patient and Public Involvement (PPI) statement

107 This research was done without patient involvement. Patients were not invited to comment
108 on the study design and were not consulted to develop patient relevant outcomes or interpret
109 the results. Patients were not invited to contribute to the writing or editing of this document
110 for readability or accuracy.

111 Database and variables.

112 We used variables such as date of diagnosis, age, sex, country of origin, department, case
113 type (imported, related), care setting (home, nursing home, hospital, intensive care unit) and
114 outcome (recovered, convalescent, deceased). The date of diagnosis was adjusted into
115 epidemiological weeks (EW), which were later grouped according to the pattern of AC
116 occurrence (Figure S1) in EW 10-15, 16-17, 18, 19-21; additionally, the variable AC [yes,
117 no] was established.

118 Statistical analysis

119 Data are presented in medians or proportions estimated with 95% CI due to the lack of
120 massive screening for COVID-19 in certain areas of the country. The geographical origin
121 and destination of imported cases was represented with a Sankey Plot (SankeyMATIC
122 (BETA). Cumulative trends and case charts were created with the number of daily cases by
123 Epid_weeks (RStudio Version 1.2.5042). In addition, a heatmap analysis was included to
124 depict a dynamic representation of daily cases by Department from March 6th through May
125 23rd, 2020 (Orange Data Mining & Fruitful Fun, Version 3.25). The proportion of
126 asymptomatic and symptomatic patients and the median age were compared with the Z and
127 U Mann Whitney tests respectively (significant p-value <0.05, two tails) [Addinsoft. 2020.

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128 XLSTAT statistical and data analysis solution. New York, USA. <https://www.xlstat.com>].

129 Age was dichotomized between 0-39 and ≥ 40 years due to its association with asymptomatic
130 and symptomatic states respectively (preliminary exploratory analysis not shown).

131 Countries of origin and departments associated with ACs were identified with a
132 Correspondence Analysis (CA). Additionally, with contribution coordinates of the columns
133 (CCC-CA), groups with a variable level of association with ACs were created [Addinsoft.
134 2020. XLSTAT statistical and data analysis solution. New York, USA.
135 <https://www.xlstat.com>].

136 To estimate the association between sociodemographic characteristics with CA (OR 95%),
137 two Logistic Regression Models (LRM) were performed, the first to establish the main
138 effects and the second a step-backward interaction model of the second level (p- value in
139 < 0.05 ; p-value out: > 0.1), which used the lowest Akaike criteria to select the best model
140 (JASP Team (2020). JASP (Version 0.12.2))

141 **RESULTS**

142 **General characteristics**

143 We identified 2,388 ACs (11.8%; 11.3-12.2%) out of 20,177 cases reported in the database.
144 Four cases were excluded due to lack of health status information. The occurrence of AC
145 state in relation to symptomatic presented a slow growth phase between EW 10-15, moderate
146 growth between EW 16-17, and a peak at EW 18, followed by a decrease between EW 19-
147 21 (Figure 1A, 1B, S1). Daily cases ranged from 1 to 203 per day, and EWs 18 and 19
148 registered the highest number of cases per day: 172 and 203, respectively.

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3 149 Additionally, we report department clusters with a high occurrence of daily COVID-19 cases,
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5 150 which follow different dynamic patterns for ACs and symptomatic patients (Figure 1C-1D).
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8 151 Meta reported the largest number of daily ACs (n: 151), with peak occurrences between April
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10 152 23rd and May 10th; followed by Amazonas, Bogotá, and Caribbean departments with peak
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12 153 reports between May 11th and 12th,

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15 154 More than half of the imported ACs came from Europe, specifically Spain, followed by North
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17 155 and South America. Those that arrived from Spain and USA were distributed mainly in
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19 156 Bogotá, Valle del Cauca and other departments of the Caribbean region. Amazonas
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21 157 department only received imported ACs from South American countries. The origin and
22
23 158 distribution of imported symptomatic patients was more diverse; however, most cases
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25 159 originated from Spain, USA, Ecuador, Mexico, Brazil, or Panama, and were mainly
26
27 160 distributed across Bogotá, Antioquia, and Valle del Cauca (Figure 2).

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29 161 About half of the ACs were located in Meta and Bogotá, and a tenth in the Amazon (Table
30
31 162 1, Table S1). Median age was 32 years old, lower than the symptomatic patients. Most of
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33 163 them were males (Table 1). The domicile was the main place of care (85.7%; 84.3-87.1%)
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35 164 and 13.9% had recovered (95%, CI, 12.5-15.3%). Four of the admitted cases had fatal
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37 165 outcomes, two from the general wards and two from the Intensive Care Units (ICU). Possibly
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39 166 these last 8 cases were treated for symptoms unrelated to COVID-19, or were diagnosed post-
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41 167 mortem.

42 43 168 **Factors associated with AC condition.**

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45 169 Using the CCC-CA, a group of six countries and three groups of departments were associated
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47 170 with AC state (Figure 3). To execute LRMs, the variables "age group 0-39 years" and "male

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3 171 sex" were transformed into dummi [0/1]. With a preliminary LRM, a higher β coefficient
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5 172 was estimated in relation to cases imported from countries associated with AC, therefore, the
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7 173 variable "geographical origin" was created, composed of the categories "imported from
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9 174 countries associated with symptomatic" [Imported CAS - referent], "imported from countries
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11 175 associated with asymptomatic" [Imported CA-AC] and "related cases". Additionally, a
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13 176 variable was created for the departments grouped with the CA [departments with low
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15 177 association - referent] and for the EW (EW 10-15 - referent). The first LRM (main effects)
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17 178 identified a significant association of all index sociodemographic categories with AC state
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19 179 (Table S2). The second model explores the following interactions: 1. Geographical origin
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21 180 and grouped departments, 2. Geographical origin and EW, 3. Age group (0-39 years) and
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23 181 gender, 4. Grouped departments and gender; and, 5. Age (0-39 years) and EW. We identified
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25 182 that the variables gender (males) and EW showed interaction with the grouped departments
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27 183 (Table 2).

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29 184 Variables "0-39 years", "departments with strong association", "imported CA-AC" and
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31 185 "related cases" were found to increase the risk of identifying AC state. It was also determined
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33 186 that the risk increased with the interaction between men in the departments with a strong and
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35 187 moderate association. In isolation (without interaction), between EWs 19-21, the risk of
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37 188 identifying AC decreased, as did EWs 16-17 in departments with a strong association.
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39 189 However, the risk increased from EW 18 to EWs 19-21 when interacting, both with moderate
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41 190 and strong association departments (Table 2).

42 191 **DISCUSSION**

43 192 We found that, in an isolated fashion, age < 40 years old, imported cases from a group of 6
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45 193 countries, autochthonous cases and the occurrence in groupings of departments were
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194 associated with AC state. Additionally, the risk of being a male AC was only identified in
195 departments with moderate or strong risk, and the risk was variable in the groupings of
196 departments throughout specific epidemiological periods.

197 Additionally, our results show that the proportion of ACs in Colombia lays between 11-12%
198 (Table 1), a lower estimate than previously described in other case series or mass screening
199 studies with reported proportions between 5-80%¹¹⁻¹⁴. Given the inclusion of
200 presymptomatic patients or the unification of AC with non-critical symptoms in some
201 reports, we cannot rule out that a non-differential classification bias influenced these
202 estimates. An adapted definition for AC in Colombia may address this limitation.

203 Figure 1 shows that the majority of imported cases to Colombia came from Spain and USA,
204 where AC rates have been estimated at 2.5% and 25%, respectively^{14,15}. Although imported
205 cases carry a distinctive genetic load that, population-wise, could manifest itself as a
206 particular phenotype¹⁶, currently there are no reports of genetic variants associated with AC
207 in general or for any of the four AC subtypes described in the literature¹⁷. Subsequent
208 research should be conducted on the possible association between ACs and phylogenetic
209 variants (or other variables) to support the differential risk identified in imported cases from
210 different regions of the world.

211 We identified that imported cases from a group of 6 countries were strongly associated with
212 AC (Figure 2, Table S1, Table 2), and although no interaction was established between the
213 country of import and the destination department (data not shown), we observed that
214 departments strongly associated with AC had less diversity of import origin. Such is the case
215 of Meta and Amazonas, which exclusively imported cases from USA and Brazil/Peru,
216 respectively (Figure 2).

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3 217 Among the demographic characteristics, the association between AC state and patients under
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5 218 40 years of age stands out. Possible explanations for this observation include: (i) the lower
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7 219 presence of co-morbid conditions and baseline health issues within this age group and (ii) the
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9 220 higher risk of exposure through work activities which are greater in this age group ¹⁸.
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11 221 However, clinical or social environment could also explain this finding, as a study in skilled
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13 222 nursing facility residents showed a high proportion of AC in those over 70 years of age,
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15 223 however this was a premature finding since most patients were later reclassified as pre-
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17 224 symptomatic or pauci-symptomatic ¹¹.

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22 225 We identified a higher frequency of men infected with COVID-19 consistent with reports
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24 226 from other countries around the world, except in Spain and Switzerland, where women
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26 227 ranked first ¹⁹. Frequent occupations performed by men, as well as certain immunological
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28 228 and genetically susceptible backgrounds have been associated with this finding ^{19,20}. In
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30 229 particular, the risk of being an AC was higher in men, and increased in geographic areas
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32 230 associated with AC. This interaction is not uncommon given that professions regularly
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34 231 carried out by men, including those such as taxi driving, private security or prison guarding,
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36 232 among other work settings, can be distributed asymmetrically within countries, a pattern that
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38 233 would explain our findings ²⁰.

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43 234 The phases on the occurrence of cases throughout EWs and the interaction with groupings
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45 235 within departments associated with AC has been previously described in Chongqing, China,
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47 236 where researchers identified significant changes in the frequency of cases after
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49 237 implementation of geographic isolation measures. In Wuhan, a study showed that one group
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51 238 of ACs was linked to imported cases while others were linked mostly to autochthonous cases
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53 239 from geographically isolated areas of Wuhan ²¹. We identified that in addition to being
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3 240 associated with a travel history to foreign countries, ACs were also associated with cases that
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5 241 appear spontaneously (related), occurring differentially as measures of geographic and social
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8 242 isolation were applied.
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11 243 The lack of mass screening for COVID-19 in Colombia is the main limitation of our study
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13 244 since the actual AC ratio and the distribution of specific characteristics may differ from those
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15 245 estimated in this report. On the other hand, although a cross-sectional design is not ideal to
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17 246 identify risk factors, to the best of our knowledge this is the first study aimed at identifying
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19 247 factors associated with AC state with population data unbiased by the inclusion of pre-
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22 248 symptomatic cases.
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25 249 The COVID-19 pandemic has had serious socioeconomic implications, including a collapse
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27 250 of healthcare systems, bankruptcy of companies as well as increasing trends in
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29 251 unemployment and crime rates^{22–25}. This has forced countries with limited resources---such
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31 252 as Colombia---to perform massive screenings in order to prematurely lift quarantine and
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33 253 isolation measures despite the latent risk of successive outbreaks caused by a potential silent
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35 254 spread of COVID-19 through cases in the pre-symptomatic phase or AC state^{26,27}.
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39 255 ACs transmit COVID-19 more efficiently than symptomatic patients for up to 21 days after
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41 256 the presumed date of infection^{28,29}. This led to their inclusion in mathematical models
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43 257 intended to estimate the probability or expected number of person-to-person infections on
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45 258 repatriation trips from Wuhan, China^{7,30}. Since then, ACs have become the target of mass
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47 259 screening in Asian and European countries effectively reducing economical losses due to
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49 260 unnecessary hospital care, controlling the spread in public or in-hospital settings, and
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51 261 allowing the execution of safe plans of social and work re-integration after quarantine and
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55 262 isolation^{26,31–35}.
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263 To date, testing of asymptomatic individuals rests at the discretion of physicians when
264 justified on a case-by-case basis. On the other hand, the utility of SARS-CoV-2 testing for
265 broad screening of asymptomatic individuals remains to be determined given the limited
266 sensitivity data available for most commercially available test kits ³⁶.

267 CONCLUSION

268 Together, our findings demonstrate sociodemographic trends strongly associated with
269 COVID-19 AC state in Colombia at a departmental and national level. We believe that the
270 implementation of massive screening campaigns to detect AC and pre-symptomatic patients
271 is paramount to further characterize this phenomenon and adequately guide public health
272 measures of containment and prevention. Additional molecular analysis of viral and host
273 genotypic characteristics should be conducted to determine possible associations with AC
274 state.

275 Authors contributorship statement

276 AT, APM and JDR designed the study. AT, GC, RPG, CH, GH, LMP, LAP and AA
277 conducted the statistical and descriptive analyses. CF, ECB provided the data for the analysis.
278 AT, APM, LAP and JDR drafted the manuscript. All authors approved the final version of
279 the manuscript.

280 **Funding:** This research received no external funding.

281 **Data sharing statement:** No additional data available

282 **Conflicts of Interest:** The authors declare no conflict of interest.

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286 **Figure Legends**

287 **Figure 1. Daily accumulation and distribution of ACs by epidemiological week in**

288 **Colombia. A.** The y-axis represents the number of cumulative ACs transformed into a base
289 10 logarithm. The number of cumulative cases per day is located in points that increase in
290 color intensity according to the occurrence of cases. **B.** The y-axis represents the number of
291 daily ACs transformed into a base 10 logarithm. The number of daily cases per day is
292 located in boxplots. **C.** Heatmap showcasing the number of ACs (top) and **B.** symptomatic
293 patients (bottom) diagnosed in every Colombian department until May 23rd, 2020.

294 **Figure 2. Origin and destination of imported asymptomatic and symptomatic cases.**

295 The left and right figures, respectively, represent the country of origin and destination
296 department of ACs and symptomatic patients. The thickness of the link tapes corresponds
297 to the number of reported cases.

298 **Figure 3. Groups of countries and departments associated with AC state.** The left

299 figure shows the group of countries associated with asymptomatic carrier (AC) state
300 identified with positive values of the CCC-CA. The right figure shows departments
301 grouped according to three intervals of CCC-CA: low association (CCC-CA: negative
302 values), moderate association (CCC-CA: $> 0 - < 0.05$), and strong association (CCC-CA:
303 ≥ 0.5).

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417 **Table 1.** Sociodemographic characteristics of the asymptomatic and symptomatic patients

Variables	Asymptomatic	Symptomatic	p-value
	n: 2388	n: 17785	
Age, years	32 (24-44)	37 (26-53)	<0.001
0-39	1603 (67.1)	9655 (54.2)	<0.001
≥40	785 (32.8)	8130 (45.7)	<0.001
Sex			
Male	1208 (75.2)	6220 (53.7)	<0.001
Female	399 (24.8)	5359 (46.3)	<0.001
Geographical source			
Related	2357 (98.7)	16972 (95.4)	<0.001
Imported	31 (1.30)	813 (4.57)	<0.001
Departments†			
Meta	749 (31.3)	219 (1.23)	<0.001

Bogotá	437 (18.3)	65.4 (36.8)	<0.001
Amazonas	238 (9.97)	1150 (6.47)	<0.001
Atlántico	203 (8.50)	1068 (6.01)	<0.001
Barranquilla	117 (4.90)	1216 (6.84)	<0.001
Imported cases			
Spain	16 (51.6)	244 (30.0)	0.011
USA	7 (22.5)	202 (24.8)	0.774
Brazil	2 (6.45)	40 (4.92)	0.700
Mexico	2 (6.45)	49 (6.03)	0.922
Argentina	1 (3.23)	3 (0.37)	0.023
Peru	1 (3.23)	11 (1.35)	0.387
Puerto Rico	1 (3.23)	12 (1.48)	0.437
Turkey	1 (3.23)	27 (3.32)	0.977

418 †: cases that appeared spontaneously in Colombia, ††: top 5 of the
 419 departments with the highest frequency of AC.

420 **Table 2.** Factors associated with asymptomatic carrier (AC) state in Colombia

Variable	Interaction model		
	B	ORc (95%, CI)	p-value
Intercept	-4.531	-	<0.001
Age			
>40 years	Ref.	-	-
0-39 years	0.451	1.569 (1.422-1.732)	<0.001
Sex			

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2				
3	Female	Ref.	-	-
4				
5	Male	-0.019	0.981 (0.850-1.132)	0.791
6				
7	Department			
8				
9	Low association [1]	Ref.	-	-
10				
11	Moderate association [2]	0.210	1.234 (0.799-1.908)	0.344
12				
13	Strong association [3]	1.130	3.095 (1.860-5.149)	<0.001
14				
15				
16	Geographical source			
17				
18	Imported CAS†	Ref.	-	-
19				
20	Imported CA-AC††	1.225	3.405 (1.491-7.775)	<0.004
21				
22	Related cases†††	1.351	4.861 (1.885-7.910)	<0.001
23				
24	EW			
25				
26	10-15 [1]	Ref.	-	
27				
28	16-17 [2]	0.657	1.410 (1.155-1.721)	<0.001
29				
30	18 [4]	0.418	1.519 (1.087-2.122)	<0.014
31				
32	19-21 [3]	-0.074	0.929 (0.758-1.138)	0.477
33				
34	Department [2] + Male	0.363	1.438 (1.035-1.998)	0.030
35				
36	Department [3] + Male	0.757	2.132 (1.723-2.638)	<0.001
37				
38	EW [2] + Department [3]	-1.052	0.349 (0.198-0.616)	<0.001
39				
40	EW [3] + Department [2]	1.474	4.368 (2.780-6.862)	<0.001
41				
42	EW [4] + Department [2]	1.219	3.385 (1.631-7.023)	0.001
43				
44	EW [4] + Department [3]	1.414	4.673 (2.273-7.447)	<0.001
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47 421 †: CAS countries associated with symptomatic patients, ††: CA-AC
 48 422 countries associated with asymptomatic carriers (AC), †††:
 49 423 spontaneous cases, **EW**: epidemiological weeks.

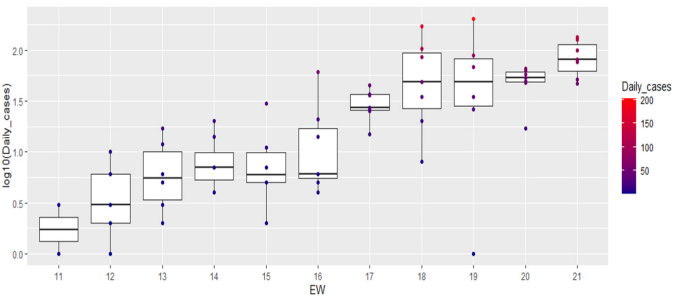
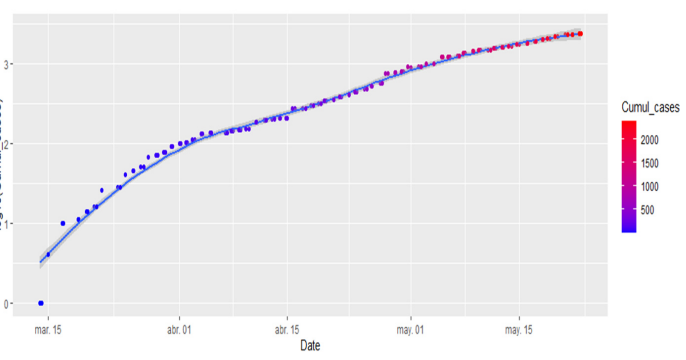
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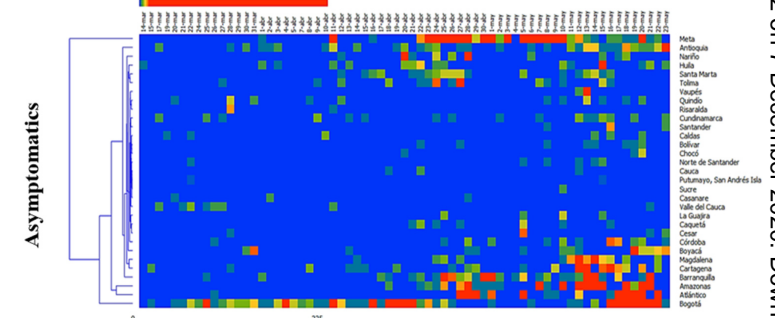
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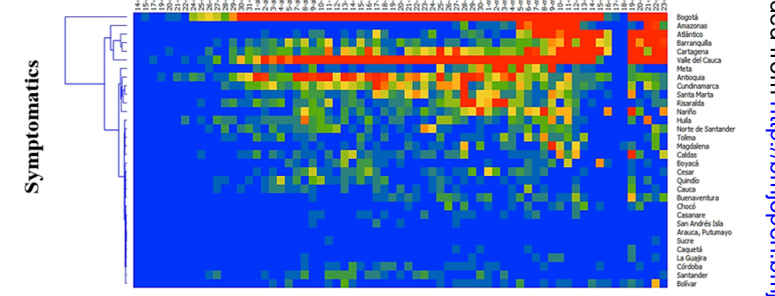
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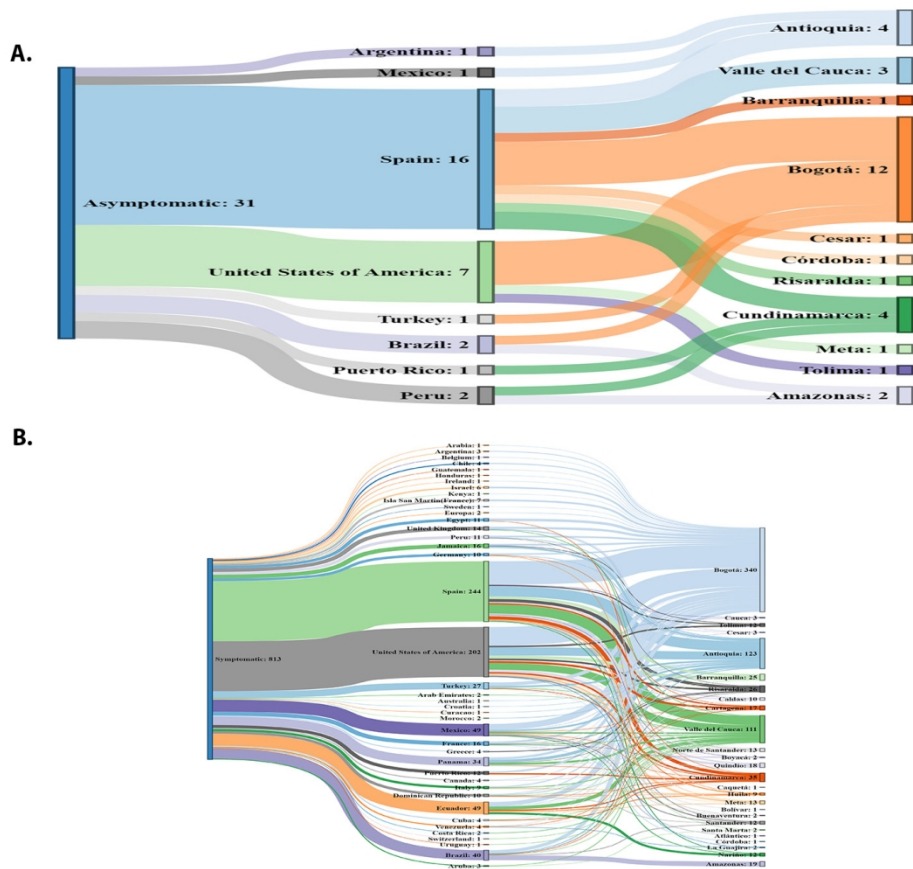


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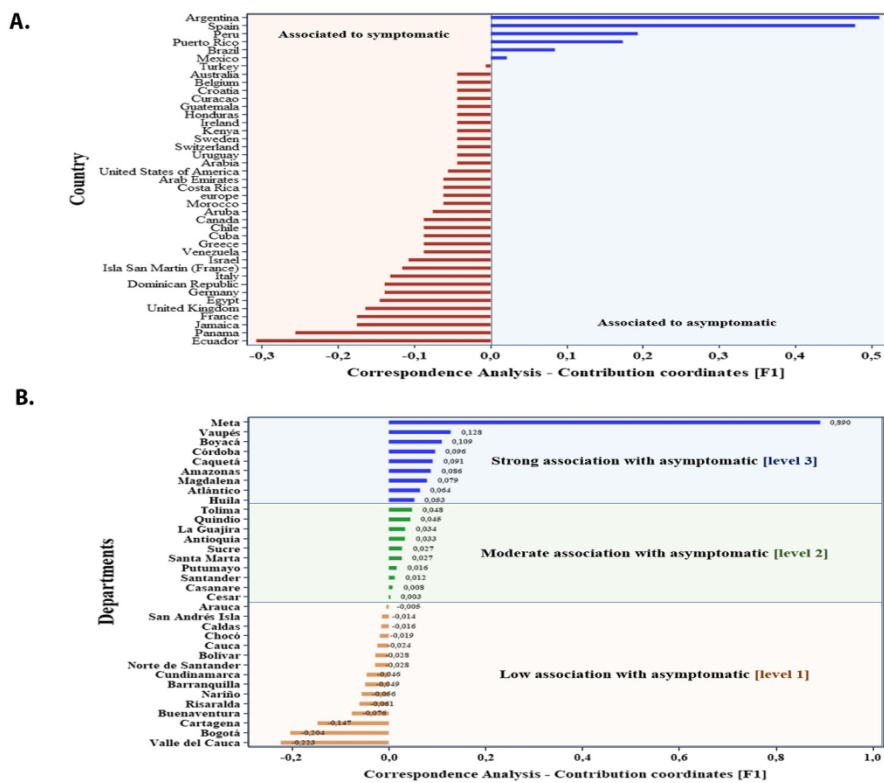


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Table S1. AC state frequency in Colombia by department

Department	Count	Proportion
Meta	749	31,37
Bogotá	437	18,3
Amazonas	238	9,97
Atlántico	203	8,5
Barranquilla	117	4,9
Antioquia	100	4,19
Cartagena	76	3,18
Magdalena	52	2,18
Boyacá	48	2,01
Huila	46	1,93
Nariño	44	1,84
Santa Marta	42	1,76
Tolima	37	1,55
Córdoba	31	1,3
Cundinamarca	28	1,17
Quindío	20	0,84
Valle del Cauca	14	0,59
Caquetá	12	0,5
Caldas	11	0,46
Cesar	11	0,46
La Guajira	11	0,46
Vaupés	11	0,46
Bolívar	9	0,38
Santander	9	0,38
Norte de	7	0,29
Risaralda	7	0,29
Chocó	6	0,25
Casanare	4	0,17
Cauca	4	0,17
Sucre	2	0,08
Putumayo	1	0,04
San Andrés Isla	1	0,04

The total number of ACs was used as the denominator to determine proportions.

Table S2. Factors associated with AC state in Colombia.

Variable	Main effects		
	B	ORa (95%, CI)	p-value
Intercept	-5.061	-	<0.001
Age,			
≥40 years old	Ref.	-	-
0-39 years old	0.449	1.566 (1.421-1.726)	<0.001
Sex			
Female	Ref.	-	-
Male	0.322	1.393 (1.264-1.537)	<0.001
Department			
Low risk	Ref.	-	-
Moderate risk	1.304	3.372 (3.134-4.330)	<0.001
Strong risk	1.909	8.310 (6.101-7.464)	<0.001
Geographical origin			
Imported CAS†	Ref.	-	-
Imported CA- AC††	1.216	3.372 (1.474-7.716)	<0.004
Related cases†††	1.472	4.356 (2.123-8.939)	<0.001
EW			
10-15	Ref.	-	-
16-17	0.344	1.410 (1.155-1.721)	<0.001
18	1.383	3.987 (3.243-4.902)	<0.001

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3 **19-21** 0.264 1.302(1.095-1.548) <0.001
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 †: CAS countries associated to symptomatic patients, ††: CA-AC countries associated to
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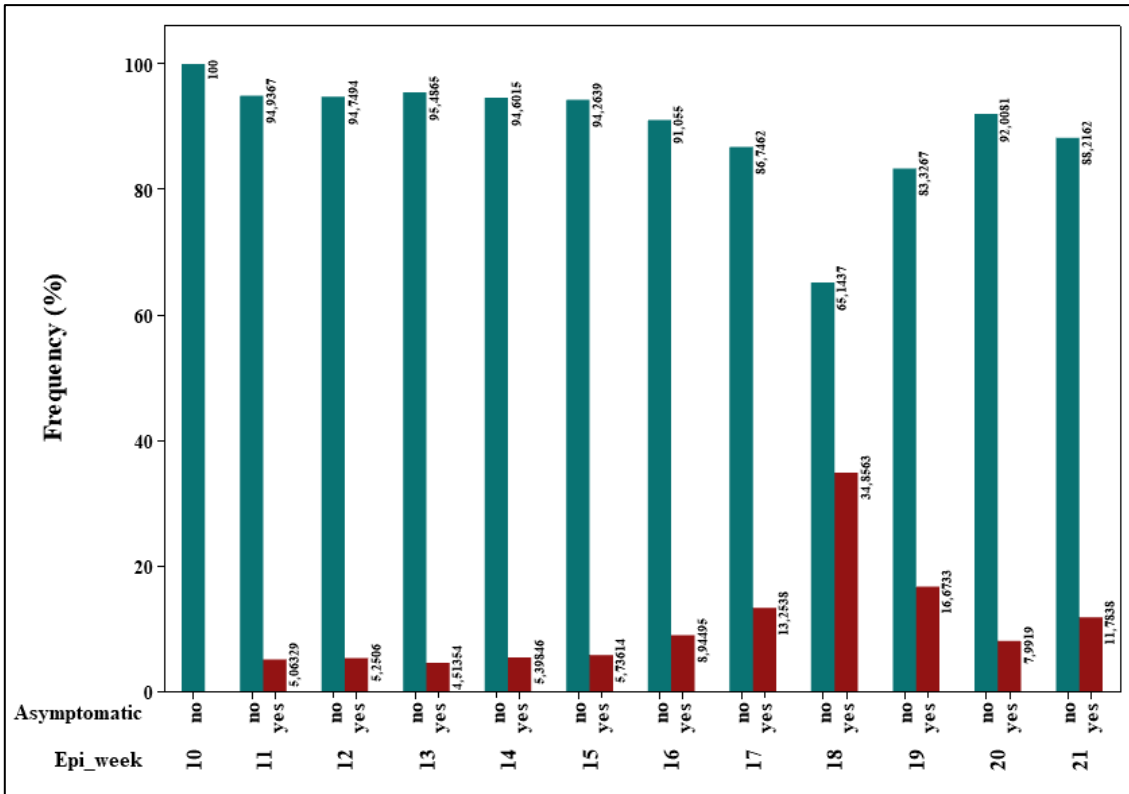
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8 ACs, †††: spontaneous cases, EW: epidemiological week.
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Figure S1. Proportion of ACs and symptomatic patients by epidemiological week in Colombia.



The number of reported ACs in Colombia by epidemiological week (EW) included: EW-11: 4/79, EW-12: 22/419, EW-13: 45/997, EW-14: 63/1167, EW-15: 60/1046, EW-16: 117/1308, EW-17: 211/1592, EW-18: 473/1357, EW-19: 421/2525, EW-20: 355/4442, EW-21: 617/5236.

BMJ Open

Epidemiological characterization of asymptomatic carriers of COVID-19 in Colombia: A cross-sectional study.

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Epidemiology
Keywords:	Epidemiology < TROPICAL MEDICINE, VIROLOGY, INFECTIOUS DISEASES

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3 **1 Epidemiological characterization of asymptomatic carriers of COVID-19 in Colombia:**4
5 **2 A cross-sectional study.**6
7
8 3 Aníbal A. Teherán^{1,2}, Gabriel Camero^{1,3}, Ronald Prado de la Guardia¹, Carolina Hernández⁴,9
10 4 Giovanni Herrera⁴, Luis M. Pombo², Albert A. Ávila⁵, Carolina Flórez⁶, Esther C. Barros⁶,11
12 5 Luis A. Perez-Garcia⁴, Alberto Paniz-Mondolfi^{7,8}, Juan David Ramírez^{4*}13
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21 **ABSTRACT (187 words)**

22 **Introduction:** Asymptomatic carriers (AC) of the new Severe Acute Respiratory Syndrome
23 Coronavirus 2 (SARS-CoV-2) represent an important source of spread for Coronavirus
24 Disease 2019 (COVID-19). Early diagnosis of these cases is a powerful tool to control the
25 pandemic. Our objective was to characterize patients with AC status and identify associated
26 sociodemographic factors.

27 **Methods:** Using a cross-sectional design and the national database of daily occurrence of
28 COVID-19, we characterized both socially and demographically all ACs. Additional
29 Correspondence Analysis and Logistic Regression Model were performed to identify
30 characteristics associated with AC state (OR, 95% CI).

31 **Results:** 76.162 ACs (12.1%; 95%CI, 12.0-12.2%) were identified, mainly before
32 epidemiological week 35 [EW]. Age \leq 26 years (1.18;1.09-1.28), male sex (1.51;1.40-1.62),
33 cases imported from Venezuela, Argentina, Brazil, Germany, Puerto Rico, Spain, United
34 States of America or Mexico (12.6;3.03-52.5) and autochthonous cases (22.6;5.62-91.4)
35 increased the risk of identifying ACs. We also identified groups of departments with
36 moderate (1.23;1.13-1.34) and strong (19.8;18.6-21.0) association with ACs.

37 **Conclusion:** Sociodemographic characteristics strongly associated with AC were identified,
38 which may explain its epidemiological relevance and usefulness to optimize mass screening
39 strategies and prevent person-to-person transmission.

40 **Key words:** COVID-19; Asymptomatic; Carrier States; Risk factors, Novel Coronavirus.

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Strengths and limitations:

- Cross-sectional studies are useful to identify possible variables associated with ACs.
- Weekly surveillance of potential cases reduced selection and classification bias of ACs.
- The large number of COVID-19 ACs included in this study allowed to draw precise estimates.
- The ongoing epidemic phase of COVID-19 in Colombia decreases the uncertainty of invisible subgroup occurrences.
- Estimates and characteristics associated with ACs may improve epidemiological surveillance in other countries.

4

63 **TEXT (2481 words)**

64 **INTRODUCTION**

65 In March 2nd, 2020, Colombia reported the first case of Coronavirus Disease 2019 (COVID-
66 19), and as of September 22nd, more than 700,000 cases have been confirmed nationwide ¹.

67 Asymptomatic carriers (AC) may be associated with the accelerated growth of cases in the
68 initial phases of the pandemic, inadvertently spreading the infection to close contacts. In this
69 case, transmission can only be limited until a diagnosis of SARS-CoV-2 infection is rendered
70 after (i) isolation due to symptom onset, (ii) contact tracing or (iii) identification during
71 massive screening strategies ^{2,3}.

72 AC and pre-symptomatic cases are epidemiologically relevant since they represent a silent
73 source of spread in various public settings (e.g. public transportation, emergency rooms,
74 supermarkets, shelters) ⁴⁻⁶. The proportion of ACs has been estimated at 15-25%, but
75 seroprevalence studies have reported values of up to 43.2% (95% CI, 32.2-54.7%).
76 Nonetheless, many pre-symptomatic patients are wrongfully classified as ACs during the
77 incubation phase; to later become pauci-symptomatic or develop respiratory manifestations
78 ranging from pneumonia to respiratory failure, or exhibit any other clinical symptoms within
79 the COVID-19 spectrum ⁴⁻⁸.

80 Epidemiological predictive models have been developed and updated to incorporate silent
81 mobility through AC phenotype in anticipation for the second and third epidemic waves of
82 COVID-19. Such is the case for the SEIR model (Susceptible, Exposed, Infected and
83 Recovered), recently updated to SEAIR (Susceptible, Exposed, Asymptomatic, Infected and
84 Recovered) ⁹. In China, estimates indicate that 60-65% of ACs remained undetected.

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85 Therefore, under the SEIR model and applying machine-learning-based transmission
86 simulators (MLSim), including the number of undetected AC within its parameters and
87 assuming 15 close contacts per day, estimates suggest that as of April 15th, 2020, the United
88 States---the country contributing the majority of cases imported to Colombia---, could have
89 presented 277,641-to-495,128 latent cases of COVID-19, potentially increasing the spread
90 of the virus ¹⁰.

91 The assessment of ACs and the identification of sociodemographic characteristics associated
92 with this subpopulation could be useful to estimate sample calculations in massive screening
93 studies, as well as adjust control and mitigation measures---especially the intensity of
94 isolation. Therefore, the objective of our study was to characterize ACs demographically and
95 socially, as well as to identify individual characteristics in interaction models associated with
96 ACs.

97 **METHODOLOGY**

98 **Design and data selection.**

99 We performed a cross-sectional study with information from the National Institute of Health
100 (INS) database on COVID-19 cases updated until August 31, 2020
101 (<https://www.ins.gov.co/Noticias/Paginas/coronavirus-casos.aspx>). By INS protocol,
102 suspected AC cases remained in quarantine for 7 days while monitoring the appearance of
103 symptoms on a daily basis; on the eighth day, a nasal swab sample was collected to identify
104 or rule out AC state. Records without health status information (symptomatic, asymptomatic)
105 were excluded. The database is public, with de-identified patient data and IRB approval was
106 thus exempt.

107 **Patient and Public Involvement (PPI) statement**

108 This research was done without patient involvement. Patients were not invited to comment
109 on the study design and were not consulted to develop patient relevant outcomes or interpret
110 the results. Patients were not invited to contribute to the writing or editing of this document
111 for readability or accuracy.

112 **Database and variables.**

113 We used variables such as date of diagnosis, age, sex, country of origin, department, case
114 type (imported, related), care setting (home, nursing home, hospital, intensive care unit) and
115 outcome (recovered, convalescent, deceased). The date of diagnosis was adjusted into
116 epidemiological weeks (EW), which were later grouped according to the pattern of AC
117 occurrence (Figure S1) in EW 10-34, ≥ 35 ; additionally, the variable AC [yes, no] was
118 established.

119 **Statistical analysis**

120 Data are presented in medians or proportions estimated with 95% CI due to the lack of
121 massive screening for COVID-19 in certain areas of the country; additionally, we estimated
122 AC rates per 100.000 population by departments using Colombian demographic estimates
123 for 2020 from the National Administrative Department of Statistics (DANE). The
124 geographical origin and destination of imported cases was represented with a Sankey Plot
125 (SankeyMATIC (BETA)). Cumulative trends and case charts were created with the number
126 of daily cases by Epid_weeks (RStudio Version 1.2.5042). In addition, a heatmap analysis
127 was included to depict a dynamic representation of daily cases by Department from March
128 6th through August 31rd, 2020 (Orange Data Mining & Fruitful Fun, Version 3.25). The

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129 proportion of asymptomatic and symptomatic patients and the median age were compared
130 with the Z and U Mann Whitney tests respectively (significant p-value <0.05, two tails)
131 [Addinsoft. 2020. XLSTAT statistical and data analysis solution. New York, USA.
132 <https://www.xlstat.com>]. Age was dichotomized between 0-26 and ≥ 27 years due to its
133 association with asymptomatic and symptomatic states respectively (preliminary exploratory
134 analysis not shown).

135 Countries of origin and departments associated with ACs were identified, respectively, with
136 a Correspondence Analysis (CA) and Factorial analysis of mixed data using PCAmix. Raw
137 data were used for CA while symptomatic and AC rates per 100.000 population were used
138 for PCAmix . Additionally, with principal coordinates (PC) obtained with both CA (PC-CA)
139 and PCAmix (PC-PCAmix), groups with a variable level of association with ACs were
140 created. [Addinsoft. 2020. XLSTAT statistical and data analysis solution. New York, USA.
141 <https://www.xlstat.com>].

142 To estimate the association between sociodemographic characteristics with ACs (OR 95%),
143 two Logistic Regression Models (LRM) were performed, the first to establish the main
144 effects and the second a step-backward interaction model of the second level (p- value in
145 <0.05; p-value out:> 0.1), which used the lowest Akaike criteria to select the best model
146 (JASP Team (2020). JASP (Version 0.12.2))

147 **RESULTS**

148 **General characteristics**

149 We identified 76.162 ACs (12.1%; 12.0-12.2%) out of 626.887 cases reported in the
150 database. Four cases were excluded due to lack of health status information. The occurrence

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151 of AC state in relation to symptomatic presented a continuous growth phase between EW 10-
152 17, and a peak at EW 18, followed by a newly increase between EW 19-34, and a steady state
153 after EW 34 (Figure 1A, 1B, S1). Daily cases ranged from 1 to 4386 per day, and EW 34
154 registered the highest number of cases per day: 4141 and 4386.

155 Additionally, we report department clusters with a high occurrence of daily COVID-19 cases,
156 which follow different dynamic patterns for ACs and symptomatic patients (Figure 1C-1D).

157 Throughout April, AC reports in Meta and Amazonas peaked; in May they peaked in
158 Cartagena, Antioquia and Bogota, with Bogota's peak lasting until August 31st; in June-July,
159 AC cases peaked in Atlantico, Barranquilla and Cordoba; and in August, they peaked in
160 Santander and Cundinamarca. Overall, the frequency of ACs in Colombia has followed a
161 dichotomic trend as shown in the lateral cluster of figure 1c: AC occurrences are distributed
162 between the highly frequent profile in Bogota during most of the epidemic and the
163 intermittent peak occurrences of the rest of Colombian departments.

164 More than half of the imported ACs came from Europe, specifically Spain, followed by North
165 and South America. Those that arrived from Spain and USA were distributed mainly in
166 Bogotá, Cundinamarca, Antioquia, and Valle del Cauca. Amazonas department only received
167 imported ACs from South American countries. The origin and distribution of imported
168 symptomatic patients was more diverse; however, most cases originated from Spain, USA,
169 Ecuador, Mexico, Brazil, or Panama, and were mainly distributed across Bogotá, Antioquia,
170 and Valle del Cauca (Figure 2).

171 More than 90% of ACs were located in Bogotá, Atlantico and Meta; However, Bogota,
172 Amazonas and Putumayo reported the highest AC rates per 100.000 population (Table 1,

173 Table S1). Median age was 37 years old, lower than the symptomatic patients. Most of them
174 were males (Table 1). By August 31st, most ACs were classified as recovered (85.8%; 85.6-
175 86.1%) or in domiciliary isolation (13.6%; 13.4-13.8%), and 356 patients (0.46%; 0.42-
176 052%) were diagnosed during their stay in ICUs (80 patients), general hospitalization
177 services (185 patients) or in post-mortem phase (91 deceased). These 356 cases may have
178 been treated for symptoms unrelated to COVID-19 or perhaps RT-PCR results arrived late,
179 with some arriving even after the patient had already passed away.

180 **Factors associated with AC condition.**

181 Using the PC-CA and PC-PCAmix, a group of six countries and three groups of departments
182 were associated with AC state (Figure 3). To execute LRMs, the variables "age group 0-26
183 years" and "male sex" were transformed into dummi [0/1]. With a preliminary LRM, a higher
184 β coefficient was estimated in relation to cases imported from countries associated with ACs,
185 therefore, the variable "geographical origin" was created, composed of the categories
186 "imported from countries associated with symptomatic" [Imported CAS - referent],
187 "imported from countries associated with ACs" [Imported CA-ACs] and "related cases".
188 Additionally, a variable was created for the departments grouped with the PCAmix
189 [departments with low association - referent] and for the EW (EW 10-34 - referent). The first
190 LRM (main effects) identified a significant association of all index sociodemographic
191 categories with ACs state (Table S2). The second model explores the following interactions:
192 1. Geographical origin and grouped departments, 2. Geographical origin and EW, 3. Age
193 group (0-26 years) and gender, 4. Grouped departments and gender; and, 5. Age (0-26 years)
194 and EW. We identified interactions between the variables "gender" (males), "age" (0-26

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195 years), and "EW" and the grouped departments; and between the variables "gender" (males)
196 and "age" (0-26 years) (Table 2).

197 Variables "age" (0-26 years), "gender" (male), "departments with moderate or strong
198 association", "imported CA-ACs" and "related cases" were found to increase the risk of
199 identifying ACs state. It was also determined that the risk increased for males (0-26 years),
200 especially for those located in departments with a strong or moderate association since EW
201 35. However it should be noted that the risk of identifying ACs has decreased since EW 35
202 when only taking isolated estimates into account (Table 2).

203 DISCUSSION

204 We found that, in an isolated fashion, age <27 years old, imported cases from a group of 6
205 countries, autochthonous cases and the occurrence in groupings of departments were
206 associated with AC state. Additionally, the risk of being a male AC was only identified in
207 departments with moderate or strong risk, and the risk was variable in the groupings of
208 departments throughout specific epidemiological periods.

209 Additionally, our results show that the proportion of ACs in Colombia lays between 12-
210 12.2% (Table 1), a lower estimate than previously described in other case series or mass
211 screening studies with reported proportions between 5-80%¹¹⁻¹⁴. Given the inclusion of pre-
212 symptomatic patients or the unification of AC with non-critical symptoms in some reports,
213 we cannot rule out that a non-differential classification bias influenced these estimates. An
214 adapted definition for AC in Colombia may address this limitation.

215 Figure 1 shows that the majority of imported cases to Colombia came from Spain and USA,
216 where AC rates have been estimated at 2.5% and 25%, respectively^{14,15}. Although imported

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3 217 cases carry a distinctive genetic load that, population-wise, could manifest itself as a
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5 218 particular phenotype¹⁶, currently there are no reports of genetic variants associated with AC
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7 219 in general or for any of the four AC subtypes described in the literature¹⁷. Subsequent
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9 220 research should be conducted on the possible association between ACs and phylogenetic
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11 221 variants (or other variables) to support the differential risk identified in imported cases from
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13 222 different regions of the world.
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17 223 We identified that imported cases from a group of 6 countries were strongly associated with
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19 224 AC (Figure 2, Table S1, Table 2), and although no interaction was established between the
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21 225 country of import and the destination department (data not shown), we observed that
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23 226 departments strongly associated with AC had less diversity of import origin. Such is the case
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25 227 of Meta and Amazonas, which exclusively imported cases from USA and Brazil/Peru,
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27 228 respectively (Figure 2).
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31 229 Among the demographic characteristics, the association between AC state and patients under
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33 230 27 years of age stands out. Possible explanations for this observation include: (i) the lower
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35 231 presence of co-morbid conditions and baseline health issues within this age group and (ii) the
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37 232 higher risk of exposure through work activities which are greater in this age group¹⁸.
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39 233 However, clinical or social environment could also explain this finding, as a study in skilled
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41 234 nursing facility residents showed a high proportion of AC in those over 70 years of age,
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43 235 however this was a premature finding since most patients were later reclassified as pre-
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45 236 symptomatic or pauci-symptomatic¹¹.
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51 237 We identified a higher frequency of men infected with COVID-19 consistent with reports
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53 238 from other countries around the world, except in Spain and Switzerland, where women
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55 239 ranked first¹⁹. Frequent occupations performed by men, as well as certain immunological
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3 240 and genetically susceptible backgrounds have been associated with this finding ^{19,20}. In
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5 241 particular, the risk of being an AC was higher in men, and increased in geographic areas
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7 242 associated with AC. This interaction is not uncommon given that professions regularly
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9 243 carried out by men, including those such as taxi driving, private security or prison guarding,
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11 244 among other work settings, can be distributed asymmetrically within countries, a pattern that
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13 245 would explain our findings ²⁰.

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17 246 The phases on the occurrence of cases throughout EWs and the interaction with groupings
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19 247 within departments associated with AC has been previously described in Chongqing, China,
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21 248 where researchers identified significant changes in the frequency of cases after
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23 249 implementation of geographic isolation measures. The dynamic changes in the detection and
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25 250 distribution of ACs throughout EWs could be explained by the surveillance strategy executed
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27 251 in Colombia known as "PRASS" (in Spanish, tests, surveillance, and sustainable selective
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29 252 isolations); this can be particularly observed from EW 30 onwards (figure S1) ²¹. In Wuhan,
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31 253 a study showed that one group of ACs was linked to imported cases while others were linked
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33 254 mostly to autochthonous cases from geographically isolated areas of Wuhan ²². We identified
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35 255 that in addition to being associated with a travel history to foreign countries, ACs were also
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37 256 associated with cases that appear spontaneously (related), occurring differentially as
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39 257 measures of geographic and social isolation were applied.

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43 258 The lack of mass screening for COVID-19 in Colombia is the main limitation of our study
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45 259 since the actual AC ratio and the distribution of specific characteristics may differ from those
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47 260 estimated in this report. On the other hand, although a cross-sectional design is not ideal to
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49 261 identify risk factors, to the best of our knowledge this is the first study aimed at identifying
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262 factors associated with AC state with population data unbiased by the inclusion of pre-
263 symptomatic cases ²³.

264 The COVID-19 pandemic has had serious socioeconomic implications, including a collapse
265 of healthcare systems, bankruptcy of companies as well as increasing trends in
266 unemployment and crime rates ^{24–27}. This has forced countries with limited resources---such
267 as Colombia---to perform massive screenings in order to prematurely lift quarantine and
268 isolation measures despite the latent risk of successive outbreaks caused by a potential silent
269 spread of COVID-19 through cases in the pre-symptomatic phase or AC state ^{28,29}.

270 ACs transmit COVID-19 more efficiently than symptomatic patients for up to 21 days after
271 the presumed date of infection ^{30,31}. This led to their inclusion in mathematical models
272 intended to estimate the probability or expected number of person-to-person infections on
273 repatriation trips from Wuhan, China ^{7,32}. Since then, ACs have become the target of mass
274 screening in Asian and European countries effectively reducing economical losses due to
275 unnecessary hospital care, controlling the spread in public or in-hospital settings, and
276 allowing the execution of safe plans of social and work re-integration after quarantine and
277 isolation ^{28,33–37}.

278 To date, testing of asymptomatic individuals' rests at the discretion of physicians when
279 justified on a case-by-case basis. On the other hand, the utility of SARS-CoV-2 testing for
280 broad screening of asymptomatic individuals remains to be determined given the limited
281 sensitivity data available for most commercially available test kits ³⁸.

282 CONCLUSION

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283 Together, our findings demonstrate sociodemographic trends strongly associated with
284 COVID-19 AC state in Colombia at a departmental and national level. We believe that the
285 implementation of massive screening campaigns to detect AC and pre-symptomatic patients
286 is paramount to further characterize this phenomenon and adequately guide public health
287 measures of containment and prevention. Additional molecular analysis of viral and host
288 genotypic characteristics should be conducted to determine possible associations with AC
289 state.

290 **Authors contributorship statement**

291 AT, APM and JDR designed the study. AT, GC, RPG, CH, GH, LMP, LAP and AA
292 conducted the statistical and descriptive analyses. CF, ECB provided the data for the analysis.
293 AT, APM, LAP and JDR drafted the manuscript. All authors approved the final version of
294 the manuscript.

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296 **Data sharing statement:** Data is freely available from the National Institute of Health (INS)
297 database on COVID-19 cases updated until August 31, 2020
298 (<https://www.ins.gov.co/Noticias/Paginas/coronavirus-casos.aspx>).

299 **Conflicts of Interest:** The authors declare no conflict of interest.

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303 **Figure Legends**

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3 304 **Figure 1. Daily accumulation and distribution of ACs by epidemiological week in**
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5 305 **Colombia. A.** The y-axis represents the number of cumulative ACs transformed into a base
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7 306 10 logarithm. The number of cumulative cases per day is located in points that increase in
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9 307 color intensity according to the occurrence of cases. **B.** The y-axis represents the number of
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11 308 daily ACs transformed into a base 10 logarithm. The number of daily cases per day is
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13 309 located in boxplots. **C.** Heatmap showcasing the number of ACs (top) and **B.** symptomatic
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15 310 patients (bottom) diagnosed in every Colombian department until August 31st, 2020.
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20 311 **Figure 2. Origin and destination of imported asymptomatic and symptomatic cases.**
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22 312 The left and right figures, respectively, represent the country of origin and destination
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24 313 department of ACs and symptomatic patients. The thickness of the link tapes corresponds
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26 314 to the number of reported cases.
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30 315 **Figure 3. Groups of countries and departments associated with AC state.** The left
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32 316 figure shows the group of countries associated with asymptomatic carrier (AC) state
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34 317 identified with positive values of the CCC-CA. The right figure shows departments
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36 318 grouped according to three intervals of CCC-CA: low association (CCC-CA: negative
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38 319 values), moderate association (CCC-CA: $> 0 - < 0.05$), and strong association (CCC-CA:
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40 320 ≥ 0.5).
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44 321 **Supplementary material Table S1.** AC state frequency in Colombia by department
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47 322 **Table S2.** Factors associated with AC state in Colombia
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50 323 **Figure S1.** The stacked bar figure represents on the y-axis the epidemiological weeks (EW)
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52 324 and on the x-axis the proportion of symptomatic (green section of the bar) and the proportion
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54 325 of asymptomatic (purple section of the bar), as well as the result of a Chi square independence
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326 test that shows statistical association between the EW variables and health status
 327 (symptomatic/asymptomatic carrier).

328 **Table 1.** Sociodemographic characteristics of the asymptomatic and symptomatic patients

Variables	Asymptomatic	Symptomatic	p-value
	n: 76162	n: 550725	
Age, years	35 (25-49)	37 (27-52)	<0.001
0-26	21310 (27.9)	129529 (23.5)	<0.001
≥27	54852 (72.0)	421196 (76.4)	<0.001
Sex			
Male	38836 (50.9)	283068 (51.4)	0.035
Female	37326 (49.0)	267657 (48.6)	0.035
Geographical source			
Related†	76108 (99.9)	549789 (99.8)	<0.001
Imported	54 (0.07)	936 (0.170)	<0.001
Departments††			
Bogotá	68143 (89.4)	148258 (26.9)	<0.001
Atlántico	1455 (1.91)	26059 (4.73)	<0.001
Meta	836 (1.10)	8532 (1.55)	<0.001
Barranquilla	737 (0.97)	34262 (6.22)	<0.001
Cundinamarca	690 (0.91)	23222 (4.22)	<0.001
Imported cases†††	53	905	958
Spain	19 (35.8)	246 (27.2)	0.170

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USA	14 (26.4)	208 (22.9)	0.565
Brazil	8 (15.1)	53 (5.86)	0.007
Mexico	3 (5.66)	51 (5.64)	0.994
Venezuela	3 (5.66)	8 (0.88)	0.002
Argentina	1 (1.89)	4 (0.44)	0.156
France	1 (1.89)	19 (2.10)	0.916
Germany	1 (1.89)	11 (1.22)	0.669
Peru	1 (1.89)	24 (2.65)	0.734
Puerto Rico	1 (1.89)	12 (1.33)	0.732
Turkey	1 (1.89)	27 (2.98)	0.645
Unknow	1	31	NA

†: cases that appeared spontaneously in Colombia, ††: top 5 of the departments with the highest frequency of AC. †††: the total number of imported asymptomatic and symptomatic cases was used as the denominator to estimate proportions by country of origin.

Table 2. Factors associated with asymptomatic carrier (AC) state in Colombia

Variable	Interaction model		
	β	ORc (95%, CI)	p-value
Intercept	-7.316	-	<0.001
Age			
>26 years	Ref.	-	-
0-26 years	0.172	1.188 (1.096-1.287)	<0.001

Sex			
Female	Ref.	-	-
Male	0.414	1.513 (1.408-1.625)	<0.001
Department			
Low association [1]	Ref.	-	-
Moderate association [2]	0.211	1.234 (1.137-1.340)	<0.001
Strong association [3]	2.986	19.81 (18.61-21.08)	<0.001
Geographical source			
Imported CAS†	Ref.	-	-
Imported CA-AC††(1)	2.536	12.62 (3.034-52.54)	<0.001
Related cases†††(2)	3.121	22.67 (5.620-91.47)	<0.001
EW			
10-34	Ref.	-	-
≥35	-1.008	0.365 (0.320-0.415)	<0.001
0-26 years + Male	0.047	1.048 (1.010-1.089)	0.014
0-26 years + Department [2]	0.174	1.190 (1.069-1.325)	0.001
0-26 years + Department [3]	-0.005	0.995 (0.919-1.077)	0.898
Department [2] + Male	-0.387	0.679 (0.615-0.749)	<0.001
Department [3] + Male	-0.377	0.686 (0.637-0.737)	<0.001
EW ≥35 + Department [2]	-0.862	0.422 (0.315-0.567)	<0.001
EW ≥35 + Department [3]	2.217	9.182 (8.045-10.47)	<0.001

335 †: CAS countries associated with symptomatic patients, ††: CA-AC
 336 countries associated with asymptomatic carriers (AC), †††:
 337 spontaneous cases, **EW**: epidemiological weeks.

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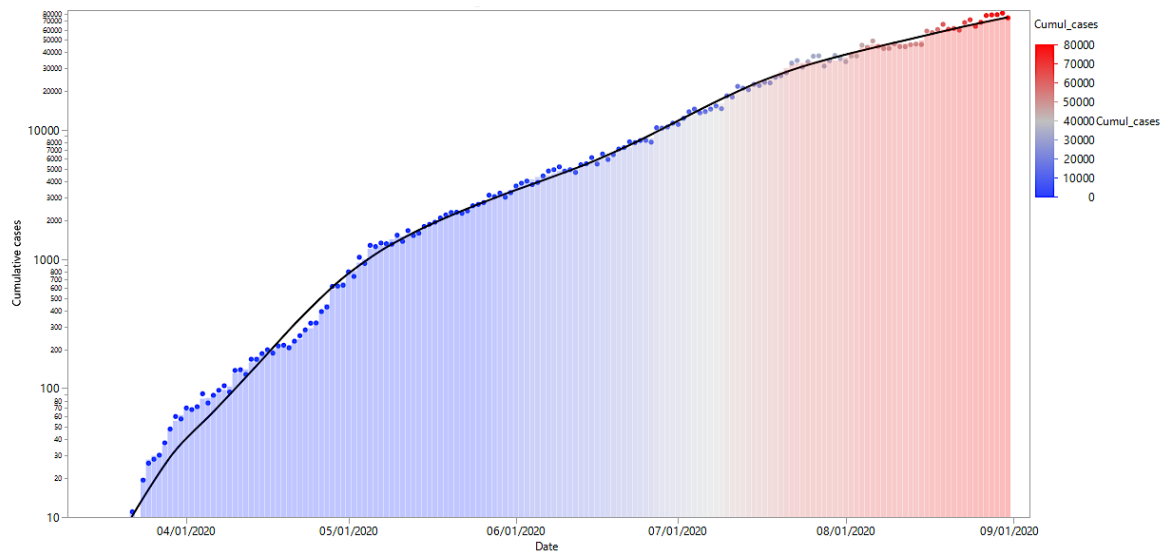
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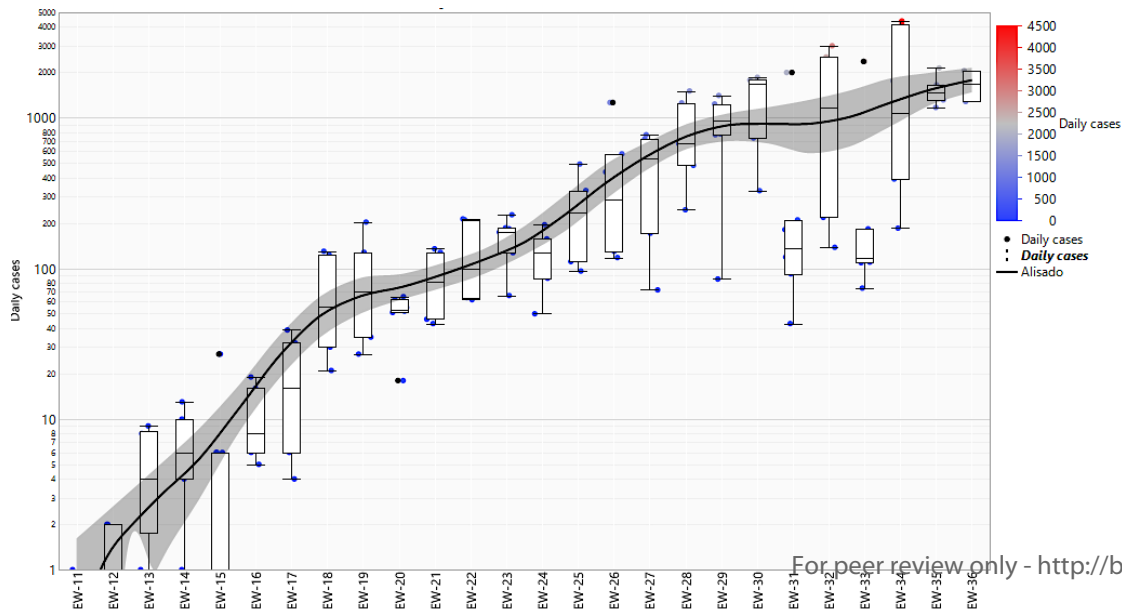
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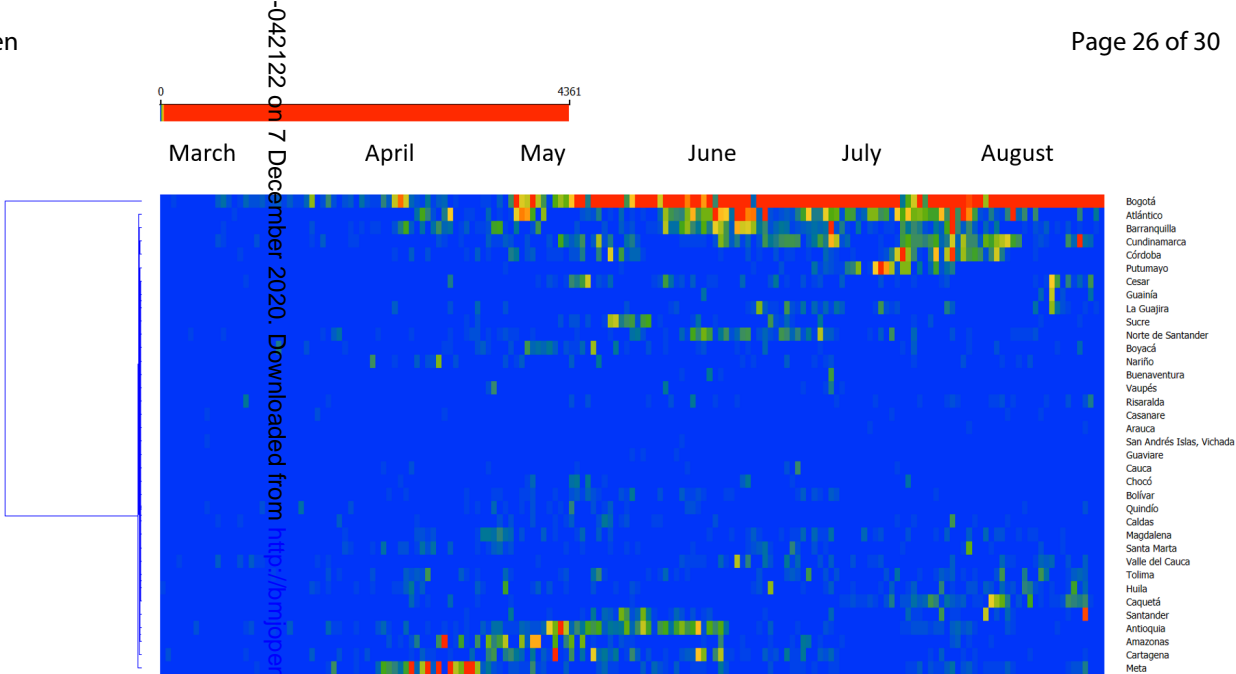
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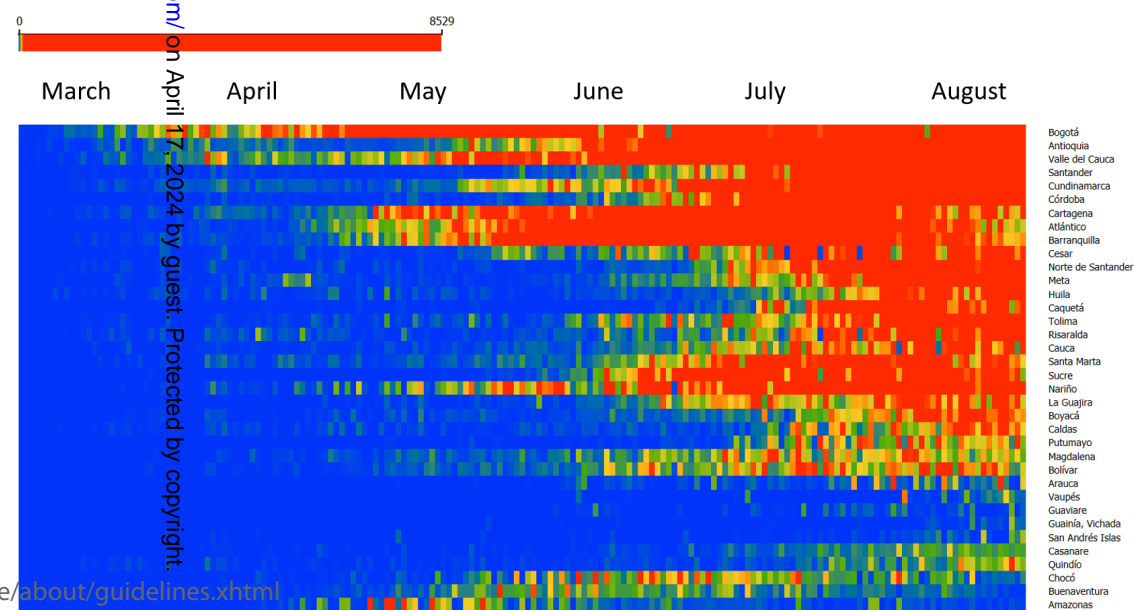
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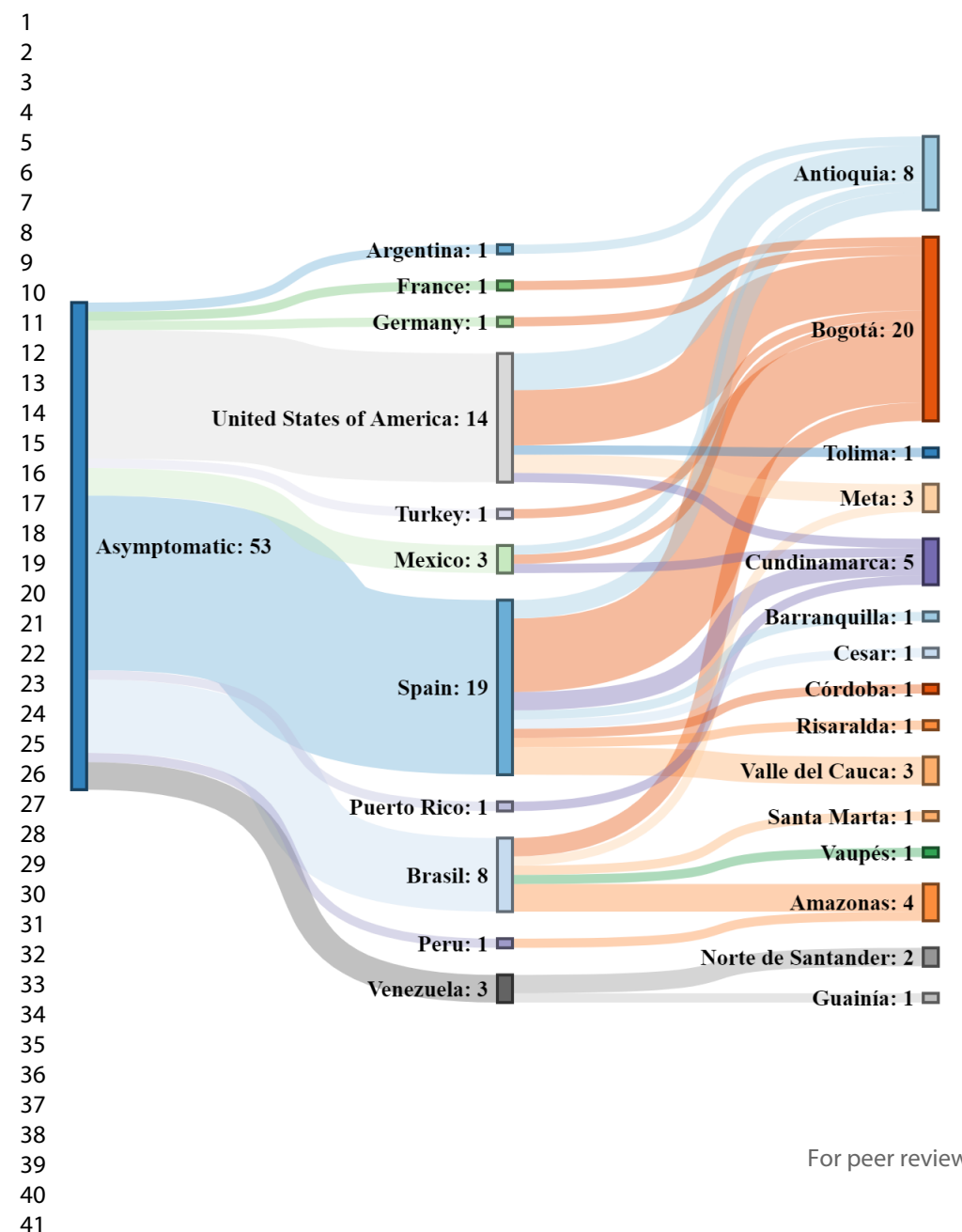
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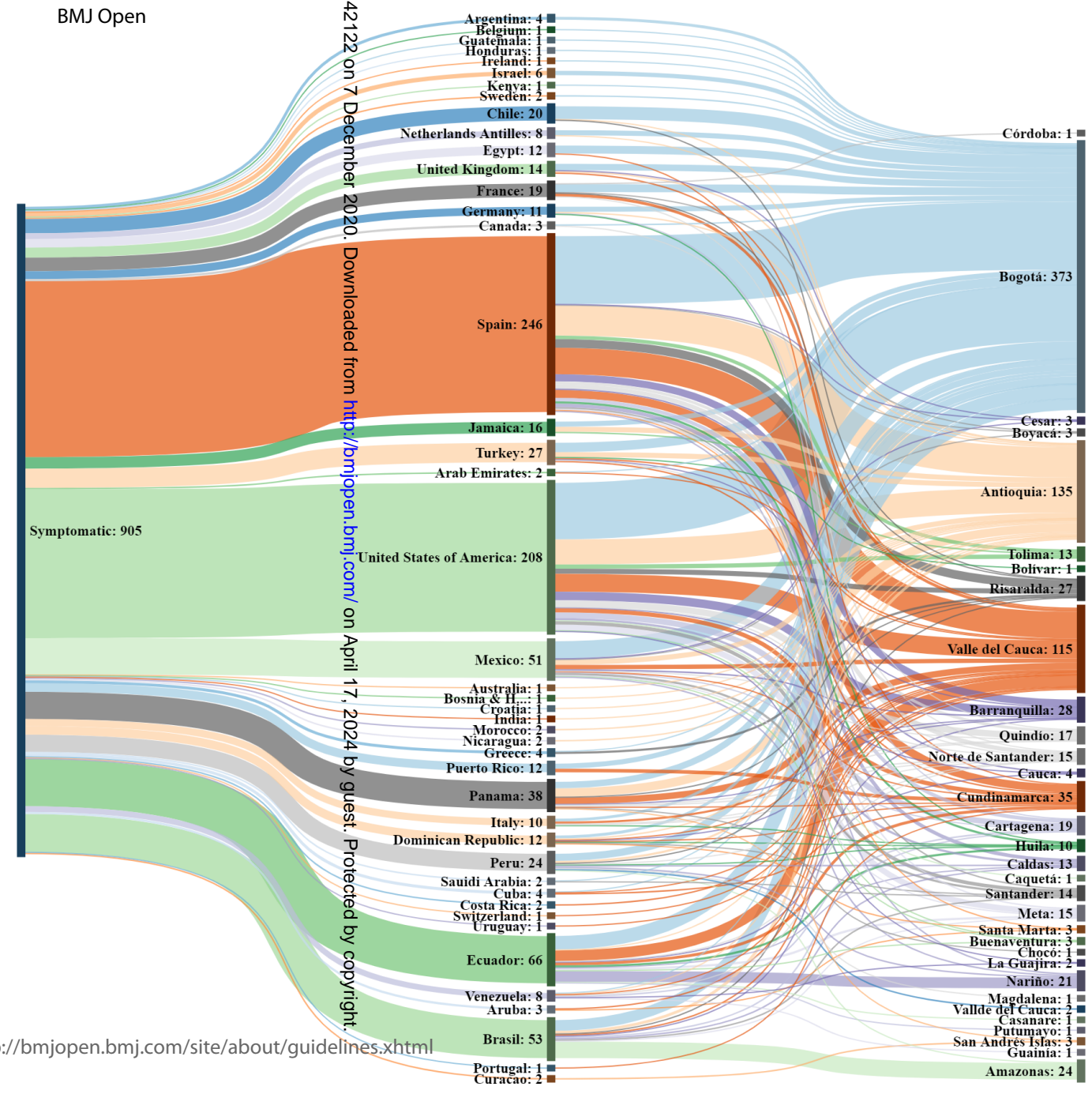
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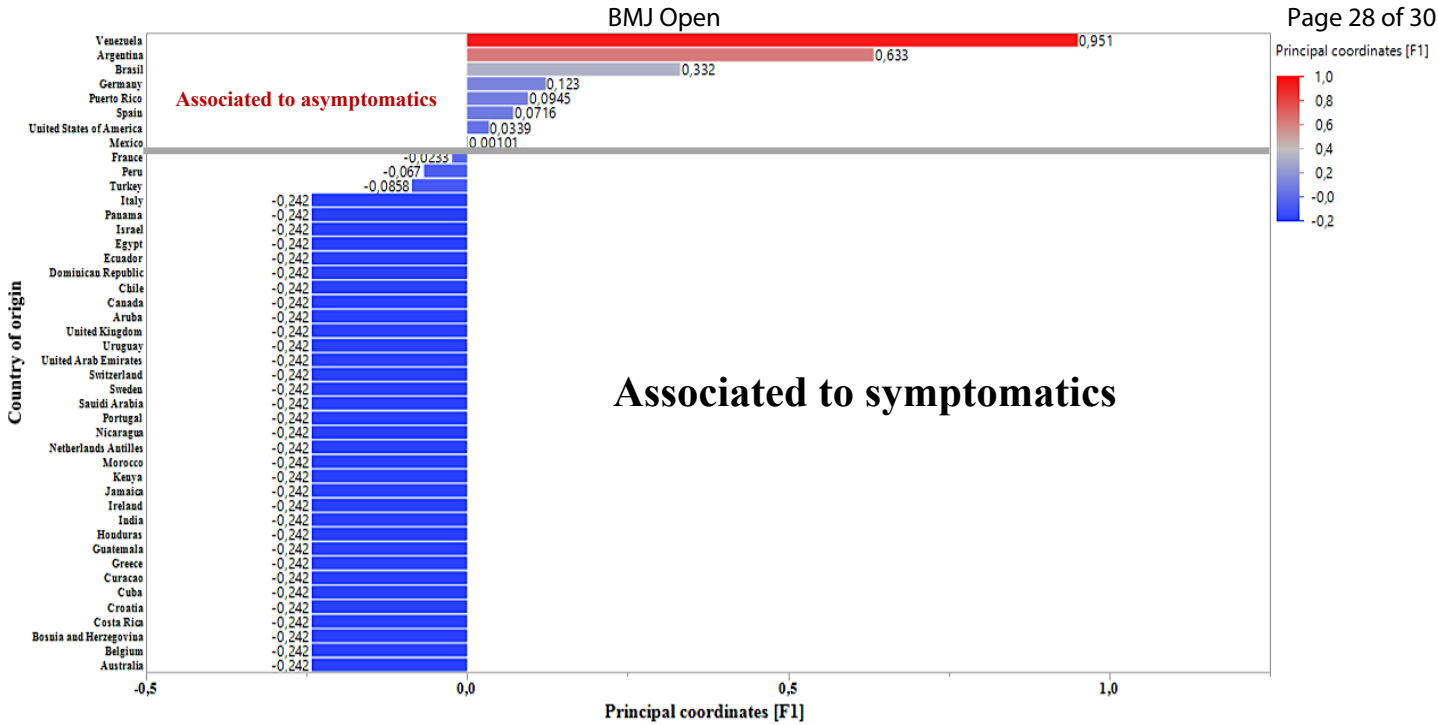


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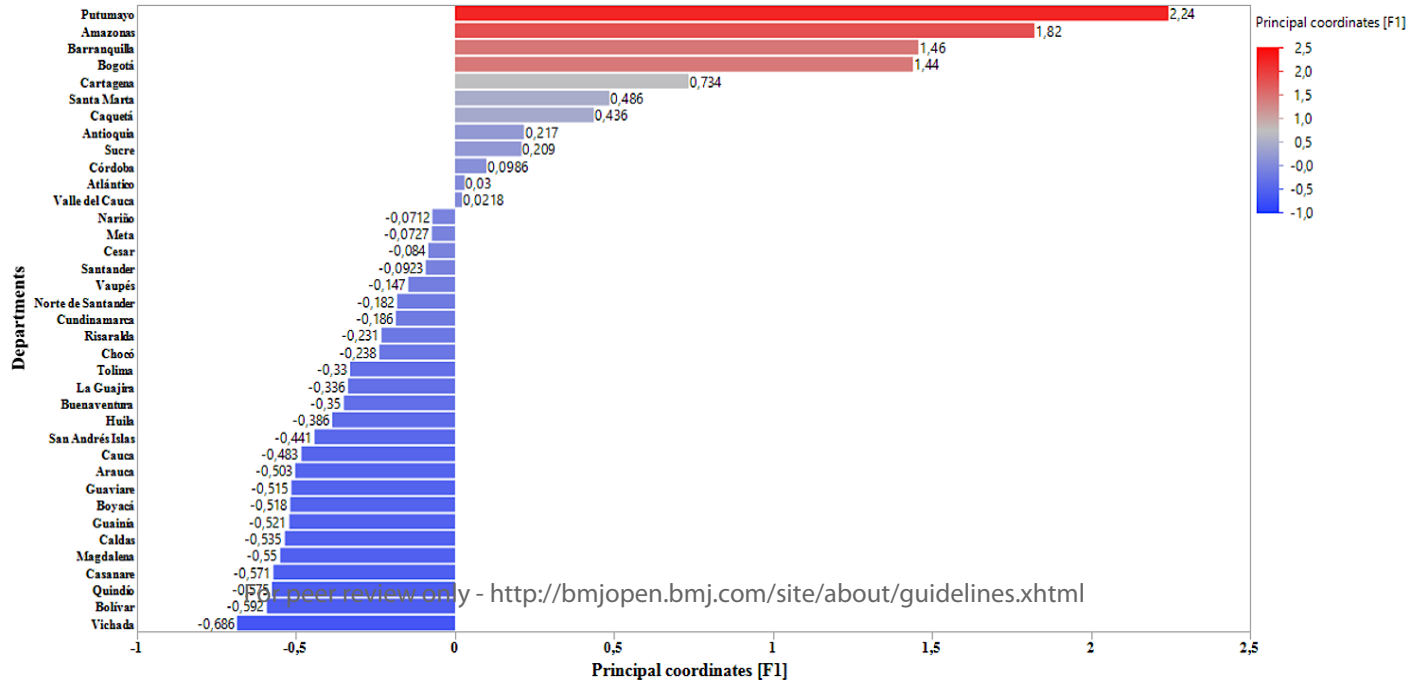


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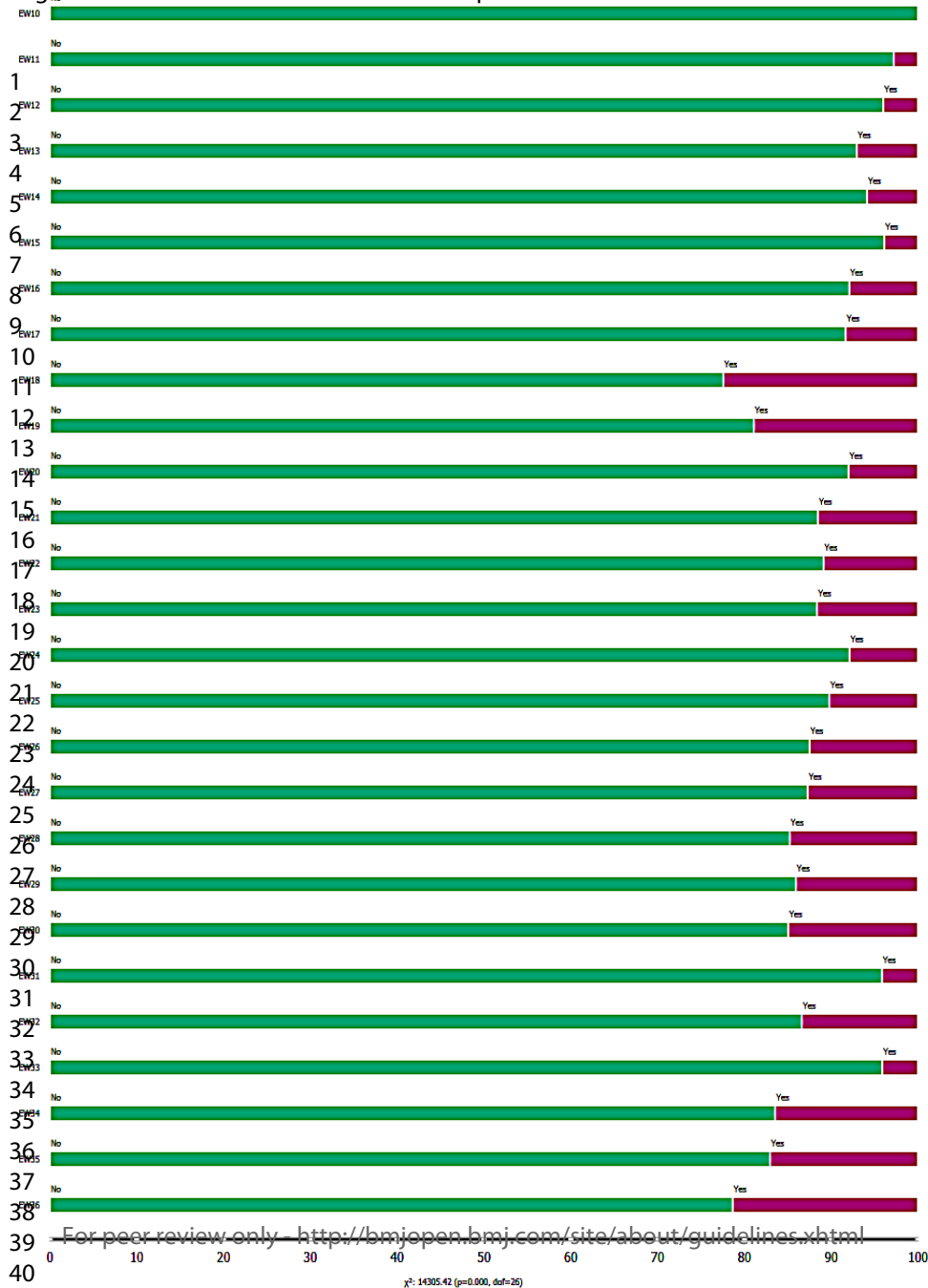


Table S1. AC state frequency in Colombia by department

Department	Asympt_cases	%	Population	Asympt_rate*	Sympt_rate*
Bogotá	68143	89.5	7743955	880,0	1914.5
Atlántico	1455	1.91	2722128	53,5	957.3
Meta	836	1.10	1063454	78,6	802.3
Barranquilla	737	0.97	1243113	59,3	2756.1
Cundinamarca	690	0.91	3242999	21,3	716.1
Antioquia	518	0.68	6677930	7,8	1239.0
Córdoba	468	0.60	1828947	25,6	1072.0
Cartagena	437	0.57	1060577	41,2	1860.5
Amazonas	333	0.44	79020	421,4	2856.2
Putumayo	262	0.34	79020	331,6	3478.9
Norte de Santander	248	0.33	1620318	15,3	727.8
Caquetá	207	0.27	410521	50,4	1474.5
Cesar	195	0.26	1295387	15,1	851.6
Santander	190	0.25	2280908	8,3	847.8
Tolima	153	0.20	1339998	11,4	544.1
Huila	151	0.20	1122622	13,5	470.6
Sucre	151	0.20	949252	15,9	1221.6
La Guajira	140	0.18	965718	14,5	533.0
Boyacá	113	0.15	1242731	9,1	308.5
Magdalena	112	0.15	1427026	7,8	269.8
Valle del Cauca	111	0.15	4532152	2,4	997.9
Santa Marta	94	0.12	538612	17,5	1569.8
Nariño	69	0.09	1627589	4,2	878.5
Bolívar	57	0.07	2180976	2,6	221.9
Caldas	51	0.07	1018453	5,0	291.0
Risaralda	46	0.06	961055	4,8	675.6
Quindío	45	0.05	555401	8,1	236.9
Chocó	39	0.05	544764	7,2	664.9
Guainía	39	0.05	50636	77,0	237.0
Vaupés	27	0.04	44712	60,4	726.9
Buenaventura	20	0.03	440989	4,5	526.1
Cauca	18	0.02	1491937	1,2	360.9
Casanare	7	0.01	435195	1,6	248.9
Arauca	3	<0.01	294206	1,0	335.8
Guaviare	3	<0.01	86657	3,5	318.5
San Andrés Islas	2	<0.01	63692	3,1	411.4
Vichada	2	<0.01	112958	1,8	103.6

The total number of Asymptomatic carriers (ACs) was used as the denominator to determine proportions. **Asympt_cases:** asymptomatic cases, **Symptomatic cases:** see in supplementary file. ***Asympt_rate:** $(\text{Asympt_cases}/\text{population}) * 100.000$ habitants. ***Sympt_rate:** $(\text{Sympt_cases}/\text{population}) * 100.000$ habitants.

Table S2. Factors associated with AC state in Colombia.

Variable	Main effects		
	β	ORa (95%, CI)	p-value
Intercept	-7.360	-	<0.001
Age,			
>26 years old	Ref.	-	-
0-26 years old	0.205	1.227 (1.205-1.250)	<0.001
Sex			
Female	Ref.	-	-
Male	0.054	1.055 (1.038-1.073)	<0.001
Department			
Low risk	Ref.	-	-
Moderate risk	1.304	3.372 (3.134-4.330)	<0.001
Strong risk	1.909	8.310 (6.101-7.464)	<0.001
Geographical origin			
Imported CAS†	Ref.	-	-
Imported CA-AC††	2.541	12.68 (3.049-52.77)	<0.001
Related cases†††	3.255	25.90 (6.425-104.4)	<0.001
EW			
10-34	Ref.	-	-
≥35	0.933	2.543 (2.484-2.603)	<0.001

†: CAS countries associated to symptomatic patients, ††: CA-AC countries associated to

ACs, †††: spontaneous cases, EW: epidemiological week.

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1 **Epidemiological characterization of asymptomatic carriers of COVID-19 in Colombia:**

2 **A cross-sectional study.**

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3 21 **ABSTRACT (187 words)**
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6 22 **Introduction:** Asymptomatic carriers (AC) of the new Severe Acute Respiratory Syndrome
7
8 23 Coronavirus 2 (SARS-CoV-2) represent an important source of spread for Coronavirus
9
10 24 Disease 2019 (COVID-19). Early diagnosis of these cases is a powerful tool to control the
11
12 25 pandemic. Our objective was to characterize patients with AC status and identify associated
13
14 26 sociodemographic factors.
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18 27 **Methods:** Using a cross-sectional design and the national database of daily occurrence of
19
20 28 COVID-19, we characterized both socially and demographically all ACs. Additional
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22 29 Correspondence Analysis and Logistic Regression Model were performed to identify
23
24 30 characteristics associated with AC state (OR, 95% CI).
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28 31 **Results:** 76.162 ACs (12.1%; 95%CI, 12.0-12.2%) were identified, mainly before
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30 32 epidemiological week 35 [EW]. Age ≤ 26 years (1.18;1.09-1.28), male sex (1.51;1.40-1.62),
31
32 33 cases imported from Venezuela, Argentina, Brazil, Germany, Puerto Rico, Spain, United
33
34 34 States of America or Mexico (12.6;3.03-52.5) and autochthonous cases (22.6;5.62-91.4)
35
36 35 increased the risk of identifying ACs. We also identified groups of departments with
37
38 36 moderate (1.23;1.13-1.34) and strong (19.8;18.6-21.0) association with ACs.
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42 37 **Conclusion:** Sociodemographic characteristics strongly associated with AC were identified,
43
44 38 which may explain its epidemiological relevance and usefulness to optimize mass screening
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46 39 strategies and prevent person-to-person transmission.
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50 40 **Key words:** COVID-19; Asymptomatic; Carrier States; Risk factors, Novel Coronavirus.
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Strengths and limitations:

- Cross-sectional studies are useful to identify possible variables associated with ACs.
- Weekly surveillance of potential cases reduced selection and classification bias of ACs.
- The large number of COVID-19 ACs included in this study allowed to draw precise estimates.
- The ongoing epidemic phase of COVID-19 in Colombia decreases the uncertainty of invisible subgroup occurrences.
- Estimates and characteristics associated with ACs may improve epidemiological surveillance in other countries.

4

63 **TEXT (2481 words)**

64 **INTRODUCTION**

65 In March 2nd, 2020, Colombia reported the first case of Coronavirus Disease 2019 (COVID-
66 19), and as of September 22nd, more than 700,000 cases have been confirmed nationwide ¹.

67 Asymptomatic carriers (AC) may be associated with the accelerated growth of cases in the
68 initial phases of the pandemic, inadvertently spreading the infection to close contacts. In this
69 case, transmission can only be limited until a diagnosis of SARS-CoV-2 infection is rendered
70 after (i) isolation due to symptom onset, (ii) contact tracing or (iii) identification during
71 massive screening strategies ^{2,3}.

72 AC and pre-symptomatic cases are epidemiologically relevant since they represent a silent
73 source of spread in various public settings (e.g. public transportation, emergency rooms,
74 supermarkets, shelters) ⁴⁻⁶. The proportion of ACs has been estimated at 15-25%, but
75 seroprevalence studies have reported values of up to 43.2% (95% CI, 32.2-54.7%).
76 Nonetheless, many pre-symptomatic patients are wrongfully classified as ACs during the
77 incubation phase; to later become pauci-symptomatic or develop respiratory manifestations
78 ranging from pneumonia to respiratory failure, or exhibit any other clinical symptoms within
79 the COVID-19 spectrum ⁴⁻⁸.

80 Epidemiological predictive models have been developed and updated to incorporate silent
81 mobility through AC phenotype in anticipation for the second and third epidemic waves of
82 COVID-19. Such is the case for the SEIR model (Susceptible, Exposed, Infected and
83 Recovered), recently updated to SEAIR (Susceptible, Exposed, Asymptomatic, Infected and
84 Recovered) ⁹. In China, estimates indicate that 60-65% of ACs remained undetected.

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85 Therefore, under the SEIR model and applying machine-learning-based transmission
86 simulators (MLSim), including the number of undetected AC within its parameters and
87 assuming 15 close contacts per day, estimates suggest that as of April 15th, 2020, the United
88 States---the country contributing the majority of cases imported to Colombia---, could have
89 presented 277,641-to-495,128 latent cases of COVID-19, potentially increasing the spread
90 of the virus ¹⁰.

91 The assessment of ACs and the identification of sociodemographic characteristics associated
92 with this subpopulation could be useful to estimate sample calculations in massive screening
93 studies, as well as adjust control and mitigation measures---especially the intensity of
94 isolation. Therefore, the objective of our study was to characterize ACs demographically and
95 socially, as well as to identify individual characteristics in interaction models associated with
96 ACs.

97 **METHODOLOGY**

98 **Design and data selection.**

99 We performed a cross-sectional study with information from the National Institute of Health
100 (INS) database on COVID-19 cases updated until August 31, 2020
101 (<https://www.ins.gov.co/Noticias/Paginas/coronavirus-casos.aspx>). By INS protocol,
102 suspected AC cases remained in quarantine for 7 days while monitoring the appearance of
103 symptoms on a daily basis; on the eighth day, a nasal swab sample was collected to identify
104 or rule out AC state. Records without health status information (symptomatic, asymptomatic)
105 were excluded. The database is public, with de-identified patient data and IRB approval was
106 thus exempt.

6

107 Patient and Public Involvement (PPI) statement

108 This research was done without patient involvement. Patients were not invited to comment
109 on the study design and were not consulted to develop patient relevant outcomes or interpret
110 the results. Patients were not invited to contribute to the writing or editing of this document
111 for readability or accuracy.

112 Database and variables.

113 We used variables such as date of diagnosis, age, sex, country of origin, department, case
114 type (imported, related), care setting (home, nursing home, hospital, intensive care unit) and
115 outcome (recovered, convalescent, deceased). The date of diagnosis was adjusted into
116 epidemiological weeks (EW), which were later grouped according to the pattern of AC
117 occurrence (Figure S1) in EW 10-34, ≥ 35 ; additionally, the variable AC [yes, no] was
118 established.

119 Statistical analysis

120 Data are presented in medians or proportions estimated with 95% CI due to the lack of
121 massive screening for COVID-19 in certain areas of the country; additionally, we estimated
122 AC rates per 100.000 population by departments using Colombian demographic estimates
123 for 2020 from the National Administrative Department of Statistics (DANE). The
124 geographical origin and destination of imported cases was represented with a Sankey Plot
125 (SankeyMATIC (BETA)). Cumulative trends and case charts were created with the number
126 of daily cases by Epid_weeks (RStudio Version 1.2.5042). In addition, a heatmap analysis
127 was included to depict a dynamic representation of daily cases by Department from March
128 6th through August 31rd, 2020 (Orange Data Mining & Fruitful Fun, Version 3.25). The

7

129 proportion of asymptomatic and symptomatic patients and the median age were compared
130 with the Z and U Mann Whitney tests respectively (significant p-value <0.05, two tails)
131 [Addinsoft. 2020. XLSTAT statistical and data analysis solution. New York, USA.
132 <https://www.xlstat.com>]. Age was dichotomized between 0-26 and ≥ 27 years due to its
133 association with asymptomatic and symptomatic states respectively (preliminary exploratory
134 analysis not shown).

135 Countries of origin and departments associated with ACs were identified, respectively, with
136 a Correspondence Analysis (CA) and Factorial analysis of mixed data using PCAmix. Raw
137 data were used for CA while symptomatic and AC rates per 100.000 population were used
138 for PCAmix . Additionally, with principal coordinates (PC) obtained with both CA (PC-CA)
139 and PCAmix (PC-PCAmix), groups with a variable level of association with ACs were
140 created. [Addinsoft. 2020. XLSTAT statistical and data analysis solution. New York, USA.
141 <https://www.xlstat.com>].

142 To estimate the association between sociodemographic characteristics with ACs (OR 95%),
143 two Logistic Regression Models (LRM) were performed, the first to establish the main
144 effects and the second a step-backward interaction model of the second level (p- value in
145 <0.05; p-value out:> 0.1), which used the lowest Akaike criteria to select the best model
146 (JASP Team (2020). JASP (Version 0.12.2))

147 **RESULTS**

148 **General characteristics**

149 We identified 76.162 ACs (12.1%; 12.0-12.2%) out of 626.887 cases reported in the
150 database. Four cases were excluded due to lack of health status information. The occurrence

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151 of AC state in relation to symptomatic presented a continuous growth phase between EW 10-
152 17, and a peak at EW 18, followed by a newly increase between EW 19-34, and a steady state
153 after EW 34 (Figure 1A, 1B, S1). Daily cases ranged from 1 to 4386 per day, and EW 34
154 registered the highest number of cases per day: 4141 and 4386.

155 Additionally, we report department clusters with a high occurrence of daily COVID-19 cases,
156 which follow different dynamic patterns for ACs and symptomatic patients (Figure 1C-1D).

157 Throughout April, AC reports in Meta and Amazonas peaked; in May they peaked in
158 Cartagena, Antioquia and Bogota, with Bogota's peak lasting until August 31st; in June-July,
159 AC cases peaked in Atlantico, Barranquilla and Cordoba; and in August, they peaked in
160 Santander and Cundinamarca. Overall, the frequency of ACs in Colombia has followed a
161 dichotomic trend as shown in the lateral cluster of figure 1c: AC occurrences are distributed
162 between the highly frequent profile in Bogota during most of the epidemic and the
163 intermittent peak occurrences of the rest of Colombian departments.

164 More than half of the imported ACs came from Europe, specifically Spain, followed by North
165 and South America. Those that arrived from Spain and USA were distributed mainly in
166 Bogotá, Cundinamarca, Antioquia, and Valle del Cauca. Amazonas department only received
167 imported ACs from South American countries. The origin and distribution of imported
168 symptomatic patients was more diverse; however, most cases originated from Spain, USA,
169 Ecuador, Mexico, Brazil, or Panama, and were mainly distributed across Bogotá, Antioquia,
170 and Valle del Cauca (Figure 2).

171 More than 90% of ACs were located in Bogotá, Atlantico and Meta; However, Bogota,
172 Amazonas and Putumayo reported the highest AC rates per 100.000 population (Table 1,

173 Table S1). Median age was 37 years old, lower than the symptomatic patients. Most of them
174 were males (Table 1). By August 31st, most ACs were classified as recovered (85.8%; 85.6-
175 86.1%) or in domiciliary isolation (13.6%; 13.4-13.8%), and 356 patients (0.46%; 0.42-
176 052%) were diagnosed during their stay in ICUs (80 patients), general hospitalization
177 services (185 patients) or in post-mortem phase (91 deceased). These 356 cases may have
178 been treated for symptoms unrelated to COVID-19 or perhaps RT-PCR results arrived late,
179 with some arriving even after the patient had already passed away.

180 **Factors associated with AC condition.**

181 Using the PC-CA and PC-PCAmix, a group of six countries and three groups of departments
182 were associated with AC state (Figure 3). To execute LRMs, the variables "age group 0-26
183 years" and "male sex" were transformed into dummi [0/1]. With a preliminary LRM, a higher
184 β coefficient was estimated in relation to cases imported from countries associated with ACs,
185 therefore, the variable "geographical origin" was created, composed of the categories
186 "imported from countries associated with symptomatic" [Imported CAS - referent],
187 "imported from countries associated with ACs" [Imported CA-ACs] and "related cases".
188 Additionally, a variable was created for the departments grouped with the PCAmix
189 [departments with low association - referent] and for the EW (EW 10-34 - referent). The first
190 LRM (main effects) identified a significant association of all index sociodemographic
191 categories with ACs state (Table S2). The second model explores the following interactions:
192 1. Geographical origin and grouped departments, 2. Geographical origin and EW, 3. Age
193 group (0-26 years) and gender, 4. Grouped departments and gender; and, 5. Age (0-26 years)
194 and EW. We identified interactions between the variables "gender" (males), "age" (0-26

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195 years), and "EW" and the grouped departments; and between the variables "gender" (males)
196 and "age" (0-26 years) (Table 2).

197 Variables "age" (0-26 years), "gender" (male), "departments with moderate or strong
198 association", "imported CA-ACs" and "related cases" were found to increase the risk of
199 identifying ACs state. It was also determined that the risk increased for males (0-26 years),
200 especially for those located in departments with a strong or moderate association since EW
201 35. However it should be noted that the risk of identifying ACs has decreased since EW 35
202 when only taking isolated estimates into account (Table 2).

203 As this is a cross-sectional study, the STROBE checklist was followed and can be revised in
204 Table S3.

205 **DISCUSSION**

206 We found that, in an isolated fashion, age <27 years old, imported cases from a group of 6
207 countries, autochthonous cases and the occurrence in groupings of departments were
208 associated with AC state. Additionally, the risk of being a male AC was only identified in
209 departments with moderate or strong risk, and the risk was variable in the groupings of
210 departments throughout specific epidemiological periods.

211 Additionally, our results show that the proportion of ACs in Colombia lays between 12-
212 12.2% (Table 1), a lower estimate than previously described in other case series or mass
213 screening studies with reported proportions between 5-80%¹¹⁻¹⁴. Given the inclusion of pre-
214 symptomatic patients or the unification of AC with non-critical symptoms in some reports,
215 we cannot rule out that a non-differential classification bias influenced these estimates. An
216 adapted definition for AC in Colombia may address this limitation.

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3 217 Figure 1 shows that the majority of imported cases to Colombia came from Spain and USA,
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5 218 where AC rates have been estimated at 2.5% and 25%, respectively ^{14,15}. Although imported
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7 219 cases carry a distinctive genetic load that, population-wise, could manifest itself as a
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9 220 particular phenotype ¹⁶, currently there are no reports of genetic variants associated with AC
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11 221 in general or for any of the four AC subtypes described in the literature ¹⁷. Subsequent
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13 222 research should be conducted on the possible association between ACs and phylogenetic
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15 223 variants (or other variables) to support the differential risk identified in imported cases from
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17 224 different regions of the world.
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22 225 We identified that imported cases from a group of 6 countries were strongly associated with
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24 226 AC (Figure 2, Table S1, Table 2), and although no interaction was established between the
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26 227 country of import and the destination department (data not shown), we observed that
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28 228 departments strongly associated with AC had less diversity of import origin. Such is the case
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30 229 of Meta and Amazonas, which exclusively imported cases from USA and Brazil/Peru,
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32 230 respectively (Figure 2).
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36 231 Among the demographic characteristics, the association between AC state and patients under
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38 232 27 years of age stands out. Possible explanations for this observation include: (i) the lower
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40 233 presence of co-morbid conditions and baseline health issues within this age group and (ii) the
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42 234 higher risk of exposure through work activities which are greater in this age group ¹⁸.
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44 235 However, clinical or social environment could also explain this finding, as a study in skilled
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46 236 nursing facility residents showed a high proportion of AC in those over 70 years of age,
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48 237 however this was a premature finding since most patients were later reclassified as pre-
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50 238 symptomatic or pauci-symptomatic ¹¹.
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3 239 We identified a higher frequency of men infected with COVID-19 consistent with reports
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5 240 from other countries around the world, except in Spain and Switzerland, where women
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7 241 ranked first¹⁹. Frequent occupations performed by men, as well as certain immunological
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9 242 and genetically susceptible backgrounds have been associated with this finding^{19,20}. In
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11 243 particular, the risk of being an AC was higher in men, and increased in geographic areas
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13 244 associated with AC. This interaction is not uncommon given that professions regularly
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15 245 carried out by men, including those such as taxi driving, private security or prison guarding,
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17 246 among other work settings, can be distributed asymmetrically within countries, a pattern that
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19 247 would explain our findings²⁰.

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24 248 The phases on the occurrence of cases throughout EWs and the interaction with groupings
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26 249 within departments associated with AC has been previously described in Chongqing, China,
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28 250 where researchers identified significant changes in the frequency of cases after
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30 251 implementation of geographic isolation measures. The dynamic changes in the detection and
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32 252 distribution of ACs throughout EWs could be explained by the surveillance strategy executed
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34 253 in Colombia known as "PRASS" (in Spanish, tests, surveillance, and sustainable selective
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36 254 isolations); this can be particularly observed from EW 30 onwards (figure S1)²¹. In Wuhan,
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38 255 a study showed that one group of ACs was linked to imported cases while others were linked
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40 256 mostly to autochthonous cases from geographically isolated areas of Wuhan²². We identified
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42 257 that in addition to being associated with a travel history to foreign countries, ACs were also
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44 258 associated with cases that appear spontaneously (related), occurring differentially as
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46 259 measures of geographic and social isolation were applied.

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52 260 The lack of mass screening for COVID-19 in Colombia is the main limitation of our study
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54 261 since the actual AC ratio and the distribution of specific characteristics may differ from those

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262 estimated in this report. On the other hand, although a cross-sectional design is not ideal to
263 identify risk factors, to the best of our knowledge this is the first study aimed at identifying
264 factors associated with AC state with population data unbiased by the inclusion of pre-
265 symptomatic cases ²³.

266 The COVID-19 pandemic has had serious socioeconomic implications, including a collapse
267 of healthcare systems, bankruptcy of companies as well as increasing trends in
268 unemployment and crime rates ²⁴⁻²⁷. This has forced countries with limited resources---such
269 as Colombia---to perform massive screenings in order to prematurely lift quarantine and
270 isolation measures despite the latent risk of successive outbreaks caused by a potential silent
271 spread of COVID-19 through cases in the pre-symptomatic phase or AC state ^{28,29}.

272 ACs transmit COVID-19 more efficiently than symptomatic patients for up to 21 days after
273 the presumed date of infection ^{30,31}. This led to their inclusion in mathematical models
274 intended to estimate the probability or expected number of person-to-person infections on
275 repatriation trips from Wuhan, China ^{7,32}. Since then, ACs have become the target of mass
276 screening in Asian and European countries effectively reducing economical losses due to
277 unnecessary hospital care, controlling the spread in public or in-hospital settings, and
278 allowing the execution of safe plans of social and work re-integration after quarantine and
279 isolation ^{28,33-37}.

280 To date, testing of asymptomatic individuals' rests at the discretion of physicians when
281 justified on a case-by-case basis. On the other hand, the utility of SARS-CoV-2 testing for
282 broad screening of asymptomatic individuals remains to be determined given the limited
283 sensitivity data available for most commercially available test kits ³⁸.

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284 CONCLUSION

285 Together, our findings demonstrate sociodemographic trends strongly associated with
286 COVID-19 AC state in Colombia at a departmental and national level. We believe that the
287 implementation of massive screening campaigns to detect AC and pre-symptomatic patients
288 is paramount to further characterize this phenomenon and adequately guide public health
289 measures of containment and prevention. Additional molecular analysis of viral and host
290 genotypic characteristics should be conducted to determine possible associations with AC
291 state.

292 Authors contributorship statement

293 AT, APM and JDR designed the study. AT, GC, RPG, CH, GH, LMP, LAP and AA
294 conducted the statistical and descriptive analyses. CF, ECB provided the data for the analysis.
295 AT, APM, LAP and JDR drafted the manuscript. All authors approved the final version of
296 the manuscript.

297 **Funding:** This research received no external funding.

298 **Data sharing statement:** Data is freely available from the National Institute of Health (INS)
299 database on COVID-19 cases updated until August 31, 2020
300 (<https://www.ins.gov.co/Noticias/Paginas/coronavirus-casos.aspx>).

301 **Conflicts of Interest:** The authors declare no conflict of interest.

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305 **Figure Legends**

306 **Figure 1. Daily accumulation and distribution of ACs by epidemiological week in**

307 **Colombia. A.** The y-axis represents the number of cumulative ACs transformed into a base
308 10 logarithm. The number of cumulative cases per day is located in points that increase in
309 color intensity according to the occurrence of cases. **B.** The y-axis represents the number of
310 daily ACs transformed into a base 10 logarithm. The number of daily cases per day is
311 located in boxplots. **C.** Heatmap showcasing the number of ACs (top) and **B.** symptomatic
312 patients (bottom) diagnosed in every Colombian department until August 31st, 2020.

313 **Figure 2. Origin and destination of imported asymptomatic and symptomatic cases.**

314 The left and right figures, respectively, represent the country of origin and destination
315 department of ACs and symptomatic patients. The thickness of the link tapes corresponds
316 to the number of reported cases.

317 **Figure 3. Groups of countries and departments associated with AC state.** The left

318 figure shows the group of countries associated with asymptomatic carrier (AC) state
319 identified with positive values of the CCC-CA. The right figure shows departments
320 grouped according to three intervals of CCC-CA: low association (CCC-CA: negative
321 values), moderate association (CCC-CA: $> 0 - < 0.05$), and strong association (CCC-CA:
322 ≥ 0.5).

323 **Supplementary material**

324 **Table S1.** AC state frequency in Colombia by department

325 **Table S2.** Factors associated with AC state in Colombia

326 **Table S3.** STROBE checklist for cross-sectional studies

Figure S1. The stacked bar figure represents on the y-axis the epidemiological weeks (EW) and on the x-axis the proportion of symptomatic (green section of the bar) and the proportion of asymptomatic (purple section of the bar), as well as the result of a Chi square independence test that shows statistical association between the EW variables and health status (symptomatic/asymptomatic carrier).

Table 1. Sociodemographic characteristics of the asymptomatic and symptomatic patients

Variables	Asymptomatic	Symptomatic	p-value
	n: 76162	n: 550725	
Age, years	35 (25-49)	37 (27-52)	<0.001
0-26	21310 (27.9)	129529 (23.5)	<0.001
≥27	54852 (72.0)	421196 (76.4)	<0.001
Sex			
Male	38836 (50.9)	283068 (51.4)	0.035
Female	37326 (49.0)	267657 (48.6)	0.035
Geographical source			
Related†	76108 (99.9)	549789 (99.8)	<0.001
Imported	54 (0.07)	936 (0.170)	<0.001
Departments††			
Bogotá	68143 (89.4)	148258 (26.9)	<0.001
Atlántico	1455 (1.91)	26059 (4.73)	<0.001
Meta	836 (1.10)	8532 (1.55)	<0.001
Barranquilla	737 (0.97)	34262 (6.22)	<0.001

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Cundinamarca	690 (0.91)	23222 (4.22)	<0.001
Imported cases†††	53	905	958
Spain	19 (35.8)	246 (27.2)	0.170
USA	14 (26.4)	208 (22.9)	0.565
Brazil	8 (15.1)	53 (5.86)	0.007
Mexico	3 (5.66)	51 (5.64)	0.994
Venezuela	3 (5.66)	8 (0.88)	0.002
Argentina	1 (1.89)	4 (0.44)	0.156
France	1 (1.89)	19 (2.10)	0.916
Germany	1 (1.89)	11 (1.22)	0.669
Peru	1 (1.89)	24 (2.65)	0.734
Puerto Rico	1 (1.89)	12 (1.33)	0.732
Turkey	1 (1.89)	27 (2.98)	0.645
Unknow	1	31	NA

†: cases that appeared spontaneously in Colombia, ††: top 5 of the departments with the highest frequency of AC. †††: the total number of imported asymptomatic and symptomatic cases was used as the denominator to estimate proportions by country of origin.

Table 2. Factors associated with asymptomatic carrier (AC) state in Colombia

Variable	Interaction model		
	β	ORc (95%, CI)	p-value
Intercept	-7.316	-	<0.001

Age				
>26 years	Ref.	-	-	
0-26 years	0.172	1.188 (1.096-1.287)	<0.001	
Sex				
Female	Ref.	-	-	
Male	0.414	1.513 (1.408-1.625)	<0.001	
Department				
Low association [1]	Ref.	-	-	
Moderate association [2]	0.211	1.234 (1.137-1.340)	<0.001	
Strong association [3]	2.986	19.81 (18.61-21.08)	<0.001	
Geographical source				
Imported CAS†	Ref.	-	-	
Imported CA-AC††(1)	2.536	12.62 (3.034-52.54)	<0.001	
Related cases†††(2)	3.121	22.67 (5.620-91.47)	<0.001	
EW				
10-34	Ref.	-		
≥35	-1.008	0.365 (0.320-0.415)	<0.001	
0-26 years + Male	0.047	1.048 (1.010-1.089)	0.014	
0-26 years + Department [2]	0.174	1.190 (1.069-1.325)	0.001	
0-26 years + Department [3]	-0.005	0.995 (0.919-1.077)	0.898	
Department [2] + Male	-0.387	0.679 (0.615-0.749)	<0.001	
Department [3] + Male	-0.377	0.686 (0.637-0.737)	<0.001	
EW ≥35 + Department [2]	-0.862	0.422 (0.315-0.567)	<0.001	
EW ≥35 + Department [3]	2.217	9.182 (8.045-10.47)	<0.001	

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3 339 †: CAS countries associated with symptomatic patients, ††: CA-AC
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5 340 countries associated with asymptomatic carriers (AC), †††:
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7 341 spontaneous cases, **EW**: epidemiological weeks.
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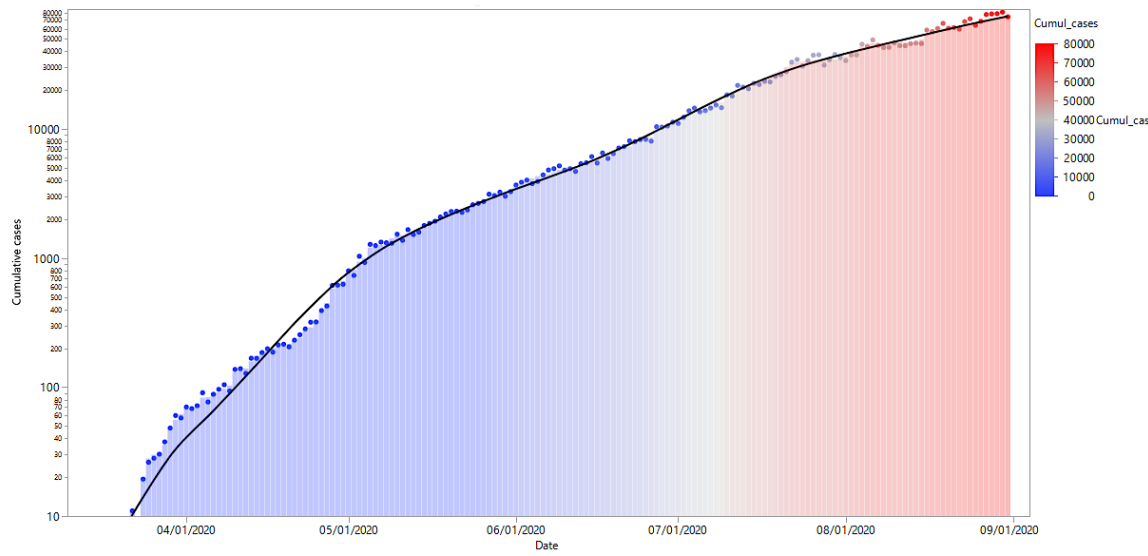
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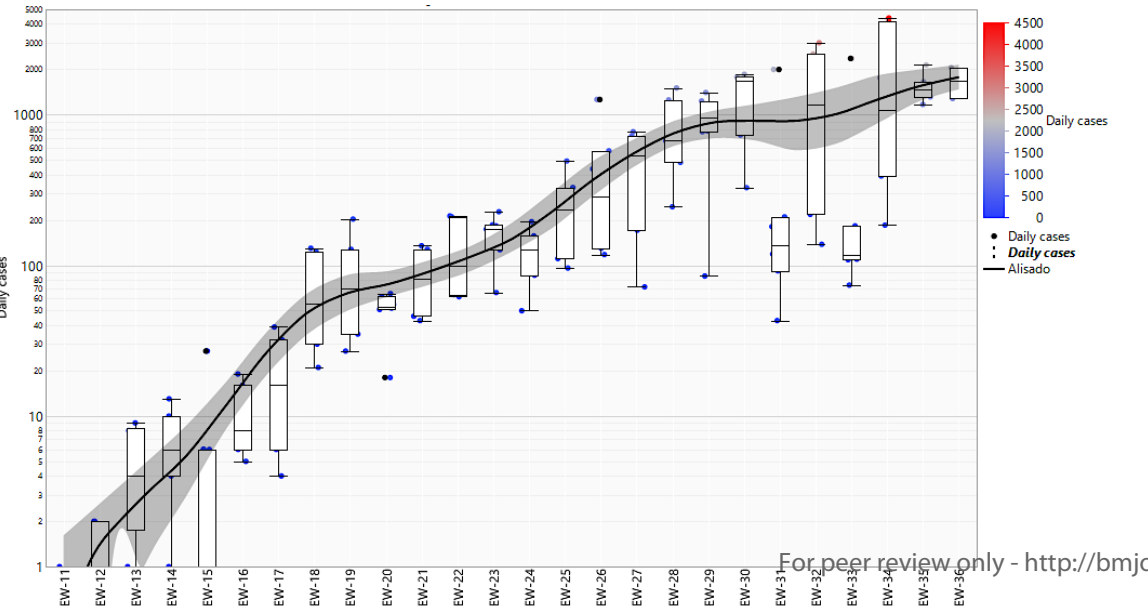
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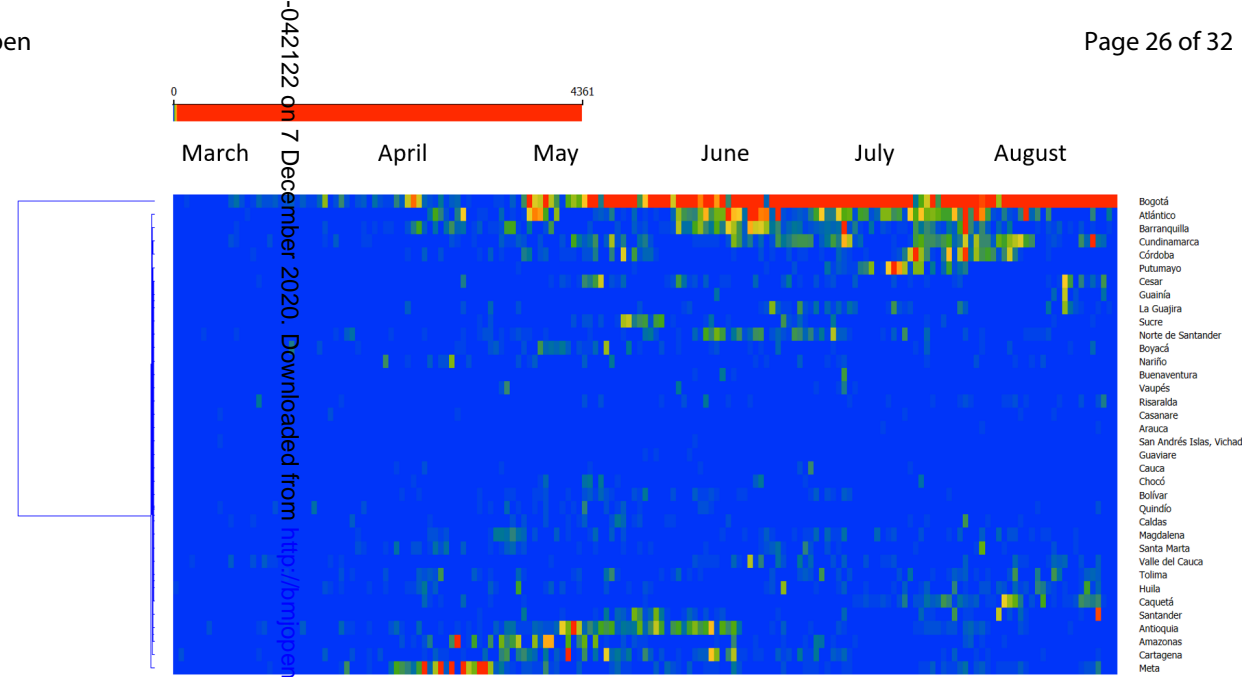
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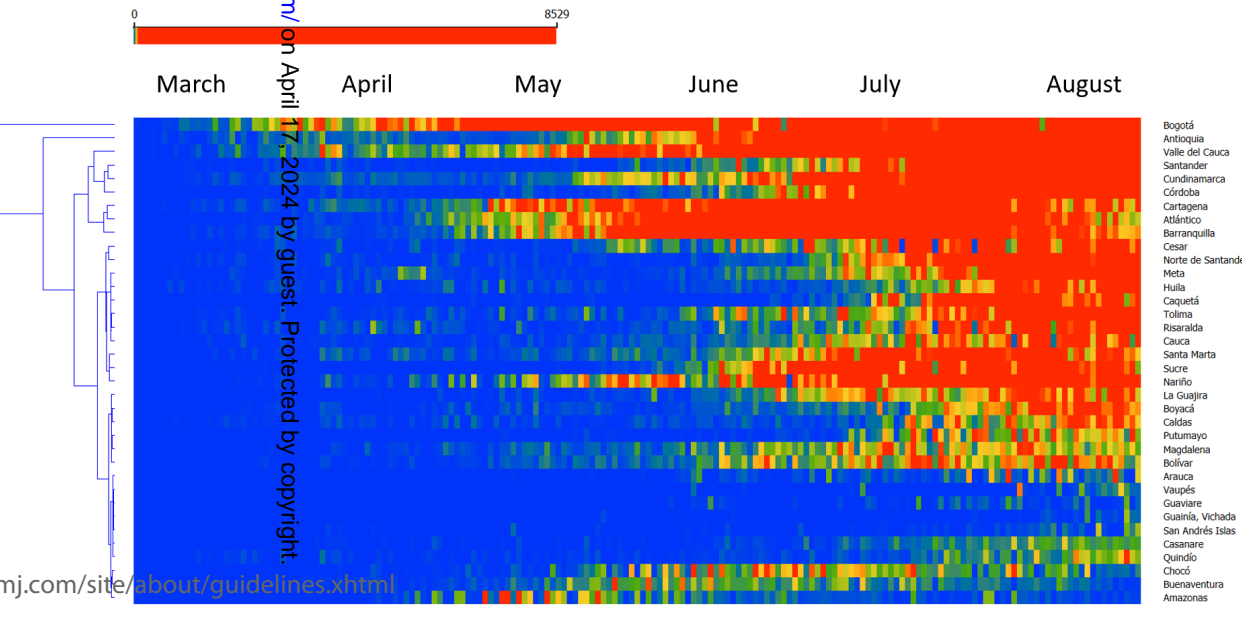


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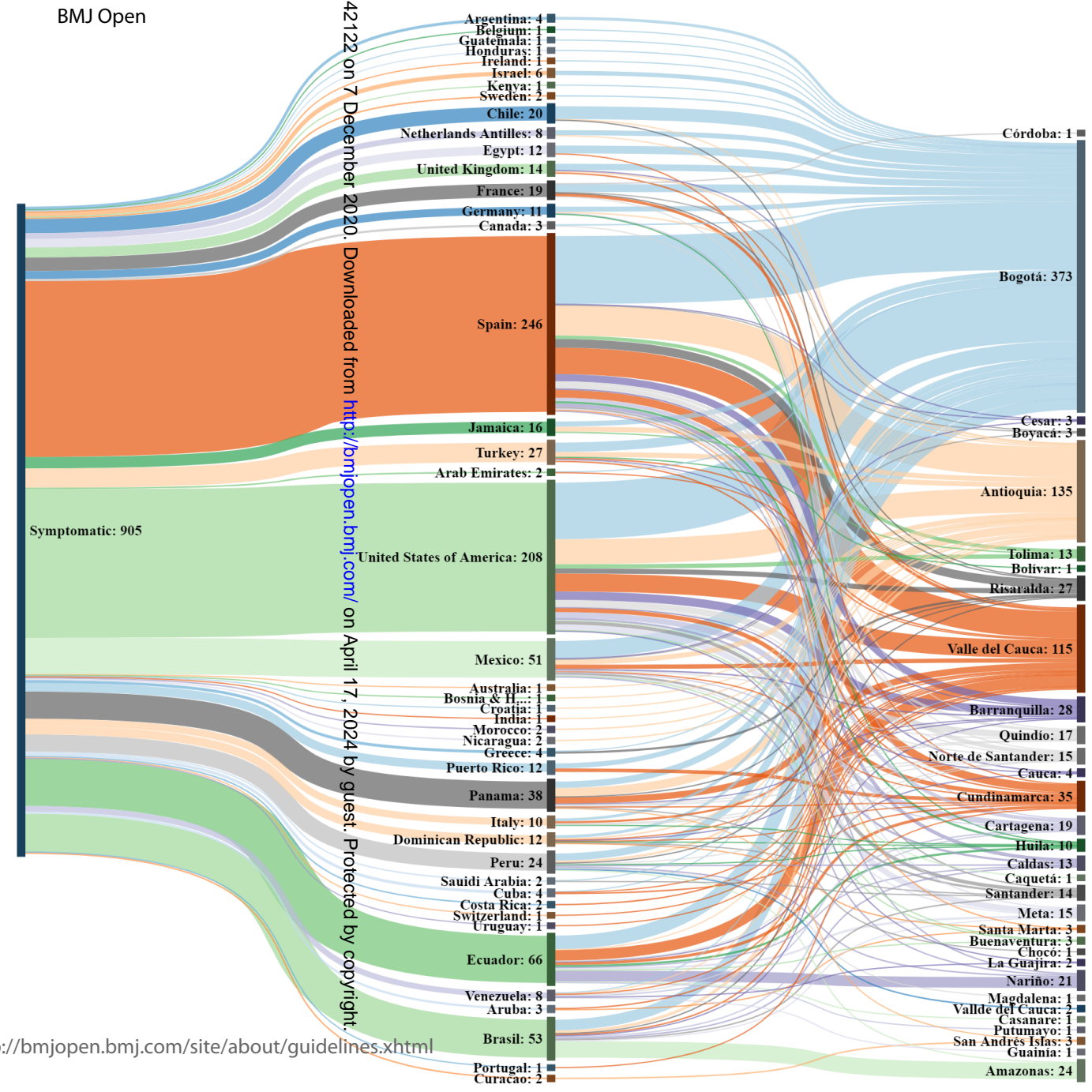
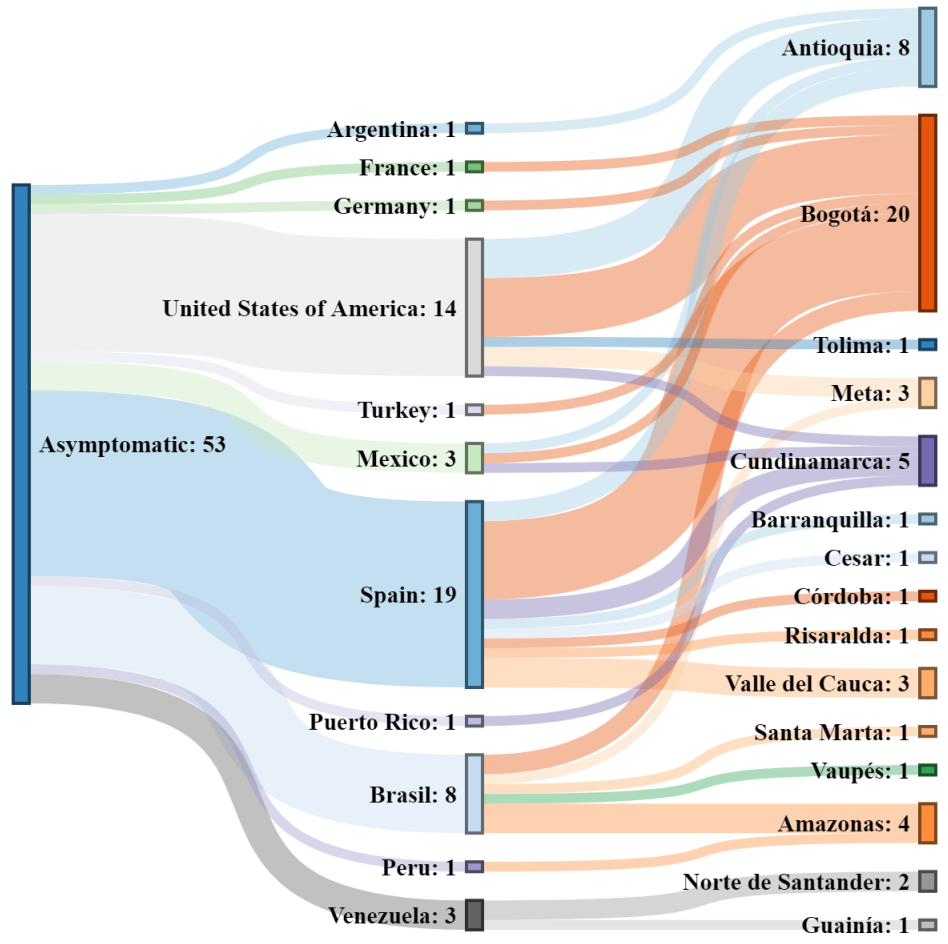
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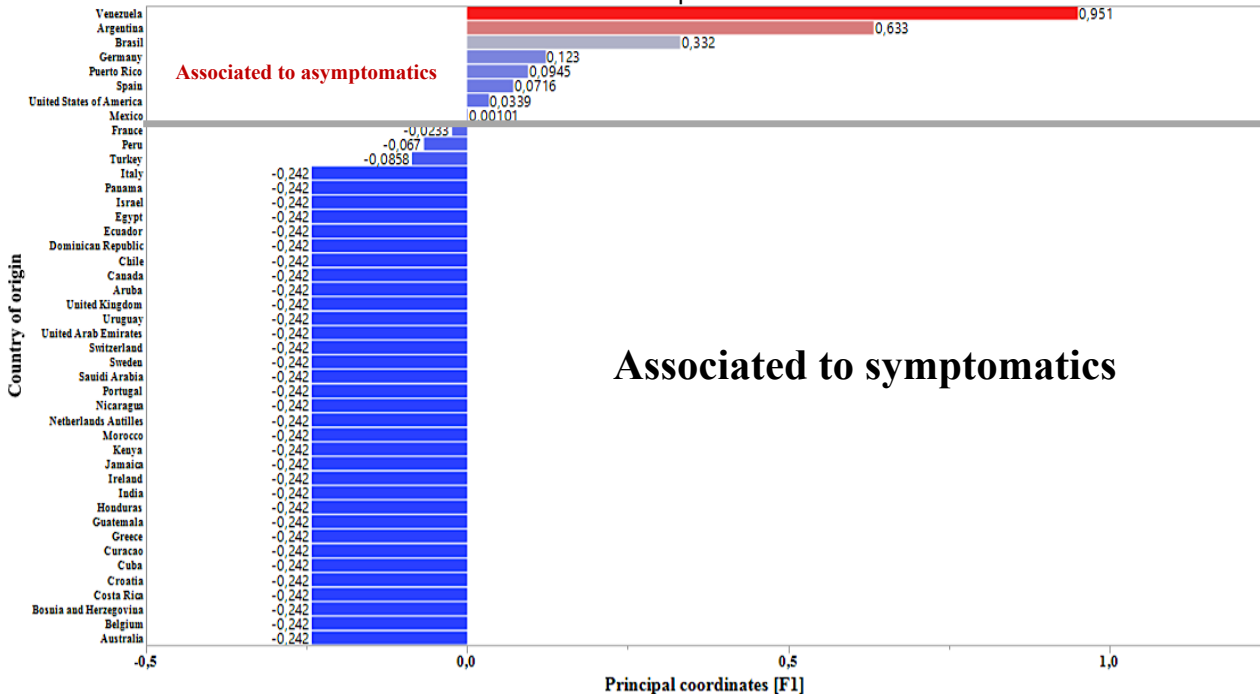
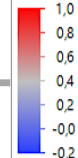


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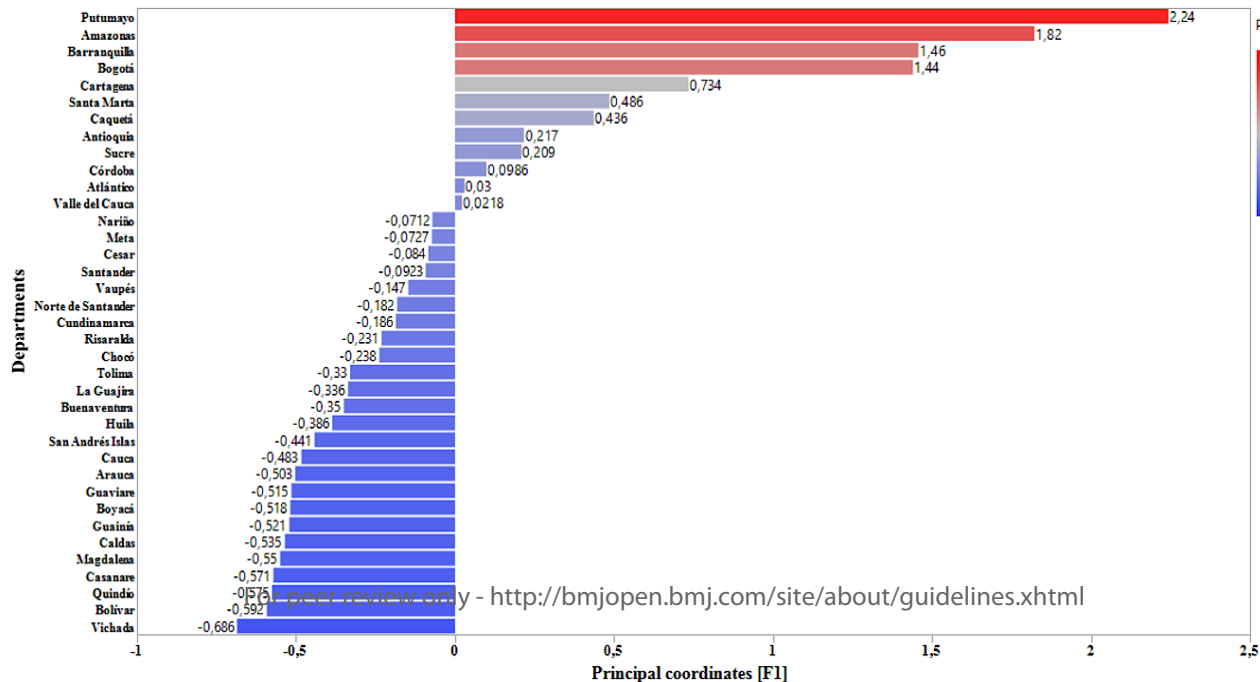
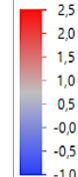
A

Principal coordinates [F1]



B

Principal coordinates [F1]



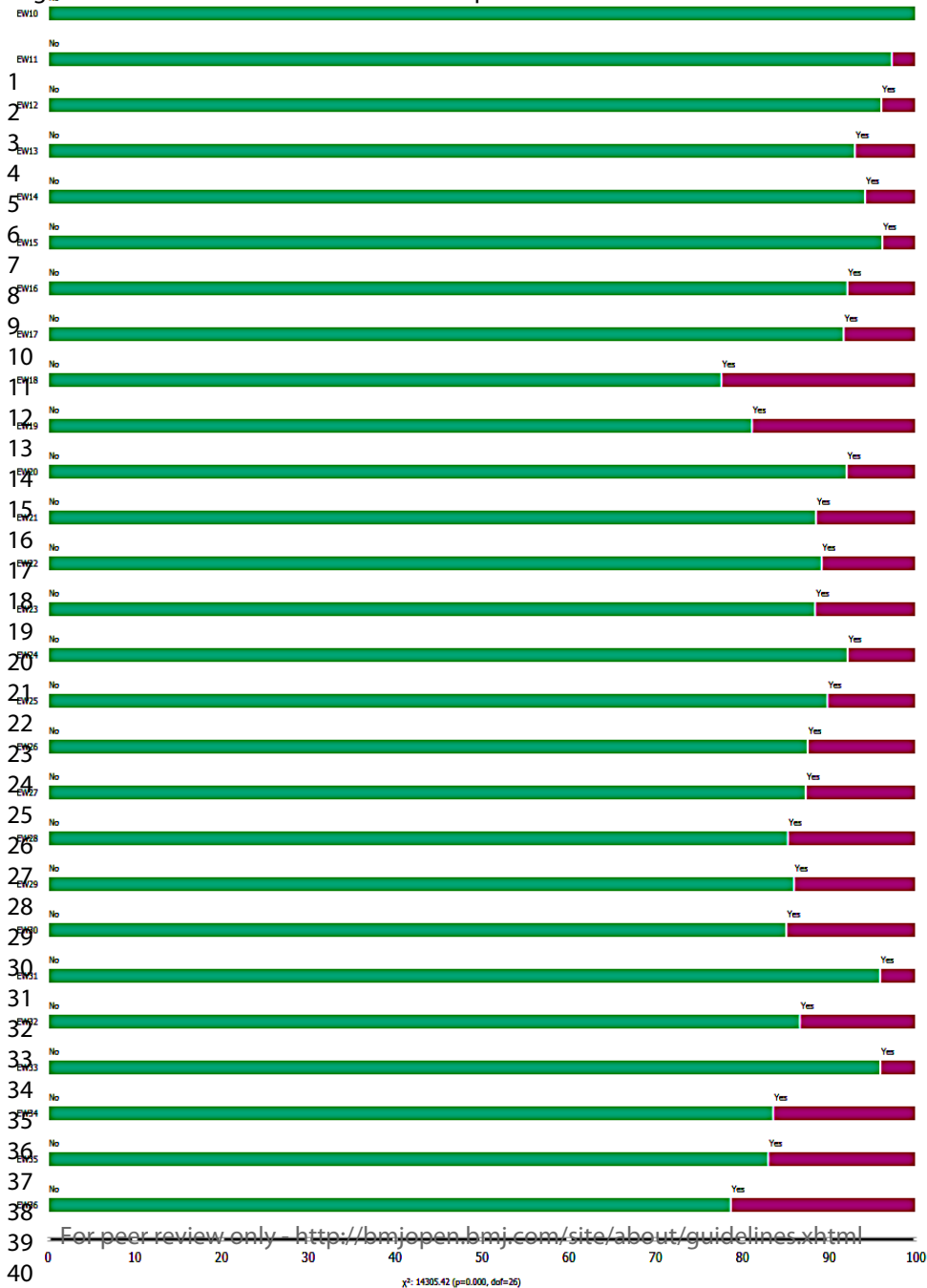


Table S1. AC state frequency in Colombia by department

Department	Asympt_cases	%	Population	Asympt_rate*	Sympt_rate*
Bogotá	68143	89.5	7743955	880,0	1914.5
Atlántico	1455	1.91	2722128	53,5	957.3
Meta	836	1.10	1063454	78,6	802.3
Barranquilla	737	0.97	1243113	59,3	2756.1
Cundinamarca	690	0.91	3242999	21,3	716.1
Antioquia	518	0.68	6677930	7,8	1239.0
Córdoba	468	0.60	1828947	25,6	1072.0
Cartagena	437	0.57	1060577	41,2	1860.5
Amazonas	333	0.44	79020	421,4	2856.2
Putumayo	262	0.34	79020	331,6	3478.9
Norte de Santander	248	0.33	1620318	15,3	727.8
Caquetá	207	0.27	410521	50,4	1474.5
Cesar	195	0.26	1295387	15,1	851.6
Santander	190	0.25	2280908	8,3	847.8
Tolima	153	0.20	1339998	11,4	544.1
Huila	151	0.20	1122622	13,5	470.6
Sucre	151	0.20	949252	15,9	1221.6
La Guajira	140	0.18	965718	14,5	533.0
Boyacá	113	0.15	1242731	9,1	308.5
Magdalena	112	0.15	1427026	7,8	269.8
Valle del Cauca	111	0.15	4532152	2,4	997.9
Santa Marta	94	0.12	538612	17,5	1569.8
Nariño	69	0.09	1627589	4,2	878.5
Bolívar	57	0.07	2180976	2,6	221.9
Caldas	51	0.07	1018453	5,0	291.0
Risaralda	46	0.06	961055	4,8	675.6
Quindío	45	0.05	555401	8,1	236.9
Chocó	39	0.05	544764	7,2	664.9
Guainía	39	0.05	50636	77,0	237.0
Vaupés	27	0.04	44712	60,4	726.9
Buenaventura	20	0.03	440989	4,5	526.1
Cauca	18	0.02	1491937	1,2	360.9
Casanare	7	0.01	435195	1,6	248.9
Arauca	3	<0.01	294206	1,0	335.8
Guaviare	3	<0.01	86657	3,5	318.5
San Andrés Islas	2	<0.01	63692	3,1	411.4
Vichada	2	<0.01	112958	1,8	103.6

The total number of Asymptomatic carriers (ACs) was used as the denominator to determine proportions. **Asympt_cases:** asymptomatic cases, **Symptomatic cases:** see in supplementary file. ***Asympt_rate:** $(\text{Asympt_cases}/\text{population}) * 100.000$ habitants. ***Sympt_rate:** $(\text{Sympt_cases}/\text{population}) * 100.000$ habitants.

Table S2. Factors associated with AC state in Colombia.

Variable	Main effects		
	β	ORa (95%, CI)	p-value
Intercept	-7.360	-	<0.001
Age,			
>26 years old	Ref.	-	-
0-26 years old	0.205	1.227 (1.205-1.250)	<0.001
Sex			
Female	Ref.	-	-
Male	0.054	1.055 (1.038-1.073)	<0.001
Department			
Low risk	Ref.	-	-
Moderate risk	1.304	3.372 (3.134-4.330)	<0.001
Strong risk	1.909	8.310 (6.101-7.464)	<0.001
Geographical origin			
Imported CAS†	Ref.	-	-
Imported CA-AC††	2.541	12.68 (3.049-52.77)	<0.001
Related cases†††	3.255	25.90 (6.425-104.4)	<0.001
EW			
10-34	Ref.	-	-
≥35	0.933	2.543 (2.484-2.603)	<0.001

†: CAS countries associated to symptomatic patients, ††: CA-AC countries associated to

ACs, †††: spontaneous cases, EW: epidemiological week.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Page and relevant text from manuscript
Title and abstract	1	(Page 1) A cross-sectional study (Page 2) It is reported in the abstract
Introduction		
Background/rationale	2	(Page 4-5)
Objectives	3	(Page 5)
Methods		
Study design	4	(Page 5)
Setting	5	(Page 5)
Participants	6	(Page 5-7) <i>Cross-sectional study</i>
Variables	7	(Page 6)
Data sources/ measurement	8*	(Page 6-7)
Bias	9	(Page 7)
Study size	10	(Page 5)
Quantitative variables	11	(Page 6)
Statistical methods	12	(Page 5-7)

Continued on next page

For peer review only

Results

Participants	13*	(Page 7-8)
Descriptive data	14*	(Page 7-9)
Outcome data	15*	(Page 7-10)
Main results	16	(Page 7-10)
Other analyses	17	NA

Discussion

Key results	18	(Page 10-11)
Limitations	19	(Page 11-12)
Interpretation	20	(Page 11-13)
Generalisability	21	(Page 13)

Other information

Funding	22	(Page 14)
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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