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1 **Co-infection of SARS-CoV-2 and influenza viruses: a systematic review and meta-analysis**

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13 **Abstract**

14 We conducted this meta-analysis to determine the proportion of co-infection with influenza
15 viruses in SARS-CoV-2 positive patients and to investigate the severity of COVID-19 in these
16 patients. We included studies with SARS-CoV-2 infection confirmed by qRT-PCR and influenza
17 virus infection (A and/or B) by nucleic acid tests. The proportion of co-infection was compared
18 between children and adults, and between critically ill or deceased patients compared to overall
19 patients. Fifty-four articles were included. The overall proportion of co-infection was 0.7%,
20 95%CI = [0.4 – 1.3]. Most influenza co-infections were due to the influenza A virus (74.4%).
21 The proportion of co-infection with influenza viruses among children (3.2%, 95% CI = [0.9 –
22 10.9]) was significantly higher than that in adult patients (0.3%, 95% CI = [0.1 – 1.2]), p-value
23 <0.01. The proportion of co-infection with influenza viruses among critically ill patients tended
24 to be higher than that in overall patients (2.2%, 95% CI = [0.3 – 22.4] versus 0.6%, 95% CI =
25 [0.3 – 1.2], respectively, p-value = 0.22). Screening for pathogens in co-infection, particularly
26 influenza viruses in patients infected with SARS-CoV-2, is necessary. This warrants close
27 surveillance and investigation of the co-incidences and interactions of SARS-CoV-2 and other
28 respiratory viruses, which is facilitated by the expansion of syndromic diagnosis approaches
29 through the use of multiplex PCR assays.

30 **Keywords:** COVID-19; SARS-CoV-2; influenza; co-infection; molecular

31 **Introduction**

32 At the end of 2019, an epidemic of severe respiratory infections and pneumonia (known as
33 COVID-19) due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began in
34 Wuhan, China. The World Health Organization (WHO) declared the global pandemic on 11
35 March 2020, less than three months after it first appeared
36 (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen>). To
37 date, the pandemic has not yet been controlled on a global scale.

38 Bacterial and viral co-infections have been described as a factor associated with more severe
39 outcomes during pandemic and seasonal influenza outbreaks [1]. COVID-19 may be overlooked
40 or diagnosed late, due to co-infections with other respiratory pathogens [2,3]. Since the onset of
41 the SARS-CoV-2 pandemic, several studies have reported influenza virus and SARS-CoV-2 co-
42 infection, with most data based on case reports or case series [4].

43 The transmissibility, clinical course, and prognosis in patients co-infected with SARS-CoV-2
44 and influenza viruses remain unclear. It has been hypothesised that treatment of influenza with
45 antivirals might improve the outcome of patients co-infected with SARS-CoV-2, although
46 response to treatment against influenza may differ between patients with and without co-
47 infection with COVID-19 [3]. Therefore, greater knowledge on morbidity and mortality in
48 COVID-19 patients co-infected with influenza viruses is needed.

49 We conducted this meta-analysis to determine the proportion of co-infection with SARS-CoV-2
50 and influenza viruses and investigate the severity of COVID-19 in these patients.

51

52 **Methods**

53 **Protocol and research strategy**

54 The protocol of this review follows the recommendations established by the Preferred Reporting
55 Items for Systematic Reviews and Meta-Analyses (PRISMA) statement ([http://www.prisma-](http://www.prisma-statement.org)
56 [statement.org](http://www.prisma-statement.org)).

57 The following databases were investigated in an attempt to identify all relevant studies published
58 on Google Scholar (<http://scholar.google.fr/>), Web of Science
59 (<https://www.webofknowledge.com/>) and PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>). The
60 most recent search was conducted on 15 July 2021. The topic search terms used were the
61 following:

62 #1: “SARS-CoV-2” OR “COVID-19”

63 #2: “influenza virus” OR “influenza viruses”

64 #3: “co-infection” OR “co-detection”

65 #4: #1 AND #2 AND #3

66 **Eligibility criteria**

67 We included published articles that reported the proportion of SARS-CoV-2 and influenza virus
68 co-infection. Preprints were also included. Only studies published in English, reporting SARS-
69 CoV-2 infection confirmed by real-time reverse transcription-polymerase chain reaction (qRT-
70 PCR) were included. Only studies reporting influenza virus infection (A and/or B) by nucleic
71 acid tests were included. . Case reports, case series, review articles, opinion articles and letters
72 which did not present original data were excluded, but reference lists were screened to identify
73 studies that might have been missed by the search.

74 To compare influenza co-infection in children and adults with SARS-CoV-2, we separated the
75 included studies into two groups: one involving children only (≤ 14 years of age) and the other
76 adults only. In studies conducted both in children and adults, subgroups were individualised.

77 To evaluate the co-infection effect on the severity of COVID-19, we separated the included
78 studies into two groups: one conducted on critically ill or deceased patients only, and the other
79 on all patients, regardless of the severity of the disease. In studies conducted in both non-severe
80 and severe patients, subgroups were individualised.

81 **Study selection**

82 After manually removing duplicates, the articles identified through the initial search were first
83 screened by title and abstract by three independent researchers (TLD, HVT and GP). The full
84 texts of relevant articles were examined for inclusion and exclusion criteria (Figure 1). In
85 addition, articles without an abstract were included for full-text screening and assessed at this
86 stage. After screening the abstracts, the full texts of the articles were assessed for eligibility by
87 the same three researchers and were selected or rejected for inclusion in the systematic review.
88 Any discordant results were discussed in a consensus meeting.

89 **Data collection process and data items**

90 Data extraction forms included information on the type of publication, the country where patients
91 were sampled, the time period of the study, the number of patients tested for both SARS-CoV-2
92 and influenza viruses, the number of patients who tested positive for SARS-CoV-2, the number
93 of COVID-19 patients with a co-infection with influenza viruses, type of sample, and influenza
94 type, if available. A fourth researcher (PC) checked the article list and data extractions to ensure

95 there were no duplicate articles or duplicate information on the same patient and also resolved
96 discrepancies about study inclusion.

97 **Assessment of risk for publication bias and statistical approach**

98 We did not evaluate publication bias with funnel plots and statistical test in this review, as the
99 usefulness of a standard publication bias test for a meta-analysis has been questioned. Although
100 publication bias may cause inflated estimates in meta-analyses for studies of treatment effect,
101 this is an unlikely scenario in this context, because we only reported the proportion of COVID-
102 19 patients co-infected with influenza viruses.

103 The meta-analysis was performed using the open-source software R [R Core team. R: A
104 language and environment for statistical computing. R foundation for statistical computing,
105 Vienna, Australia, 2020. URL: [<http://www.r-project.org>]. and using a random effects model.
106 This software made it possible to include dichotomous outcomes (number of events out of the
107 total). We performed subgroup analyses by group of patients (adult versus children) and by
108 severity of the studied population (critically ill patients or deceased patients versus overall
109 infected patients with COVID-19). A p-value <0.05 was considered significant.

110

111 **Results**

112 **Study selection and characteristics**

113 The study selection process is presented in the flow-diagram (Figure 1). The search algorithm
114 produced 1248 articles from the Google Scholar, Web of Science and PubMed databases.
115 Nineteen articles were added from other sources. After removing duplicates, 426 articles were

116 scanned, based on their title and abstract. A total of 169 articles were processed for full text
117 screening. Fifty-four articles met the inclusion criteria and were included in the qualitative
118 synthesis of the systematic review and meta-analysis (Figure 1) [5-58].

119 Of the 54 included articles (Table 1), all were peer-reviewed papers. Most studies were
120 conducted in China (n= 15), followed by the USA (12), France (7), Spain (3), Switzerland (2),
121 Saudi Arabia (2), the UK (1), Singapore (1), Iran (1), Japan (1), Russia (1), Finland (1), Italy (1),
122 Taiwan (1), Brazil (1), Canada (1), Korea (1), India (1) and Thailand (1). All studies were
123 conducted in 2020 with the majority before May 2020, corresponding to the first phase of the
124 COVID-19 pandemic. Forty-nine articles reported the study dates (Table 1). Of these, 28
125 (51.9%) were conducted during the descending phase of the influenza season and 11 (20.4%)
126 were conducted at the end of the influenza season in the related countries (Supplementary data).
127 Eleven studies lasted \leq two weeks, 15, 15 and eight lasted respectively from three to five weeks,
128 from six to ten week and $>$ ten weeks (Table 1). Fifteen studies were conducted in adults only,
129 nine in children only and one compared the co-infection in adults and children. Thirty studies
130 were conducted in any classes of age or did not reported the age of the studied population. Most
131 studies were conducted on patients at various stages of disease severity, while five studies were
132 limited to critically ill patients or patients who died. No eligible study that compared severe
133 versus non-severe COVID-19 co-infected patients was available.

134 **Proportion of co-infection with influenza viruses in COVID-19 patients**

135 The proportion of co-infection with influenza viruses in COVID-19 patients varied according to
136 period of study and to countries where studies were conducted. Table 1 shows the proportion of
137 co-infection with influenza viruses and SARS-CoV-2 and influenza surveillance information
138 related to countries, respectively. This review included 18,021 patients infected with SARS-

139 CoV-2 who were tested for influenza viruses. Of them, 143 patients were co-infected. Hence, the
140 overall proportion of co-infection was 0.7%, 95%CI = [0.4 – 1.3] and heterogeneity (I^2) was
141 87.4%. Most of 143 influenza co-infections were due to the influenza A virus (106, 74.1%) and
142 29 cases (20.3%) involved the influenza B virus. One patient was coinfecting with three viruses
143 (SARS-CoV-2, influenza A virus and influenza B virus). The type of influenza virus was not
144 identified in nine patients. Influenza A virus subtypes were identified in 23 cases, with H1N1
145 being the most frequent (38, 77.6%) and H3N2 in 11 cases , (22.4%).

146 **Proportion of co-infection with influenza viruses in child and adult COVID-19 patients**

147 The proportion of co-infection in children was 3.2%, 95% CI = [0.9 – 10.9] and that among adult
148 patients was 0.3%, 95% CI = [0.1 – 1.2] (Figure 2). The difference was significant with a p-value
149 <0.01 and heterogeneity (I^2) was 54.0% and 26.0%, respectively.

150 **Effect of co-infection with influenza viruses on the severity of COVID-19**

151 The proportion of co-infection in critically ill or deceased patients was 2.2%, 95% CI = [0.3 –
152 22.4] and among overall population of co-infected patients was 0.6%, 95% CI = [0.3 – 1.2]
153 (Figure 3). The difference was not significant with a p-value = 0.22 and heterogeneity (I^2) was
154 0% and 85%, respectively.

155

156

157 **Discussion**

158 The co-infection rate varied according to country and period of study. Influenza viruses circulate
159 all over the world. In temperate regions, influenza is seasonal epidemic disease, occurring

160 typically in the winter season: from November to April in the northern hemisphere and from
161 April to September in the southern hemisphere
162 (https://www.who.int/ith/diseases/influenza_seasonal/en/). In tropical territories, there is no clear
163 seasonal pattern and influenza circulates year-round, albeit typically with several peaks during
164 rainy seasons (https://www.who.int/ith/diseases/influenza_seasonal/en/). In addition, the number
165 of COVID-19 cases also varies widely between countries around the world
166 (<https://www.worldometers.info/coronavirus/>). Consequently, the proportion of SARS-CoV-2
167 and influenza co-infection varies from country to country. Also because of the seasonal pattern
168 of influenza, the reported rate of co-infected patients depends on the time when the study was
169 conducted. Our analysis shows that the actual proportion of co-infections may have been
170 underestimated, because over 70% of included studies were conducted during descending and
171 late phases of the influenza season in the relevant countries (Supplementary data).

172 On other hand, the detection of co-infection with influenza virus (or other viruses) and SARS-
173 CoV-2 depends on the dynamic of infection of each pathogen. This adds to the challenge of
174 diagnosing COVID-19, especially when the patient may test negative for SARS-CoV-2 but
175 positive for other viruses, and very shortly thereafter turns SARS-CoV-2 positive. In this case,
176 COVID-19 may be under-estimated, and medical treatment could be delayed [2,59]. In fact,
177 influenza viruses have shorter mean incubation and viral shedding times than SARS-CoV-2 virus
178 (two days vs. six days and three days vs. 17 days, respectively) [60-62]. It is likely that in some
179 patients getting infected with the two viruses simultaneously, the influenza virus is no longer
180 detectable at the time the SARS-CoV-2 infection is diagnosed and the time window of co-
181 detectability may be too short to adequately identify all co-infections with influenza and SARS-
182 CoV-2 using molecular tests.

183 Our analysis shows that the proportion of co-infections with influenza virus in COVID-19
184 children was significantly higher than in infected adults. In a comparative study by Pigny *et al.*,
185 viral co-infection (with any viruses) was more frequent in SARS-CoV-2 children than in adults
186 living in the same household [43]. Although no cases of influenza virus infection have been
187 found, possibly due to the study being conducted during the recession phase of the influenza
188 epidemic in the USA, this study showed that COVID-19 paediatric patients are at a higher risk of
189 viral co-infection. Interestingly, despite partial lockdowns with creches and schools being closed,
190 COVID-19 children were co-infected with other respiratory viruses while their families were not
191 [43]. In addition, a higher frequency of viral respiratory co-infections in children than in adults
192 had been shown in the pre-COVID-19 pandemic [63]. This suggests that the pathogen infection
193 and co-infection also depend on the host body.

194 Although the difference was not statistically significant, the proportion of co-infection in severe
195 COVID-19 patients was three times higher than in the total population of patients in our analysis.
196 In previous studies, the clinical presentation in COVID-19 patients coinfecting with influenza
197 viruses was not different to that of patients with a single SARS-CoV-2 infection, but the clinical
198 outcome was more severe among co-infected patients [64-67]. In a comparative study by Ma *et*
199 *al.*, conducted on 93 critically ill COVID-19 patients and including 44 deaths, no significant
200 difference was observed in the proportion of co-infection with influenza virus and SARS-CoV-2
201 between the two groups: survivors and non-survivors [64]. However, in patients who died, the
202 incidence of acute cardiac injury was significantly higher in patients who were co-infected with
203 influenza viruses than in those with SARS-CoV-2 mono-infection (86.4% versus 54.5%
204 respectively, $p < 0.05$) [64]. In another study, Yue *et al.* showed that patients coinfecting with
205 SARS-CoV-2 and influenza B virus were more likely to develop poor outcomes, compared with

206 those with a single SARS-CoV-2 infection and SARS-CoV-2- influenza A virus co-infection
207 [65]. Stowe *et al.* analysed the risk of mortality among individuals with COVID-19 and influenza
208 virus co-infection [67]. Of the 19,256 patients tested, 4,500 were positive for SARS-CoV-2, of
209 whom 58 were co-infected. Their analysis showed that co-infected patients had a two-fold higher
210 risk of dying than patients only infected with SARS-CoV-2. The lack of a significant difference
211 in the co-infection rate according to COVID-19 severity in our analysis can be explained by the
212 limited number of studies conducted on patients with severe forms of the disease (only five).
213 Interestingly, the proportion of influenza virus co-infections was proportional to the mortality
214 rate in the four studies with available mortality data. In fact, the proportion of co-infections was
215 0.1%, 0.6%, 9.5% and 21.9% in studies reporting a mortality rate of 32.1%, 48.9%, 52.4% and
216 100%, respectively [55-58].

217 In addition, Zhang *et al.* conducted an animal model study on simultaneous or sequential co-
218 infection with influenza A(H1N1)pdm09 and SARS-CoV-2 [68]. Their results showed that co-
219 infected hamsters had a more severe disease than hamsters infected with a single virus.
220 Simultaneous co-infection lowered SARS-CoV-2 loads in the respiratory tract but was associated
221 with delayed resolution of lung damage. Moreover, co-infected hamsters had lower levels of the
222 SARS-CoV-2 neutralising antibody in the serum and longer SARS-CoV-2 shedding in oral
223 swabs [68]. These results suggest an interaction effect between the two viruses compared to
224 mono-infection with SARS-CoV-2.

225 Our study has some limitations. First, seven out of 54 studies were conducted on fewer than 20
226 patients. Furthermore, a high heterogeneity was also observed across all studies and all subgroup
227 analyses (divided by age of the population studied or severity of patients). The high variance
228 between studies in our meta-analysis may be due to methodological factors, clinical factors,

229 sample size, and particularly to the period of time when the studies were conducted, as the rate of
230 co-infection depends on the rate of epidemiological co-incidence of the viruses [5]. This is
231 important, because influenza is a seasonal infection in many regions.

232 While there are more than 108 vaccines in clinical development for COVID-19
233 (<https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>), only
234 a few vaccines have been licensed by WHO. After 20 months of the pandemic, the value of
235 therapeutics against COVID-19 remains controversial. In contrast, antivirals and vaccines are
236 available for influenza. Influenza vaccines reduce not only hospitalisation due to influenza
237 infections but may possibly also reduce their subsequent impact on COVID- 19 mortality.
238 However, access to influenza vaccination as well as to COVID-19 vaccination is not identical
239 around the world. In any case, individual non-pharmaceutical preventive measures should be
240 improved. It is noteworthy that cases of the influenza decreased dramatically following the
241 application of control measures against COVID-19 [69,70], as confirmed by the national
242 surveillance data presented here (Supplementary data). It is very difficult to confirm whether this
243 decrease is related to the interaction between pathogens or to the effectiveness of preventive
244 measures against COVID-19. Since the future of the epidemics is unpredictable, close
245 surveillance and investigation of the co-incidences and interactions of SARS-CoV-2 and other
246 respiratory viruses, including influenza viruses is needed. An expansion of syndromic diagnosis
247 approaches through the use of multiplex PCR assays is definitely also required [71].

248

249 **Ethical Approval**

250 NA

251 **Consent to participate**

252 NA

253 **Consent to Publish**

254 NA

255 **Authors' Contributions**

256 Conceptualisation: Thi Loi Dao, Van Thuan Hoang, Philippe Gautret

257 Methodology: Thi Loi Dao, Van Thuan Hoang, Matthieu Million, Philippe Gautret

258 Data collection: Thi Loi Dao, Van Thuan Hoang

259 Formal analysis and investigation: Thi Loi Dao, Van Thuan Hoang, Philippe Colson, Matthieu

260 Million, Philippe Gautret

261 Writing original draft and preparation: Thi Loi Dao

262 Writing – review and editing: Van Thuan Hoang, Philippe Colson, Matthieu Million, Philippe

263 Gautret

264 Supervision: Philippe Gautret

265

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268

269 **Conflict of Interest**

270 Thi Loi Dao, Van Thuan Hoang, Philippe Colson, Matthieu Million and Philippe Gautret declare
271 that they have no conflict of interest.

272

273 **Availability of data and materials**

274 The datasets generated during and/or analysed during the current study are available in the
275 manuscript.

276

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Table 1: Characteristics of included studies.

Reference	Type of study	Country	Period of study	Duration of study (week)	Number of patients tested	Number of patients positive for SARS-CoV-2	Number (proportion, %) of co-infected patients	Type of sample	Age	Number (proportion) of critically ill patients, and mortality rate
Influenza co-infection in all COVID-19 patients										
[5]	Cross-sectional	France	1 March to 30 April 2020	9	4,222 patients were tested for both SARS-CoV-2 and influenza viruses	643	4 (0.6%) (IAV = 2, IBV = 2)	Nasopharyngeal swabs	Adults and children	NA
[6]	Cross-sectional	France	25 January to 29 March 2020	9	1,423	301	5 (1.7%) type of influenza was not reported	Upper and lower respiratory tract samples	Adults and children	Critically ill = 20% in overall patients
[7]	Retrospective analysis	USA	10 March to 23 March 2020	2	500	51, but only 46 patients were tested for influenza by qPCR	1 (2.2%) (IAV)	Nasopharyngeal swabs	Adults and children	ND
[8]	Retrospective cohort	China	1 January to 20 January 2020	3	-	99	0 (0%)	-	Adults	Critically ill (23%), mortality (11%)
[9]	Cross-sectional	France	7 February to 22 February 2020	2	-	13	1 (7.7%) (IAV H1N1)	Nasopharyngeal swabs	Adults and children	ND
[10]	Cross-sectional	USA	12 March to 15 April 2020	5	2,458	459	3 (0.7%) (IAV)	Nasopharyngeal swabs	ND	ND

[11]	Cross-sectional	Japan	10 March to 7 May 2020	8	191	8	0 (0%)	Nasopharyngeal swabs	ND	ND
[12]	Retrospective study	UK	20 February to 30 April 2020	10	-	836, but only 250 were tested for influenza viruses	0 (0%)	Sputum or bronchoalveolar	Adults	Mortality (262/836, 31.3%)
[13]	Cross-sectional	China	24 January to 29 February 2020	5	164	3	0 (0%)	Oropharyngeal swabs	ND	ND
[14]	Retrospective	China	1 December 2019 to 16 January 2020	7	161	2	0 (0%)	Nasopharyngeal swab, sputum or bronchoalveolar lavage fluid	Children	ND
[15]	Cross-sectional	USA	3 March to 25 March 2020	3	1,206	115	1 (0.9%) (IAV)	Nasopharyngeal swabs	Adults and children	ND
[16]	prospective cohort	Switzerland and	1 January to 29 March 2020	13	7,663 but 1816 were tested for influenza viruses	309/1,816	2 (0.6%) (IAV)	Nasopharyngeal/oropharyngeal swabs	Adults and children	Critically ill (67/1966 hospitalized patients, 3.4%)
[14]	Retrospective cohort	China	1 January to 1 March 2020	9	-	32	0 (0%)	Sputum	Adults	Critically ill (10/32, 31.3%)
[18]	Cross-sectional	China	20 January to 1 February 2020	2	186	92	0 (0%)	Sputum, nasal or throat swab	Adults and children	ND

[19]	Retrospective cohort	China	4-28 February 2020	3	-	354 hospitalised patients, but only 76 were tested for influenza viruses	0 (0%)	Sputum	Adults	Critically ill (84/354, 23.7%), mortality (11/354, 3.1%)
[20]	Cross-sectional	China	19 January to 26 February 2020	5	-	250	3 (1.2%) (IAV = 2, IBV = 1)	Sputum or nasopharyngeal swabs	ND	Critically ill (8/11 co-infected patients with respiratory viruses, 72.7%)
[21]	Cross-sectional	USA	25 March to 22 April 2020	4	12,075	1,690	0 (0%)	Nasopharyngeal swabs	Adults and children	ND
[22]	Retrospective cohort	USA	16 March to 20 April 2020	5	10,194	8,990, but only 1,204 patients were tested for influenza virus	1 (0.1%) (IAV)	-	ND	ND
[23]	Cross-sectional	Thailand	8-31 January 2020	3	-	11 hospitalised patients	1 (9.1%) (IAV)	Nasopharyngeal, oropharyngeal swabs and sputum	Adults	Critically ill (0%), mortality (0%)
[21]	Retrospective cohort	USA	1 March to 4 April 2020	5	-	5700, but only 1,996 patients were tested for influenza virus	1 (0.1%) (IAV)	Nasopharyngeal swabs	Adults and children	2,634 patients with available clinical data, Critically ill (373/2,634, 14.2%), mortality (553/2,634, 21%)

[25]	Retrospective cohort	USA	3 February to 31 March 2020	8	316. Of whom, 270 were tested for influenza virus by qPCR and 97 patients were tested by mNGS	33	0 (0%)	oropharyngeal and/or nasopharyngeal swab	Adults	186 were hospitalised, Critically ill (53/186, 28.5%), mortality (16/186, 8.6%)
[26]	Retrospective cohort	Russia	2 March to 30 April 2020 (set 1) and 5 May to 20 June 2020 (set 2)	16	7,864 (set 1) and 4,458 (set 2)	455 were tested for influenza viruses	0 (0%)	Nasopharyngeal swabs	Adults and children	ICU (1.4%), mortality (1%) in overall patients
[24]	Retrospective cohort	China	21 January to 29 February 2020	6	2,188	24	0 (0%)	Nasopharyngeal swabs	ND	ND
[28]	Cross-sectional	Singapore	5 February to 15 April 2020	10	736	431	0 (0%)	oropharyngeal and/or nasopharyngeal swab	ND	Critically ill (16/736, 2.2%)
[29]	Retrospective cohort	China	20 January to 27 February 2020	5	-	74 infected children. But only 34 were screened for influenza viruses	1 (2.9%) (IAV and IBV)	Nasopharyngeal swabs	Children	Critically ill (0%)
[30]	Retrospective cohort	France	26 February to 14 March, 2020	2	-	70	0 (0%)	Respiratory samples	Adults	Critically ill (11/70, 15.7%), mortality (4/70, 5.7%)

[31]	Retrospective cohort	USA	9 March to 30 April 2020	7	3,669 ill children. But only 767 patients were tested for both SARS-CoV-2 and influenza virus	101/767	1 (1.0%) (IAV)	-	Children	ND
[32]	Retrospective cohort	China	27 January to 23 February 2020	4	57 children	34	9 (26.5%) (IAV = 3, IBV = 6)	Nasopharyngeal or throat swabs	Children	Mortality (0%)
[33]	Cross-sectional	China	22 January to 2 February 2020	2	-	257	7 (2.7%) (IAV = 2, IBV = 5)	Throat samples	Adults and children	Critically ill (17/257, 6.6%), mortality (0%)
[34]	-	China	-	-	-	162	3 (1.9%) (IVA H3N2)	Nasopharynx swabs and sputum	ND	ND
[35]	Cross-sectional	China	23 January to 8 February 2020	2	-	20	3 (15.0%) (IAV = 1, IBV = 2)	Pharyngeal swabs	Children	Mortality (0%)
[36]	Retrospective	Spain	2-16 March 2020	2	365	41	2 (4.9%) (IBV)	-	Children	Critically ill (22/365, 6.0%)
[37]	Retrospective	China	1-10 February 2020	1	-	25	2 (8.0%) (IBV)	Nasopharyngeal and throat swabs	Children	Critically ill (2/25, 8.0%)
[38]	Cross-sectional	Reunion Island,	18 March to 15 April	4	-	36, but only 31 patients were	1 (3.2%) (H1N1)	Nasopharyngeal swab or	ND	Critically ill (10/36, 27.8%)

		France	2020			tested for influenza viruses		tracheal aspirate		
[39]	Prospective cohort	Finland	2 December 2019 to 30 April 2020	21	213	28, but only 21 were tested for influenza viruses	0 (0%)	Respiratory samples	Adults	ND
[40]	Retrospective	Taiwan	February to August 2020	-	205	55	0 (0%)	Nasopharyngeal swabs	Adults and children	ND
[41]	Cross-sectional	Italia	21 January to 7 February 2020	2	126	3	0 (0%)	Nasopharyngeal swabs	ND	ND
[42]	Cross-sectional	Spain	28 February to 22 April 2020	8	-	989	5 (0.5%) (IAV = 4, IBV = 1)	Respiratory samples	ND	ND
[43]	Cross-sectional	Switzerland	-	-	-	71	0 (0%)	Nasopharyngeal swabs	Adults (41), children (30)	ND
[44]	Retrospective	USA	25 March to 15 May 2020	7	-	54	0 (0%)	Nasopharyngeal swabs	Children	ND
[45]	Cross-sectional	Spain	4-28 March 2020			183 but 103 were tested for influenza viruses	1 (1.0%) (IAV H1)	Nasopharyngeal swabs	Adults	ND
[46]	Cross-sectional	USA	1 February to 31 May 2020		17,4746	3,757	15 (%) (IAV = 12, IBV = 3)		ND	Mortality (512/3,757, 13.6%)
[47]	Retrospective cohort	India	1 August 2020 to 31 December 2020			101	9 (H3N2 = 8, H1N1 = 1)	Upper respiratory tract samples	ND	Mortality (9/92 (9.8%) in COVID-19 only patients and 3/9 (33.3%) in co-infected patients)

[48]	Retrospective cohort	Saudi Arabia	-	-	-	48	17 (35.4%) (H1N1)	Respiratory tract samples	Adult and Children (1-92 years)	14 ICU (6 co-infected) patients and 34 mild (11 co-infected) patients
[49]	Retrospective cohort	China	11 January 2020 to 1 March 2020		-	408 but only 348 patients were tested for influenza viruses	4 (1.1%) (Influenza A = 1, Influenza B = 3)	Nasopharyngeal swabs	ND	Mortality (3, 0.7%)
[50]	Observational study	Brazil	March to December, 2020		987	418	6 (1.4%) (Influenza A)	Respiratory tract samples	Adults and children	ND
[51]	Cross-sectional study	France	25 January to 30 April, 2020		3768	806	4 (0.5%)	Respiratory tract samples	Adults	Mortality (19.1%)
[52]	Retrospective cohort	Korea	7 to 23 February, 2020		20,054	342	3 (0.9%) (Influenza A)	Respiratory tract samples	ND	ND
[54]	Retrospective study	Canada	7 March to 28 May, 2020		255627	6717, but only 1020 patients were tested for influenza viruses	1 (0.1%) (Influenza A)	Respiratory tract samples	ND	ND
Influenza co-infection in critically ill or died COVID-19 patients										
[54]	Retrospective cohort	USA	-	-	-	8	1 (12.5%) (IBV)	Upper and lower respiratory tract samples	Adults	Mortality was not available
[55]	Retrospective cohort	KSA	20 March to 31 May 2020	10	-	352	0 (0%)	Nasopharyngeal swabs	Adults	Mortality (32.1%)

[56]	Retrospective cohort	France	13 March to 16 April 2020	5	-	92 but only 82 were tested for influenza viruses	0 (0%)	Nasopharyngeal swabs	Adults	Mortality (48.9%)
[57]	Cross-sectional	USA	20 February to 5 March 2020	2	-	21	2 (9.5%) (IAV)	Nasopharyngeal swabs	Adults	Mortality (52.4%)
[58]	Retrospective	Iran	2 March to 20 April 2020	7		105 patients died	23 (21.9%) IAV H1N1 = 18, IAV non-H1N1 = 5, IBV = 0)	Nasopharyngeal and throat swabs	Adults and children	Mortality (100%)

ND: not documented, IAV: influenza A virus, IBV: influenza B virus, ICU: intensive care unit

Figure 1: Flow chart.

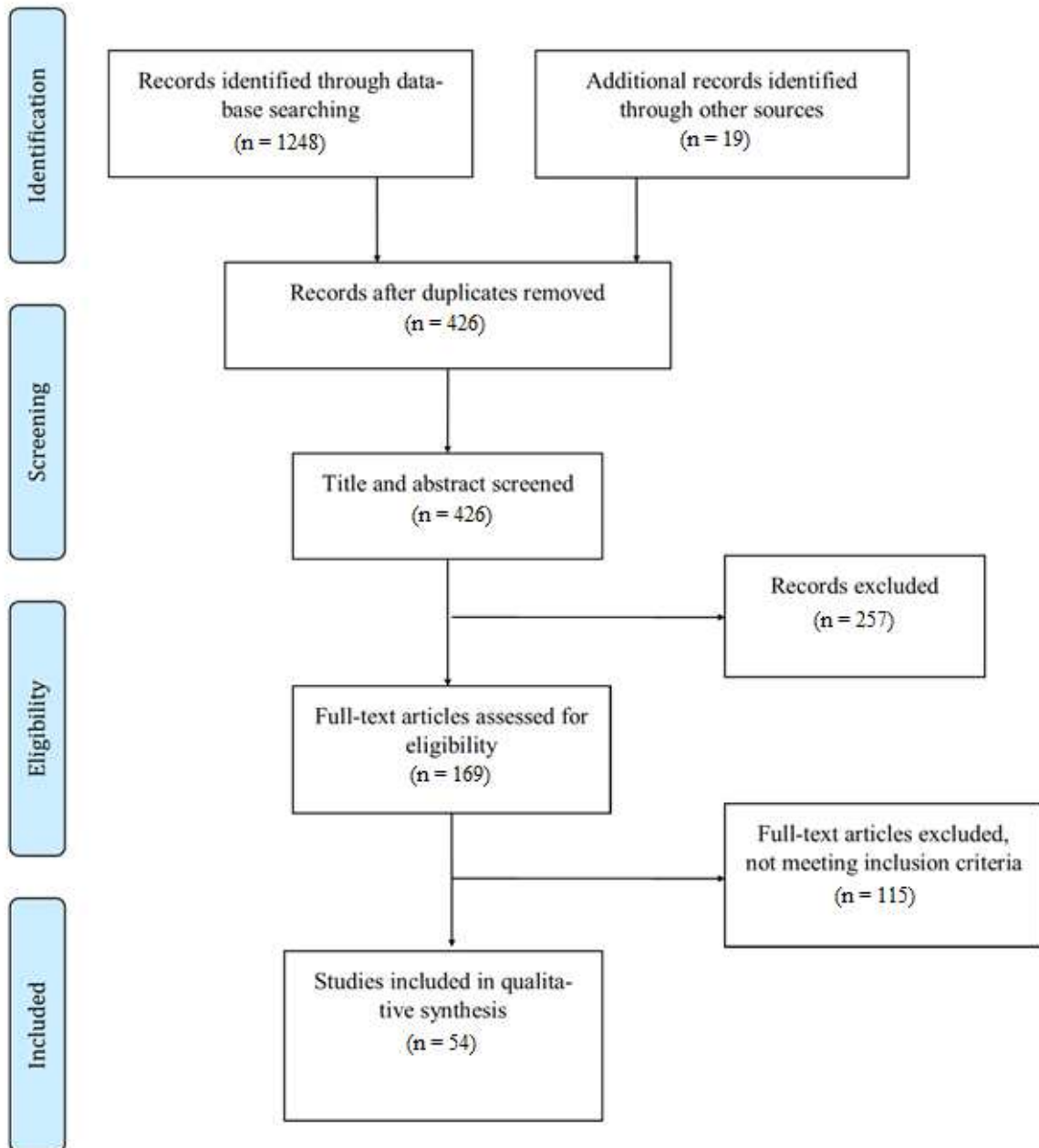


Figure 2: Rates of co-infection with SARS-CoV-2 and influenza virus in COVID-19 children and adult patients.

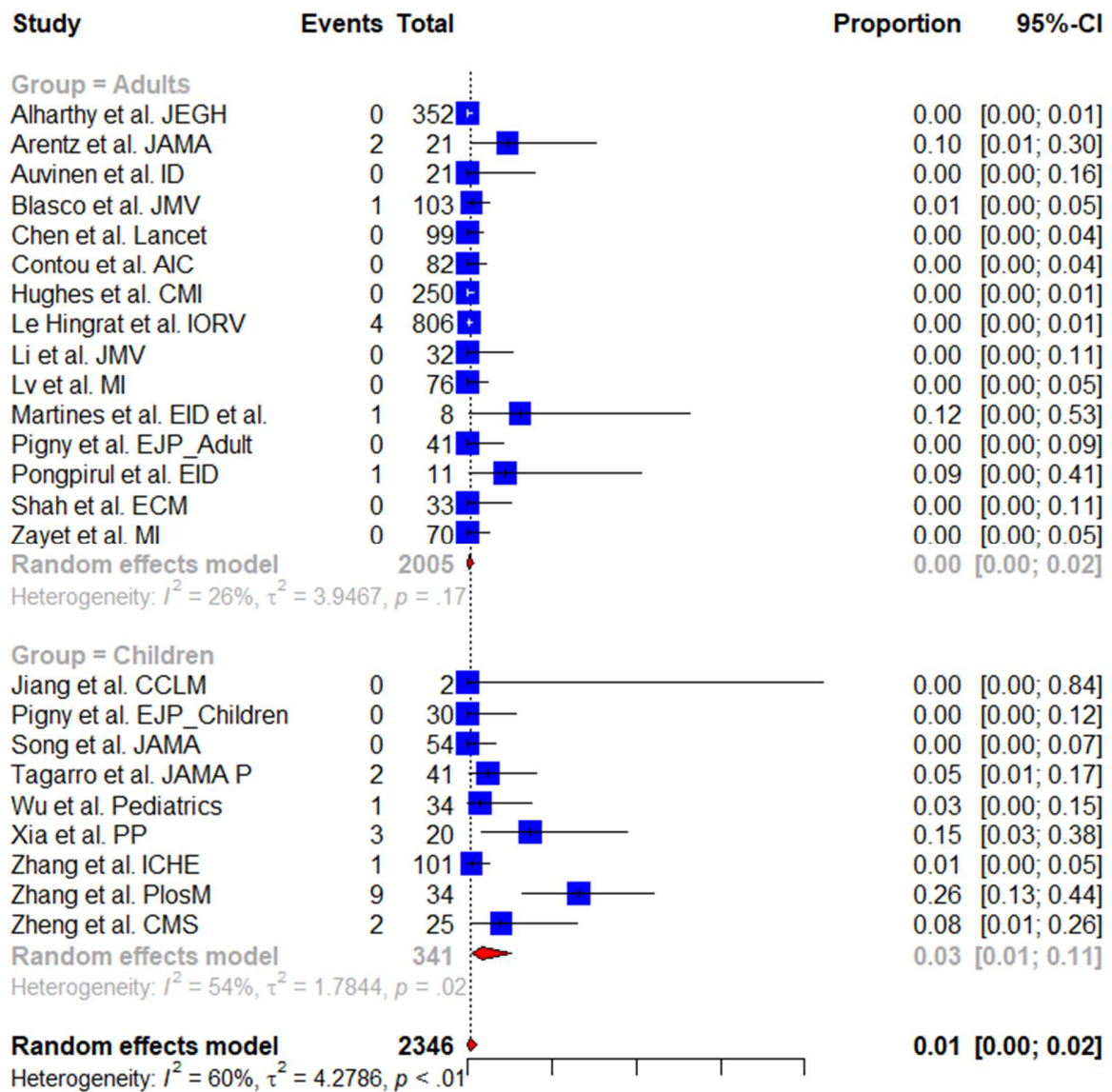


Figure 4: Rates of co-infection with SARS-CoV-2 and influenza virus in total population of patients and in critically ill or deceased patients.

