

Epidemiology of respiratory pathogen carriage in the homeless population within two shelters in Marseille, France, 2015–2017: cross sectional 1-day surveys

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1 **Epidemiology of respiratory pathogen carriage in the homeless population within 2**
2 **shelters in Marseille, France, 2015-2017: Cross sectional one-day surveys**

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14

15 **Running title:** Respiratory pathogens in sheltered homeless people

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19

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24 **Abstract**

25 **Objectives.** To assess risk factors for respiratory tract infection symptoms and signs in sheltered
26 homeless people in Marseille during the winter season, including pathogen carriage.

27 **Methods.** Data on 479 male participants within 2 shelters who completed questionnaires and
28 a total of 950 nasal and pharyngeal samples were collected during the winters of 2015-2017.
29 Respiratory pathogen carriage including 7 viruses and 4 bacteria was assessed by quantitative
30 polymerase chain reaction.

31 **Results.** The homeless population was characterized by a majority of individuals of North
32 African origin (300/479, 62.6%) with a relatively high prevalence of chronic homelessness
33 (175/465, 37.6%). We evidenced a high prevalence of respiratory symptoms and signs
34 (168/476, 35.3%), a very high prevalence of bacterial carriage (313/477, 65.6%), especially
35 *Haemophilus influenzae* (280/477, 58.7%) and a lower prevalence of virus carriage (51/473,
36 10.8%) with human rhinovirus being the most frequent (25/473, 5.3%). Differences were
37 observed between the microbial communities of the nose and throat. Duration of homelessness
38 (OR=1.77, p=0.017), chronic respiratory diseases (OR=5.27, p<0.0001) and visiting countries
39 of origin for migrants (OR=1.68, p=0.035) were identified as independent risk factors for
40 respiratory symptoms and signs. A strong association between virus (OR=2.40, p=0.012) or
41 *Streptococcus pneumoniae* (OR=2.32, p=0.014) carriage and respiratory symptoms and signs
42 was also found.

43 **Conclusions.** These findings allowed identifying the individuals at higher risk for contracting
44 respiratory tract infections to better target preventive measures aiming at limiting the
45 transmission of these diseases in this setting.

46

47 **Introduction**

48 Given their lack of customary and regular access to a conventional dwelling or residence,
49 homeless people reside in the street and/or in shelters. The challenge of poor environmental
50 conditions, poor physical state, smoking habit, alcohol abuse or illicit drug consumption
51 significantly impairs their health status. Behind the frequent association with mental disease
52 and unintentional injuries, homeless people are also predisposed to infectious diseases,
53 especially respiratory infections such as tuberculosis and pneumonia [1]. A high prevalence of
54 chronic respiratory diseases was recorded in the homeless, including bronchitis, asthma and
55 chronic obstructive pulmonary disease [2]. Respiratory diseases are frequently associated with
56 death among homeless individuals [3]. Pulmonary tuberculosis is frequent in the homeless
57 population and has been extensively studied [4, 5].

58 In Marseille, there are an estimated 1500 homeless individuals including more than 800
59 sleeping in the street and approximately 600 living temporarily at the 2 main shelters of the
60 city [6]. Infectious diseases are frequent among Marseille's sheltered homeless people,
61 including lice and *Bartonella quintana* infection, hepatitis E and C, *Tropheryma whipplei*
62 infection, skin infections and respiratory tract infections [7]. A 50% rate of respiratory
63 symptoms and signs was observed in this population, in winter 2005 [8]. About 8.7% carried
64 at least one respiratory virus, with rhinovirus being the most frequent when sampled during
65 the winters of 2010-2011 [9]. These preliminary finding demonstrated that respiratory
66 infections might be frequent among sheltered homeless people in Marseille, warranting
67 further investigation.

68 We described socio-demographic characteristics, underlying chronic medical conditions and
69 addictions, clinical respiratory symptoms and signs, and prevalence of respiratory viruses and
70 bacteria (other than *Mycobacterium tuberculosis*) in the homeless population in 2 shelters of
71 Marseille over the 2015-2017 period of time and investigated potential risk factors.

72 The main objective of the study was the assessment of risk factors for respiratory tract
73 infection symptoms and signs in sheltered homeless people during the French winter season,
74 including pathogen carriage. We hypothesize that carriage of viral pathogens may be
75 associated with clinical signs and symptoms since it is admitted that the vast majority of
76 respiratory infections in adults are caused by rhinoviruses, coronaviruses and influenza
77 viruses [10]; whereas carriage of bacterial pathogens may not necessarily be associated with
78 clinical signs and symptoms since bacterial microorganisms that are potential aetiological
79 agents of respiratory tract infections are also part of the resident microbiome [11]. The
80 secondary objective was to investigate the possible association between viral-bacterial co-
81 carriage or dual bacterial infections and respiratory symptoms and signs, since the pathogenic
82 role of respiratory viruses in virus-bacteria co-infected patients remains unclear [12] and
83 because interspecies interactions in patients infected with several respiratory bacteria is
84 suspected [13].

85 **Methods**

86 **Study population and data collection.** Ethical approvals were obtained from the Institutional
87 Review Board and Ethics Committee of Marseille (2010-A01406-33). Cross sectional one-day
88 surveys were organized on February 17, 2015, March 7-10, 2016 and February 6-8, 2017 in 2
89 shelters (A and B) in Marseille, France, housing 600 homeless persons, for the night only, with
90 a high turnover. Shelter A has a special (day-night) unit with a 35-bed capacity, dedicated to
91 high-risk sedentary homeless people who are characterized by a high level of poverty, poor
92 hygiene, alcoholism and mental illness. Adult homeless people were recruited on a voluntary
93 basis. A medical doctor administered a standardized questionnaire addressing demographics,
94 chronic medical conditions, chronic respiratory disease (CRDs) status (defined as suffering
95 from one of the following conditions: asthma, chronic obstructive pulmonary disease,
96 occupational lung diseases and pulmonary hypertension), substance abuse, vaccination status,

97 symptoms and signs (cough, expectoration, rhinorrhea, dyspnea, sore throat, sibilants, rhonchi,
98 crackles, headache, myalgia, conjunctivitis, fever) at enrollment and physically examined the
99 participants. All patients signed an informed consent. The homeless people screened were
100 offered treatment or further evaluation based on the symptom assessment, since qPCR data
101 were obtained long after the surveys were done.

102 **Respiratory specimens.** Nasal and pharyngeal swabs were collected from each participant,
103 transferred to Sigma-Virocult® medium and stored at -80°C. The DNA and RNA extractions
104 were concurrently performed using the EZ1 Advanced XL (Qiagen, German) with the Virus
105 Mini Kit v2.0 (Qiagen) according to the manufacturer's recommendation. All quantitative
106 real-time PCR (qPCR) reactions were performed using a C1000 Touch™ Thermal Cycle
107 (Bio-Rad, USA). Negative control (PCR mix + sterilized water) and positive control (DNA
108 from bacterial strain or RNA from viral strain) were included in each run. Positive results of
109 bacteria or virus amplification were defined as those with a cycle threshold (CT) value ≤ 35 .
110 Patients having at least one nasal or pharyngeal positive sample were considered positive
111 cases.

112 **Identification of respiratory bacteria.** Real-time PCR amplifications were carried out by
113 using LightCycler® 480 Probes Master kit (Roche diagnostics, France) according to the
114 manufacturer's recommendations. The *SHD* gene of *Haemophilus influenzae*, *phoE* gene of
115 *Klebsiella pneumoniae*, *NucA* gene of *Staphylococcus aureus*, and *lytA* gene of *Streptococcus*
116 *pneumoniae* were detected with internal controls T4 phage as previously described [14, 15]

117 **Identification of respiratory viruses:** One-step duplex qRT-PCR amplifications by
118 HCoV/HPIV-R Gene Kit (REF: 71-045, Biomerieux®, France) were used for the detection of
119 human coronavirus (HCoV) and human para-influenzavirus (HPIV), according to the
120 manufacturer's recommendations. One-step simplex real-time qRT-PCR amplifications were
121 performed by using Multiplex RNA Virus Master Kit (Roche diagnostics, France) for

122 influenza A (FLUA), influenza B (FLUB), human rhinovirus (HRV), human
123 metapneumovirus (HMPV), human respiratory syncytial virus (HRSV) and internal controls
124 MS2 phage [14]. HCoV positive samples were further screened for HCoV-HKU1, HCoV-
125 NL63, HCoV-229E, and HCoV-OC43 [16].

126

127 **Statistical analysis**

128 Statistical analysis was conducted using STATA software (version 11.1). Differences in the
129 proportions (percentages and odds ratio (OR) with 95% confidence interval (CI) estimations)
130 were tested by Pearson's chi-square or Fisher's exact tests when appropriate. Two-tailed tests
131 were used for comparisons. Univariate analysis was used to examine unadjusted associations
132 between multiple factors (demographic, chronic medical condition), respiratory symptoms or
133 physical finding and prevalence of respiratory pathogen carriage. A p value <0.05 was
134 considered statistically significant. Only the variables with a prevalence $\geq 5.0\%$ were
135 considered for statistical analysis. Variables with p values of <0.2 from the univariate analysis
136 were included in the multivariate analysis. Analysis of multicollinearity among the
137 independent variables was performed using the phi coefficient to test for correlation among
138 binary variables; and for pairs of variables that were highly correlated (Absolute value of
139 correlation coefficient >0.7), only one variable was entered into the multivariate model.
140 Multivariable logistic regression (created by step-wise regression) was used to determine
141 factors associated with respiratory symptoms and signs. Log likelihood Ratio Tests were
142 performed to determine these multivariable modeling.

143

144 **Results**

145 Since only 2 women were identified, they were excluded. Of the 479 male individuals who
146 answered the questionnaire and signed consent forms, 477 patients agreed to undergo nasal or
147 pharyngeal sampling. About 11550 qPCR reactions were performed.

148 **Characteristics and clinical status of the homeless participants**

149 The socio-demographic characteristics, substance abuse, chronic disease and clinical features of
150 participants are shown in Table 1 and Figure 1. The population was characterized by middle-
151 aged males (43.6 ± 16 years old) of North African origin, with a relatively high proportion of
152 chronic homelessness (more than one year) reported by 37.2% of individuals and with a 61.2%
153 prevalence of tobacco smoking. About 8% reported suffering from CRDs. The prevalence rate
154 of at least one respiratory symptom or sign was of 35.3% with cough, rhinorrhea and dyspnea as
155 the most frequent symptoms. Most symptomatic individuals (70.8%, 119 out of 168) were
156 smoking tobacco or suffering from CRDs.

157 **Prevalence of respiratory pathogens by real-time PCR**

158 We evidenced a high prevalence of respiratory carriage of bacteria (65.6%, 313 of 477),
159 notably, the proportion of individuals colonized by *H. influenzae* in nasal and/or pharyngeal
160 swabs was of 58.7% (n=280) and that of *S. pneumoniae* was of 12.4% (n=59). Fifty-one
161 patients (10.8%) were also tested positive for at least one virus by qRT-PCR. When comparing
162 nasal and pharyngeal sampling sites, we found that *H. influenzae* was significantly more
163 frequently detected in pharyngeal samples compared to nasal samples, while the prevalence of
164 *S. aureus* and HRV in nasal samples was significantly higher than in pharyngeal samples
165 (shown in Table 2). Co-infections were frequently observed with the most frequent being *H.*
166 *influenzae*-virus and *H. influenzae*-*S. pneumoniae* co-infections (Table 1).

167 **Association between demographics, chronic medical conditions, respiratory pathogen** 168 **carriage and clinical findings according to respiratory symptoms and signs in univariate** 169 **analysis and multivariate analysis**

170 Respiratory symptom and signs prevalence significantly increased with the duration of
171 homelessness (Table 1). The prevalence of symptoms and signs was higher in individuals ≥ 50
172 years of age, suffering from chronic respiratory diseases and in individuals born in France but

173 was lower in individuals born in Sub-Saharan Africa. Among migrants, the symptom and sign
174 prevalence was significantly higher in those visiting their country of origin compared to others.
175 Individuals carrying at least one virus, *S. pneumoniae* or *H. influenzae*-*S. pneumoniae* co-
176 infection were more likely to present with at least one respiratory symptom or sign. In the
177 multivariate analysis, only individuals experiencing chronic homelessness (OR=1.77 [1.11-
178 2.83], p=0.017), those visiting their country of origin (OR=1.68 [1.04-2.71], p=0.035), those
179 suffering from chronic respiratory diseases (OR=5.27 [2.24-12.41], p<0.0001), and those
180 carrying at least one virus (OR=2.40 [1.21-4.74], p=0.012) or *S. pneumoniae* (OR=2.32 [1.18-
181 5.3], p=0.014) remained associated with an increased prevalence of respiratory symptoms and
182 signs (Table 3). Overall, individuals carrying at least one virus were more likely to present with
183 cough, expectoration, rhinorrhea and sore throat. Carriage of *S. pneumoniae* was associated
184 with cough (Table 4).

185 **Discussion**

186 The sheltered homeless population in our study was characterized by a high proportion of
187 migrants of North African origin with a high prevalence of smoking habits and CRDs. We
188 observed a high prevalence of respiratory symptoms and signs (35%) in line with the results of
189 a survey conducted in Italy and The Netherlands [17, 18]. Dry or productive cough, rhinorrhea
190 and dyspnea were the symptoms most frequently observed, suggesting that both upper and
191 lower tract respiratory infections affect a significant proportion of sheltered homeless people
192 during winter. We found relatively low rates of influenza virus infections. Cross sectional
193 surveys took place when influenza was epidemic in the region of Marseille. Influenza
194 vaccination rate in the homeless population screened in our surveys was in the same range in
195 Marseille's overall population [19, 20]. This result may indicate that the social isolation of
196 homeless people might have a protective impact against community influenza virus
197 transmission. One of the most important findings of this study is the very high prevalence of

198 bacterial colonization by respiratory bacteria with *H. influenzae* (59%), and *S. pneumoniae*
199 (13%), which were the most frequent. A high prevalence of *H. influenzae* carriage (70%) was
200 also observed by direct PCR, in healthy infants from the Western region of Gambia [21] and a
201 rate of 40.9% was reported among children aged ≤ 6 years in day-care centers in eastern France
202 [22]. In surveys conducted among healthy adults in the Australian Aboriginal population, the
203 prevalence of non-typeable *H. influenzae* reached approximately 22.9% when culturing
204 nasopharyngeal samples [23]. A 2.3% *H. influenzae* nasal prevalence was observed in
205 Marseille's individuals originating from North-Africa by qPCR in 2013 [17], however, the
206 survey was conducted in October, which may account for a lower prevalence, as shown in
207 another healthy Italian children population [24]. *K. pneumoniae* naso-pharyngeal carriage rates
208 have been reported to range from 3 to 15%, which is in agreement with our results [25]. This
209 bacterium is known to be frequently multidrug-resistant [25] and further studies on drug
210 resistance in bacteria isolated from homeless people would be of interest.

211 We identified chronic homelessness, chronic respiratory diseases and visiting countries of
212 origin for migrants as independent risk factors for respiratory symptoms and signs. We
213 found a strong association between virus or *S. pneumoniae* carriage and respiratory symptoms
214 and signs, reinforcing the need to increase vaccination rates in this population.

215 Additionally, data obtained in this study emphasizes the difference between the microbial
216 communities of the nose and throat, indicating the need for both nasal and pharyngeal swabs
217 sampling in future studies to better assess upper respiratory microbiological carriage.

218 Our study has several limitations. The first is that we did not use a control group for
219 evaluation of background carriage in the healthy adult population. The second limitation is
220 that our survey took place in winter, so we could not have an overview about seasonal
221 variations of carriage in the homeless, whereas it was demonstrated to have impacted the
222 airway microbial community in adults and children [24, 26]. Future studies will be conducted

223 at least twice a year (in winter and in summer). The questionnaire design did not allow a clear
224 distinction between acute (short-term) and chronic (going on) respiratory symptoms which
225 needs to be considered in further studies. Finally, the level of precariousness of the homeless
226 was limited to the duration of homelessness and more detailed information should be recorded
227 in future studies.

228 In summary, we confirm the high prevalence of respiratory symptoms and signs in sheltered
229 homeless people associated with a high level of bacterial carriage in the respiratory tract.
230 Several risk factors for respiratory symptoms and signs were identified, allowing a better
231 identification of individuals at higher risk on whom to base targeted preventive interventions,
232 including notably vaccination against influenza and *S. pneumoniae* infections. Such an approach
233 has proven effective in identifying individuals at higher risk for body lice in the same
234 population [27] and the results of our study will benefit to homeless people in the future.

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239 **Potential conflicts of interest**

240 No reported conflicts of interest.

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243 recruiting, interviewing and examining participants and collecting samples, as well as
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320 **Table 1. Risk factors for respiratory disease: univariate analysis**

Characteristics	Total (N)	At least one respiratory symptom or sign N (%)	No respiratory symptom and no sign N (%)	Univariate analysis Odds ratio (95%CI), p-value
Total		168 (35.3)	308(64.3)	
Year of study*				
2015	125 (26.1)	37 (29.6)	88 (70.4)	
2016	156 (32.6)	74 (47.4)	82 (52.6)	
2017	198 (41.3)	57 (29.2)	138 (70.8)	
Shelter				
A	311 (64.9)	107 (35.2)	201 (65.3)	0.93 [0.63-1.38], p=0.73
B	168 (35.1)	61 (36.3)	107 (63.7)	Ref
Age				
Mean age (SD)	43.6±16 years	NA		
Age range	18-84 years	NA		
≤50 years of age	318 (66.8)	98 (30.8)	220 (69.2)	Ref
>50 years of age	158 (33.2)	69 (44.2)	87 (55.8)	1.78 [1.20-2.64], p=0.004
Birthplace				
France (mainland)	71 (14.8)	39 (54.9)	32 (45.1)	Ref
France (overseas territories)	1 (0.2)	0 (0)	1 (100)	NA
North Africa	300 (62.6)	100 (33.4)	199 (66.6)	0.41 [0.25-0.70], p=0.001
Sub-Saharan Africa	43 (9.0)	7 (16.3)	36 (83.7)	0.16 [0.63-0.41], p<0.0001
East Europe	35 (7.3)	13 (39.4)	20 (60.6)	0.53 [0.23-1.24], p=0.14
West Europe	9 (1.9)	2 (22.2)	7 (77.8)	0.23 [0.04-1.21], p=0.08
Asia	20 (4.2)	7 (35.0)	13 (65.0)	0.44 [0.16-1.24], p=0.12
Other	0 (0)			NA
Mean duration of residence in France (SD)				
9.88 (0-25.4)		NA	NA	
Range of duration of residence in France				
0-65 years		NA	NA	
≥ 1 year	220 (55.3)	79 (35.9)	141 (64.1)	1.52 [0.99-2.32], p=0.06
< 1 year	178 (44.7)	48 (27.0)	130 (73.0)	Ref
Visit to country of origin since immigration				
126 (31.9)		51 (40.5)	75 (59.5)	1.76 [1.13-2.74], p=0.012
No visits to country of origin since immigration				
269 (68.1)		75 (27.9)	194 (72.1)	Ref
Mean duration of homelessness (SD)				
2.66 years (0-7.8)		NA	NA	
Range of duration of homelessness				
0-52 years				

≥ 1 year	175 (37.6)	80 (45.7)	95 (70.6)	2.02 [1.37-2.99], p<0.0001
<1 year	290 (62.4)	85 (29.4)	204 (70.6)	Ref
Addiction				
Alcohol				
Frequent	52 (10.9)	24 (47.1)	27 (52.9)	1.75 [0.98-3.14], p=0.06
Rare or never	424 (89.1)	143 (33.7)	281 (66.3)	Ref
Tobacco				
Yes	293 (61.2)	113 (38.7)	179 (61.3)	1.48 [1.00-2.20], p=0.05
Never	185 (38.7)	55 (30.3)	129 (70.1)	Ref
Cannabis	75 (15.7)	28 (37.3)	47 (62.7)	1.11 [0.67-1.85], p=0.69
Injected substances	2 (0.4)	0 (0)	2 (100)	
Snorted substances	13 (2.7)	4 (30.8)	9 (66.2)	
Drug substitutes	1 (0.2)	1(100)	0 (0)	
Chronic diseases				
Chronic respiratory diseases	38 (8.1)	27 (71.0)	11 (28.9)	5.12 [2.47-10.62], p<0.0001
Diabetes mellitus	36 (7.6)	14 (38.9)	22 (61.1)	1.18 [0.59-2.37], p=0.65
Cancer	5 (1.1)	1 (20)	4 (80)	
Hepatitis	10 (2.1)	8 (80)	2 (20)	
Body mass index				
Mean body mass index	24.4 ± 4.0 (kg/m ²)	NA	NA	
Range of Body mass index				
Normal weight	251 (55.9)	86 (34.3)	165 (65.7)	Ref
Underweight	17 (3.8)	9 (52.9)	8 (47.1)	0.46 [0.17-0.24], p=0.12
Overweight	138 (30.7)	47 (34.1)	91 (65.9)	1.00 [0.65-1.56], p=0.97
Obesity	43 (9.6)	12 (27.9)	31 (72.1)	1.35 [0.65-2.75], p=0.41
Seasonal vaccination against influenza	71 (15.1)	31 (43.7)	40 (56.3)	1.50 [0.90-2.5], p=0.12
Respiratory carriage				
<i>Haemophilus influenzae</i>	280 (59.6)	90 (32.4)	189 (67.7)	0.73 [0.50-1.08], p=0.11
<i>Streptococcus pneumoniae</i>	59 (12.4)	32 (54.2)	27 (45.8)	2.45 [1.42-4.29], p= 0.001
<i>Staphylococcus aureus</i>	35 (7.3)	10 (26.8)	25 (71.4)	0.72 [0.33-1.53], p=0.4
<i>Klebsiella pneumoniae</i>	35 (7.3)	11 (31.4)	24 (68.6)	0.83 [0.40-1.75], p=0.63
At least one virus	51 (10.8)	26 (51)	25 (49)	2.09 [1.17-3.49], p=0.012
Human rhinovirus	25 (5.3)	11 (44)	14 (56)	1.48 [0.65-3.34], p=0.34
Human coronavirus	10 (2.1)	5 (50)	5 (50)	
Influenza A	7 (1.5)	4 (57.1)	3 (42.9)	
Influenza B	7 (1.5)	5 (71.4)	2 (28.6)	

Human respiratory syncytial virus	3(0.6)	1(33.3)	2 (66.6)	
Human para-influenza virus	1(0.2)	1(100)	0	
Human metapneumovirus	0	0	0	
Co-infection				
<i>H. influenzae</i> + <i>S. pneumoniae</i>	43 (9.0)	24 (55.8)	19 (44.2)	2.55 [1.35-4.82], p=0.003
<i>H. influenzae</i> + virus	33 (7.0)	14 (42.2)	19 (57.6)	1.4 [0.68-2.85], p=0.36
<i>H. influenzae</i> + <i>K. pneumoniae</i>	25 (5.2)	6 (24)	19 (76)	0.57 [0.22-1.45], p=0.23
<i>H. influenzae</i> + <i>S. aureus</i>	24 (5.0)	8 (33.3)	16 (66.7)	0.92 [0.38-2.19], p=0.85
<i>S. pneumoniae</i> + virus	12(2.5)	9 (75)	3 (25)	
<i>S. pneumoniae</i> + <i>S. aureus</i>	9 (1.9)	4(44.4)	5(55.6)	
<i>S. pneumoniae</i> + <i>K. pneumoniae</i>	5 (1.0)	3 (60)	2 (40)	
<i>S. aureus</i> + <i>K. pneumoniae</i>	4 (0.8)	0	4(100)	
<i>S. aureus</i> + virus	4 (0.8)	3 (75)	1 (25)	

321 Abbreviations: SD, standard deviation; NA, not applicable, Ref, Reference category

322 *Year of study was not included in the analysis, given that no intervention could be done based on this criterion.

323

324 **Table 2. Prevalence (%) of bacteria and viruses detected by qPCR**

Respiratory pathogen	Positive carriage			
	Nasal specimen, N (%)	Pharyngeal specimen, N (%)	p-value	Nasal or pharyngeal, N (%)
Total	476 (100)*	474 (100)*		477 (100)*
Bacteria	105 (22.1)	280 (59.1)	<0.0001	313 (65.6)
<i>Haemophilus influenzae</i>	46 (9.8)	266 (56.4)	<0.0001	280 (58.7)
<i>Klebsiella pneumoniae</i>	17 (3.5)	20 (4.2)	0.61	35 (7.3)
<i>Staphylococcus aureus</i>	28 (5.9)	12 (2.5)	<0.001	35 (7.3)
<i>Streptococcus pneumoniae</i>	33 (7.0)	36 (7.6)	0.69	59 (12.4)
Virus	34 (7.1)	24 (5.1)	0.18	51 (10.8)
Influenza A	4 (0.8)	4 (1.0)	-	7 (1.5)
Influenza B	4 (0.8)	6 (1.3)	-	7 (1.5)
Human rhinovirus	20 (4.3)	7 (1.5)	<0.001	25 (5.3)
Human respiratory syncytial virus	1 (0.2)	2 (0.4)	-	3 (0.6)
Human metapneumovirus	0 (0)	0 (0)	-	0 (0)
Human coronavirus	5 (1.1)	5 (1.1)	0.99	10 (2.1)
HCoV-HKU1	0 (0)	1 (0.2)	-	1 (0.2)
HCoV-E229	3 (0.6)	1 (0.2)	-	4 (0.8)
HCoV-NL63	1 (0.2)	0 (0)	-	1 (0.2)
HCoV-OC43	1 (0.2)	3 (0.6)	-	4 (0.8)
Human para-influenza virus	0 (0)	1 (0.2)	-	1 (0.2)

325 *473 patients had both nasal and pharyngeal sampling; 3 patients had only nasal swabs and 1 patient had only
326 pharyngeal swabs. Patients having at least one nasal or pharyngeal positive sample were considered positive
327 cases.

328 **Table 3. Risk factors for respiratory disease: multivariate analysis**

Characteristics*	Multivariate analysis Odds ratio (95%CI), p-value
Age ≥ 50 years vs others	-
Birthplace	-
Range of duration of residence in France ≥ 1 year vs others	-
Visit to country of origin since immigration	1.68 [1.04-2.71], p=0.035
Range of duration of homelessness ≥ 1 year vs others	1.77 [1.11-2.83], p=0.017
Alcohol	-
Tobacco	-
Chronic respiratory diseases	5.27 [2.24-12.41], p<0.0001
Seasonal vaccination against influenza	-
Respiratory pathogen	
<i>Haemophilus influenzae</i>	-
<i>Streptococcus pneumoniae</i>	2.32 [1.18-5.3], p=0.014
At least one virus	2.40 [1.21-4.74], p=0.012
<i>H. influenzae</i> + <i>S. pneumoniae</i> co-infection	-

329 Abbreviations: vs, versus

330 * Only variables with p values of <0.2 in the univariate analysis and with a paired correlation coefficient < 0.7 were included in
331 the multivariate analysis.

332 **Table 4. Association between respiratory pathogen carriage and clinical findings in**
 333 **univariate analysis according to respiratory symptoms and signs**

Respiratory pathogen	Odds ratio (95%CI), p-value				
	Cough	Expectoration ^a	Rhinorrhea ^a	Dyspnea	Sore throat
<i>Streptococcus pneumoniae</i>	2.5 [1.41-4.41], p=0.001	1.3 [0.59-2.95], p=0.51	1.03 [0.3-3.59] p=0.965	1.10 [0.41-2.95] p=0.85	1.13 [0.38-3.37], p=0.83
At least one virus	2.5 [1.37-4.58], p=0.002	2.15 [1.01-4.60] p=0.044	2.5 [1.00-6.12], p=0.047	1.68 [0.66-4.24], p=0.27	7.3 [3.26-16.42], p<0.0001

334

335 **Figure 1. Prevalence of clinical signs and symptoms over the 2015-2017 period (N=479**
336 **individuals).**

337 Abbreviations: CRDs, chronic respiratory diseases.

