

Characteristics of human metapneumovirus infection in adults hospitalized for community-acquired influenza-like illness in France, 2012-2018: a retrospective observational study

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1 2 3	Characteristics of Human Metapneumovirus Infection in Adults Hospitalized for Community-acquired Influenza-Like Illness in France, 2012-2018: a retrospective observational study
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44 Abstract

Objectives. To describe the prevalence, clinical features and complications of human
metapneumovirus (hMPV) infections in a population of adults hospitalized with influenza-like
illness (ILI).

48 Methods. This was a retrospective, observational, multicenter cohort study using prospectively collected data from adult patients hospitalized during influenza virus circulation, 49 for at least 24h, for community-acquired ILI (with symptom onset <7 days). Data were 50 51 collected from five French teaching hospitals over six consecutive winters (2012-2018). 52 Respiratory viruses were identified by multiplex RT-PCR on nasopharyngeal specimens. 53 hMPV+ patients were compared to hMPV- patients, influenza+ and respiratory syncytial virus (RSV)+ patients using multivariate logistic regressions. Primary outcome was the 54 prevalence of hMPV in patients hospitalized for ILI. 55

Results. Among the 3148 patients included (1449 (46%) women, 1988 (63%) aged 65 and 56 over; 2508 (80%) with chronic disease), at least one respiratory virus was detected in 1604 57 (51%, 95%CI [49-53]), including 100 cases of hMPV (100/3148, 3% 95%CI [3-4]), of which 58 10 (10%) were viral co-infection. In the hMPV+ patients, mean length of stay was 7 days, 59 62% (56/90) developed a complication, 21% (14/68) were admitted to intensive care unit and 60 4% (4/90) died during hospitalization. In comparison with influenza+ patients, hMPV+ 61 patients were more frequently > 65 years old (aOR=3.3, 95%CI[1.9-6.3]) and presented more 62 acute heart failure during hospitalization (aOR=1.8, 95%CI[1.0-2.9]). Compared to RSV+ 63 patients, hMPV+ patients had less cancer (aOR=0.4, 95%CI[0.2-0.9]) and were less likely to 64 65 smoke (aOR=0.5, 95%CI[0.2-0.9]) but had similar outcomes especially high rate of respiratory and cardiovascular complications. 66

67 Conclusions. Adult hMPV infections mainly affect the elderly and patients with chronic
68 conditions and are responsible for frequent cardiac and pulmonary complications similar to

- 69 those of RSV infections. At-risk populations would benefit from the development of antivirals
- 70 and vaccines targeting hMPV.
- 71 Key words: human Metapneumovirus; Influenza; Respiratory Syncytial Virus; Adults

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Journal Prevention

73 Introduction

During winter, community-acquired influenza-like illness (ILI), mostly caused by respiratory 74 75 viruses, is very common. The most frequent viruses seen in primary care are influenza viruses A/B, rhinovirus, coronavirus, respiratory syncytial virus (RSV) and human 76 metapneumovirus (hMPV) [1,2]. In the hospital setting, adults with ILI are commonly tested 77 only for influenza, resulting in limited data concerning other respiratory viruses. The use of 78 79 multiplex RT-PCR allows identification of multiple viruses simultaneously but remains a second-line test in non-immunocompromised patients in emergency departments because of 80 81 its cost and the limited therapeutic options [3].

Human MPV, discovered in 2001, is phylogenetically similar to RSV and has been frequently 82 83 found associated with respiratory tract illnesses [1,4,5]. Its circulation occurs with a seasonal distribution from January to March in the Northern hemisphere, often overlapping or following 84 85 RSV infection season [6,7]. Human MPV is a major pediatric respiratory pathogen [8] but can affect all age groups, especially persons with chronic conditions [9], leading to diverse 86 87 clinical presentation from upper respiratory tract symptoms to severe pneumonia [10,11]. 88 While hMPV is known to contribute substantially to the burden of wintertime respiratory illnesses in adults [12], data on its frequency and comparison to other respiratory viruses in 89 large adult populations are scarce. 90

91 We aimed to (i) describe the clinical characteristics and outcome of hMPV infection and (ii) 92 compare hMPV to influenza and RSV infections in adults hospitalized for community-93 acquired ILI in France in winter between 2012 and 2018.

95 Methods

96 Study design

We performed a post-hoc, retrospective analysis of the FLUVAC study. FLUVAC is a French 97 prospective case-test negative design study evaluating influenza vaccine effectiveness on 98 influenza-associated hospitalization conducted in five (2012/13, 2015/16 to 2017/18) or six 99 (2013/14 to 2014/15) teaching hospitals. All adults hospitalized for at least 24 h for ILI during 100 101 influenza circulation period, with symptom onset <7 days before screening, were included in FLUVAC. ILI was defined according to the European Centre for Disease Prevention and 102 103 Control (ECDC) definition [13] as a combination of the following: (a) at least one of the 104 following systemic symptoms: fever or feverishness, headache, myalgia or malaise, and (b) 105 at least one of the following respiratory symptoms: cough, sore throat or dyspnea. Patient with contra-indication for influenza immunization, those who had previously tested positive 106 107 for influenza virus in the same season and those without French social security affiliation were excluded. Each participant was interviewed, and nasopharyngeal samples were 108 obtained at enrolment to screen for influenza and other respiratory viruses. 109

110 In the present study, we included all the patients from the first six FLUVAC seasons 111 (2012/13, 2013/14, 2014/15, 2015/16, 2016/17, 2017/18) for whom virologic results on 112 respiratory viruses were available (Figure 1).

113

114 Outcomes

115 The primary outcome was the prevalence of confirmed hMPV infection in patients 116 hospitalized with ILI. Secondary outcomes were the demographic characteristics, chronic 117 underlying diseases and treatments, clinical presentation of the ILI episode and 118 complications, intensive care unit admission or death in patients with hMPV infections.

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125 Microbiological data

Respiratory viruses were identified using multiplex RT-PCR performed on nasopharyngeal 126 swabs. Clinical bronchoalveolar lavage fluid samples and tracheal aspirates were also 127 tested. Samples were first tested in the virology laboratory of each participating hospital 128 using real-time (RT) influenza A and B PCR after manual nucleic acid extraction. All samples 129 130 were then sent to the French National Influenza Reference Centre (CNR-Lyon) for influenza confirmation and screening for other respiratory viruses (adenoviruses, bocaviruses, hMPV, 131 picornavirus, RSV, coronaviruses, parainfluenza viruses (since 2013)) by RT-PCR using the 132 Respiratory Multiwell System r-gene® on an ABI 7300 analyzer between 2012/13 and 133 2014/15. Since 2015/16, all the virology laboratories of the five sites used the same Eurobio 134 135 kit and only B lineage was provided by the CNR-Lyon.

136

137 Statistical analysis

138 Quantitative variables were expressed as mean and standard deviation (SD) or median and 139 interquartile range (IQR), and qualitative variables as number and percentage. Qualitative 140 variables were compared using the χ^2 and Fisher's exact tests, as appropriate. Quantitative 141 variables were compared by Wilcoxon rank sum test. Missing data for each variable were 142 excluded from the denominator.

Patients with multiple viral infections were excluded from the analyses. Univariate analysis 143 144 was used to asses risk factors for the detection of hMPV infection, influenza infection, RSV infection and acute heart failure. We performed two multivariate analyses using a backward 145 stepwise logistic regression model using hMPV test result (positive/negative) and acute heart 146 147 failure (yes/no) as the dependent variable in the first and second model respectively. 148 Covariates with a p-value <0.2 in univariate analysis were tested in the multivariate model. Results from regression models are expressed as crude odds ratios (OR) and adjusted ORs 149 (aOR) with 95% CI. A p-value of <0.05 was considered statistically significant. Analyses were 150

151 performed using R software (Version 1.1.463).

Ethics 152

- The FLUVAC study (clinicaltrials.gov NCT02027233) followed Good Epidemiological and 153
- 154 Clinical Practices in Clinical Research, and the Declaration of Helsinki, and was approved by
- the regional ethics committees. All the study participants gave their informed consent for 155
- 156 respiratory virus testing.

Results 157

Comparison of hMPV+ and hMPV- patients 158

ound

Of the 3148 patients included in the FLUVAC study, 1604 (51%, 95%CI [49-53]) tested 159 positive for at least one respiratory virus. Most had influenza (1123/1604, 70%, 95%CI [68-160 161 72]), while 167 had picornavirus (10%, 95%CI [9-12]), 145 had RSV (9%, 95%CI [8-10]), 100 had hMPV (6%, 95%CI [5-7]), 38 had adenovirus (2%, 95%CI [2-3]) and 23 had bocavirus 162 (1%, 95%CI [1-2]) (Figure 1 and Table S1). Ten of the 100 hMPV infections (10%) were co-163 infection cases with at least one other virus: 3 with influenza A virus, 1 with coronavirus, 1 164 with both influenza A virus and coronavirus, 2 with picornavirus, 1 with parainfluenza virus, 1 165 166 with adenovirus and 1 with RSV.

Overall, 3% (95%CI[3-4]) of people with ILI symptoms (90/3148) tested positive for hMPV. 167 168 Peak hMPV detection occurred between mid-January and mid-February (Supplementary Figure 1 & 2). While patients with hMPV infections were generally older than those without 169 170 (median age 78 years [IQR 70-86] versus 71 years [IQR 57-83], p<.001), other demographic characteristics were similar. Most patients with hMPV presented at least one chronic 171 172 condition (81%, 73/90), mostly cardiac (50%, 45/90) and respiratory (44%, 40/90) chronic diseases, 17% under immunosuppressive treatment (15/90), 14% active smokers (12/87) 173 and 41% (37/90) hospitalized in the 12 months preceding the study (Table 1). 174

The median time from symptom onset to admission was similar between hMPV+ and hMPVpatients (2 days (IQR, 1-3)) as well as the main symptoms at inclusion except for weakness/malaise that was less frequent in hMPV+ patients (13/90 (14%) vs 27%, p<.007).

There was no difference between hMPV+ and hMPV- groups in terms of median length of stay, number of complications during hospitalization, intensive care unit (ICU) admission and death. However, hMPV+ patients were more likely to have an acute heart failure during hospitalization (25% (22/89) vs 14% (377/2722), p<.004).

182 There was no difference in sociodemographic characteristics, clinical presentation or

183 outcomes between hMPV and viral coinfection and patients with hMPV infections alone.

In the multivariate analysis, when comparing hMPV+ patients to all hMPV- patients, age > 65
years (aOR 95% CI 3.3 [1.9;6.1], p<0.001) was significantly associated with hMPV detection.
In contrast, the sudden onset of symptoms, defined as the occurrence of malaise/weakness,
was associated with the absence of hMPV infection (aOR 95% CI 0.4 [0.2;0.8], p=0.008)
(Table 1).

After adjustment for chronic heart disease, age, gender, smoking status and influenza vaccination, hMPV infection was significantly associated with occurrence of acute heart failure during hospitalization (aOR 95% CI 1.8 [1.1;3.0], p=0.02).

192 Comparison of hMPV and influenza+ patients

In univariate analysis, in comparison to influenza+ patients, hMPV+ patients were older (median age 78 IQR [70-86] versus 69 IQR [54-82] years old, respectively, p<0.001), more vaccinated against influenza (58% versus 39% respectively, p<0.001), presented more dyspnea at inclusion (p=0.05) but less weakness (p=0.01), headache (p=0.01) and sore throat (p=0.008). They were more likely to present acute heart failure during the hospital stay (p=0.002). Other outcomes were not significantly different (**Table 2**).

In the final model from multivariate analysis, in comparison with influenza+ patients, hMPV+
patients were more frequently > 65 years old (aOR 3.3 [1.9-6.3], p<0.001).

201

202 **Comparison of hMPV+ and RSV+ patients**

In univariate analysis, hMPV+ patients had less chronic disease (p=0.04), including chronic renal failure (p=0.04) and cancer (p=0.05) and were less likely to smoke (p=0.05) than RSV+ patients.

In the final multivariate model, in comparison with RSV+ patients, hMPV+ patients had less cancer (aOR=0.4 [0.2-0.9], p=0.02) and were less likely to smoke (aOR=0.5 [0.2-0.9], p=0.04). Clinical presentation and outcomes were similar between the two groups (**Table 2**).

210 **Discussion**

In our post-hoc analysis of 3148 hospitalized adult patients with community-acquired ILI, 211 212 hMPV was found in 3% of the samples. These patients were older, had chronic conditions, frequent respiratory and cardiac chronic diseases, and frequently presented complications. 213 This prevalence is consistent with several studies that found hMPV in 3 to 6% of adult 214 215 patients with lower respiratory tract infection in primary care [1,14–16] and in 6% of patients 216 hospitalized for acute respiratory infection (ARI) [17]. This frequency may vary according to 217 the inclusion criteria, especially temperature cut-off, as hMPV infection frequently causes 218 non-febrile illness [5].

219 Our hospitalized hMPV+ adults were mostly older and/or high risk patients as previously

described in the literature [5,10,18–20]. Complications were frequent (62%), as well as ICU
admission (17%) and death (4%). These rates were similar to those of the 91 hospitalized
patients with hMPV from the Walsh *et al.* study in 2008 in the USA [10], but lower than those
of the 128 critically ill adults with hMPV infection (31% required ICU admission and 8% died)

from the Hasvold *et al.* study in 2016 [20].

The majority of hMPV+ patients presented several respiratory signs (cough, dyspnea), whereas sudden onset of symptoms was associated with the absence of hMPV infection. There were differences in clinical presentation between hMPV+ patients and influenza+ patients (less frequent constitutional symptoms (headache, weakness, myalgia) but more dyspnea) but not between hMPV+ patients and RSV+ patients. These points emphasize the difficulty of distinguishing respiratory viruses based on clinical signs alone and question the relevance of the current ILI definition to detect hMPV infection.

232 Interestingly, we also found that hMPV+ patients were older and presented more chronic

233 cardiac conditions and acute heart failure during the hospitalization than influenza+ patients.

Although, influenza [21] and RSV [22] are known to worsen heart failure, no study has

specifically assessed hMPV [21,22]. In our study, hMPV infection was independently

associated with the occurrence of acute heart failure.

237 Several limitations should be acknowledged. First, we enrolled patients during influenza virus circulation whereas hMPV circulation does not always match that of influenza. Second, we 238 239 had no data to support causality between the detection of hMPV in nasopharyngeal samples and the ILI hospital admission. Other pathogens such as respiratory bacteria may have been 240 involved and hMPV may been a concomitant infectious agent with no role in the symptoms 241 reported. The absence of data on bacteriological results prevents us from addressing this 242 243 issue. Finally, although asymptomatic carriage of hMPV appears to be uncommon [26], we 244 had no control population (i.e. hospitalized adults without ILI symptoms) to help evaluate hMPV pathogenicity. 245

In conclusion, adult hMPV infections concerned 3% of patients hospitalized with ILI in tertiary care hospitals over six consecutive influenza seasons in France. Most of the patients were older, had associated chronic conditions and developed pulmonary and cardiac complications. The relation between hMPV infection and worsening of heart failure needs further investigation. These at-risk populations would benefit from the development of antivirals and vaccines targeting hMPV.

253 Transparency declaration

- The authors declare no competing interest related to the study. P Loubet has received
- 255 personal fees and non-financial support from Pfizer and Sanofi Pasteur. O Launay is an
- 256 investigator for clinical trials sponsored by Janssen, GSK, Pfizer, Sanofi Pasteur and MSD
- and received travel support to attend scientific meetings from pharmaceutical companies.

258 Authors' Contributions

- PL and OL conceptualized the study. PL developed the methodology. PM did the analysis.
- PL and PM wrote the original manuscript. NL, FG, FL, ZL, PV, XD, DP, SA, SR, GL, ASL,
- 261 VF, NH, BL and FC critically reviewed the manuscript. OL supervised the research.

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Table 1. Clinical characteristics and outcomes of hospitalized patients infected with human Metapneumovirus compared to patient without human Metapneumovirus, 2012-2018

	hMPV-	hMPV+	Univariate			Multivariate analysis			
	(n=3048)	(n=90)	analysis	Crude OR		p-value Adju		Adjusted OR	p-value
Baseline characteristics									
Gender			0.00		[4 0 0 0]				
women, n (%)	1390/3048 (46%)	50/90 (56%)	0.06	1.5	[1.0;2.3]	0.08			
Men, n (%)	1658/3048 (54%)	40/90 (44%)							
Age	71 (50 02)	70 (70 00)	-0.001						
Median age, years (IQR)	/1 (50-82)	78 (70-86)	<0.001	2.0		0.001	2.2	[1.0.0.1]	-0.001
Age > 65, ft (%) Modian BML $k_{\rm fr}$ (kOD)	1904/3048 (62%)	76/90 (84%) 24.9 (21.5.29.5)	<0.001	2.9	[1.6;5.7]	0.001	3.3	[1.9;6.1]	<0.001
median bivil, kg/m2 (IQK)	24.8 (21.5 - 28.5)	24.8 (21.5 - 28.5)							
	641/2020	12/07/140/)	0.07	0.0		0.94			
Sinoker, $n (\%)$	041/2938	12/8/(14%)	0.07	0.9	[0.5;1.7]	0.84			
Non smoker, n (%)	9/3/2938	28/87 (32%) 17/97 (E10/)	0.93						
Chronic diseases (at least and) n (%)	1324/2330	72/00 (91%)	0.12						
Chronic diseases (at least one), it (%)	2428/3048 (80%) 1261/2048 (4E%)	/3/90 (81%)	0.74						
Chronic heart disease, n (%)	1301/3040 (43%)	40/90 (44%) 45/00 (50%)	0.90	1 1	[0 7.1 9]	0.57			
Diabotos n (%)	714/2048 (22%)	43/90 (30%)	0.12	1.1	[0.7,1.0]	0.57			
Chronic ronal failure n (%)	/14/3040 (23%) /68/20/8 (15%)	10/90(20%)	0.32	0.5	[0 2.1 0]	0.08			
Cancor n (%)	400/3040 (1370) 515/2048 (17%)	$\frac{3}{30}(10\%)$	0.17	0.5	[0.2,1.0]	0.08			
Cirrhosis n (%)	109/3035 (1%)	13/90 (14/0)	0.45						
Immunosunnressive treatment n (%)	514/30/3 (17%)	4/30 (4%)	0.55						
Pregnancy n (% of women of childbearing age)	28/339 (8%)	0	1						
Influenza vaccination n (%)	1418/3011 (47%)	52/90 (58%)	0.03	1 1	[0 7.1 7]	0.69			
Hospitalization in the previous 12 months $n(\%)$	1405/3031 (46%)	37/90 (41%)	0.03	1.1	[0.7,1.7]	0.05			
Presence of child/children <5 in the household in (%)	182/3025 (6%)	5/90 (6%)	0.80						
Clinical presentation	101/0010 (0/0/	5,55 (0,0)	0100						
Median time from symptom onset to hospitalization, days (IOR)	2 (1-3)	2 (1-3)	0.7						
Symptoms	- ()	- ()	•••						
Fever or feverishness. n (%)	2562/3045 (84%)	79/90 (88%)	0.40						
Cough. n (%)	2360/3045 (78%)	75/90 (83%)	0.18	1.5	[0.9:2.7]	0.18			
Dyspnea, n (%)	1739/2199 (79%)	76/90 (84%)	0.54		, 1				
Weakness/malaise. n (%)	821/3041 (27%)	13/90 (14%)	0.007	0.5	[0.2:0.8]	0.01	0.4	[0.2:0.8]	0.008
Headache. n (%)	755/3032 (25%)	16/90 (18%)	0.08	0.8	[0.4:1.4]	0.44		[0/0.0]	
Myalgia, n (%)	734/3029 (24%)	19/90 (21%)	0.45		. , ,				
Sore throat. n (%)	439/3024 (15%)	8/90 (9%)	0.10	0.8	[0.3:1.5]	0.48			
Outcome	, , ,	, , ,			. , ,				
At least one complication during the hospital stay, n (%)	1648/3148 (52%)	56/90 (62%)	0.13						
Pneumonia*, n (%)	918/3124 (29%)	32/89 (36%)	0.27						
Respiratory failure, n (%)	873/3124 (28%)	32/89 (36%)	0.17						
A suite le sent failure en (0/)	420/3122 (13%)	22/89 (25%)	0.004						
Acute neart failure, fi (%)	257/2122 (00/)	2/20 (0%)	0.95						
Acute respiratory distress syndrome, n (%)	257/3123 (8%) E (2.0)	8/89 (9%) 7 (4 12)	0.85						
iviedian length of stay, days (IQK)	2 (2-9) E 12 /2202 (210/)	/ (4-13) 15/00 (17%)	0.50						
The automation after nospitalization in acute care, n (%) Death in $l(x)$	343/2203 (24%) 127/2121 (40/)	13/30(11/%)	0.00						
	131/3131 (4%)	4/30 (4%)	T						

Table 2. Sociodemographic, clinical characteristics and outcome of hospitalized patients infected with human Metapneumovirus, compared to RSV and influenza virus infected patients, 2012-2018

	hMPV+ (n=90)	Influenza+ (n=908)	p-value	RSV+ (n=129)	p-value
Baseline characteristics					
Gender					
Women, n (%)	50/90 (56%)	430/908 (47%)	0.14	67/129 (52%)	0.60
Men, n (%)	40/90 (44%)	478/908 (53%)		62/129 (48%)	
Age					
Median age, years (IQR)	78 (70-86)	69 (54 - 82)	<0.001	74 (64-84)	0.06
Age > 65, n (%)	76/90 (84%)	538/908 (59%)	<0.001	95/129 (74%)	0.06
Median BMI, kg/m2 (IQR)	24.8 (21.5 -28.5)	25.1 (22.1 - 28.4)	0.85	24.6 (21.6-28.8)	0.91
Smoking status					
Smoker, n (%)	12/87(14%)	178/874 (21%)	0.12	31/126 (25%)	0.05
Ex-smoker, n (%)	28/87 (32%)	260/874 (30%)	0.72	44/126 (35%)	0.70
Non-smoker, n (%)	47/87 (54%)	420/874 (49%)	0.37	51/126 (40%)	0.05
Chronic diseases (at least one), n (%)	73/90 (81%)	678/908 (75%)	0.18	117/129 (91%)	0.04
Chronic respiratory disease, n (%)	40/90 (44%)	344/908 (38%)	0.22	70/129 (54%)	0.15
Chronic heart disease, n (%)	45/90 (50%)	362/908 (40%)	0.06	64/129 (50%)	0.96
Diabetes, n (%)	18/90 (20%)	204/908 (22%)	0.59	30/129 (23%)	0.57
Chronic renal failure, n (%)	9/90 (10%)	116/908 (13%)	0.45	26/129 (20%)	0.04
Cancer, n (%)	13/90 (14%)	131/908 (14%)	0.99	33/129 (26%)	0.05
Cirrhosis, n (%)	4/90 (4%)	28/922 (3%)	0.52	4/129 (3%)	0.60
Immunosuppressive treatment, n (%)	15/90 (17%)	151/904 (17%)	0.99	26/128 (20%)	0.50
Pregnancy, n (% of women of childbearing age)	0	13/123 (11%)	1.00	0	1.00
Influenza vaccination, n (%)	52/90 (58%)	351/919 (39%)	<0.001	70/126 (56%)	0.68
Hospitalization in the previous 12 months, n (%)	37/90 (41%)	360/908 (40%)	0.79	64/129 (50%)	0.21
Presence of child/children <5 in the household, n (%)	5/90 (6%)	69/915 (8%)	0.67	8/129 (6%)	0.84
Clinical presentation					
Median time from symptom onset to hospitalization, days (IQR) Symptoms	2 (1-3)	2 (1-4)	0.23	2 (1-3)	0.7
Fever or feverishness, n (%)	79/90 (88%)	811/907 (89%)	0.63	109/128 (85%)	0.58
Cough, n (%)	75/90 (83%)	784/908 (86%)	0.43	106/128 (83%)	0.92
Dyspnea, n (%)	76/90 (84%)	650/908 (71%)	0.05	112/128 (88%)	0.42
Weakness/malaise, n (%)	13/90 (14%)	244/904 (27%)	0.01	29/128 (23%)	0.13
Headache, n (%)	16/90 (18%)	277/902 (31%)	0.01	30/128 (23%)	0.31
Myalgia, n (%)	19/90 (21%)	260/897 (29%)	0.11	19/128 (15%)	0.23
Sore throat, n (%)	8/90 (9%)	184/901 (20%)	0.008	22/126 (17%)	0.07
Outcome					
At least one complication during the hospital stay, n (%)	56/90 (62%)	473/908 (52%)	0.07	85/129 (66%)	0.58
Pneumonia, n (%)	32/89 (36%)	257/904 (28%)	0.14	50/128 (39%)	0.64
Respiratory failure, n (%)	32/89 (36%)	254/904 (28%)	0.12	47/128 (37%)	0.91

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Acute heart failure, n (%)	22/89 (25%)	114/903 (13%)	0.002	21/128 (16%)	0.13
Acute respiratory distress syndrome, n (%)	8/89 (9%)	83/904 (9%)	0.95	15/128 (12%)	0.52
Median length of stay, days (IQR)	7 (4-13)	6 (3-10)	0.06	7 (5-14)	0.50
ICU admission after hospitalization in acute care, n (%)	15/90 (17%)	155/908 (17%)	0.88	33/128 (26%)	0.20
Death, n (%)	4/90 (4%)	36/906 (4%)	0.78	9/129 (7%)	0.44

hMPV: human Metapneumovirus, RSV : Respiratory Syncytial Virus, BMI : body mass index, IQR : inter quartile range

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FIGURE

Figure 1. Flowchart.



ILI: Influenza-like Illness RSV: Respiratory Syncytial Virus hMPV: human Metapneumovirus