

Online supplement

to “Epidemiology of Human Metapneumovirus among Children with Severe or Very Severe Pneumonia and Community Controls in Resource-Limited Settings: the PERCH study experience”

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Table S1. hMPV-positivity among cases vs. controls, chest X-ray positive vs. negative cases, and controls with vs. without RTI

Characteristic, <i>n</i> (%)	Detection of hMPV in NP/OP						Adjusted Odds Ratios of hMPV Positivity (95% CI)											
	Cases			Controls			All Cases vs All Controls		p value		CXR+ Cases vs CXR- Cases		p value		RTI Controls vs Controls without RTI		p value	
	All (<i>n</i> = 3887)	CXR-pos (<i>n</i> =1725)	CXR-neg (<i>n</i> =1601)	All (<i>n</i> =4976)	RTI (<i>n</i> =1180)	No RTI (<i>n</i> =3796)												
All	267 (6.9)	147 (8.5)	88 (5.5)	115 (2.3)	45 (3.8)	70 (1.8)	3.03 (2.42 – 3.80)	<0.0001	1.62 (1.23-2.13)	0.001	2.81 (1.87-4.24)	<0.0001						
Site								0.09*		0.09		0.003						
Kenya (n=628)	46 (7.3)	25 (8.9)	15 (5.3)	22 (2.6)	9 (4.3)	13 (2.0)	2.97 (1.76 – 5.00)	<0.0001	1.69 (0.87-3.28)	0.12	2.26 (0.95-5.39)	0.07						
Gambia (n=609)	40 (6.6)	19 (7.0)	21 (6.8)	13 (2.1)	8 (5.1)	5 (1.1)	3.24 (1.70 – 6.15)	<0.0001	1.03 (0.54-1.96)	0.93	5.02 (1.62-15.59)	0.005						
Mali (n=650)	41 (6.3)	23 (9.6)	10 (3.7)	9 (1.2)	7 (2.3)	2 (0.5)	5.71 (2.72 – 11.97)	<0.0001	2.78 (1.29-5.97)	0.009	5.14 (1.05-25.08)	0.04						
Zambia (n=460)	41 (8.9)	26 (14.0)	10 (6.9)	10 (1.9)	5 (9.6)	5 (1.0)	5.08 (2.51 – 10.28)	<0.0001	2.19 (1.02-4.71)	0.04	9.95 (2.75-35.92)	<0.0001						
South Africa (n=794)	52 (6.6)	31 (7.2)	10 (4.1)	27 (3.3)	1 (2.2)	26 (3.3)	2.09 (1.29 – 3.39)	0.003	1.85 (0.89-3.86)	0.10	0.66 (0.09-4.96)	0.69						
Thailand (n=221)	8 (3.6)	4 (4.1)	4 (4.2)	10 (1.5)	6 (2.4)	4 (1.0)	2.39 (0.93 – 6.17)	0.07	0.96 (0.23-3.96)	0.95	2.43 (0.68-8.68)	0.17						
Bangladesh (n=525)	39 (7.4)	19 (8.7)	18 (7.1)	24 (3.1)	9 (5.3)	15 (2.5)	2.43 (1.44 – 4.10)	0.001	1.26 (0.64-2.47)	0.50	2.13 (0.91-4.99)	0.08						
Age group								0.10		0.06		0.71						
28 days-5 months(n=1580)	96 (6.1)	51 (7.6)	31 (4.9)	35 (2.3)	12 (4.1)	23 (1.8)	2.90 (1.95 – 4.32)	<0.0001	1.61 (1.01-2.57)	0.05	3.06 (1.40-6.69)	0.005						
28d-2 m (n=804)	44 (5.5)	25 (7.4)	14 (4.5)	4 (0.9)	0 (0.0)	4 (1.1)	6.19 (2.20 – 17.45)	0.001	1.85 (0.93-3.67)	0.08	N/A	N/A						
3-5 m (n=776)	52 (6.7)	26 (7.7)	17 (5.3)	31 (2.8)	12 (5.2)	19 (2.1)	2.67 (1.68 – 4.23)	<0.0001	1.44 (0.76-2.76)	0.27	3.68 (1.63-8.33)	0.002						
6-11 months (n=884)	78 (8.8)	46 (11.2)	22 (6.5)	24 (2.0)	10 (3.3)	14 (1.6)	4.51 (2.82 – 7.22)	<0.0001	1.83 (1.07-3.13)	0.03	2.86 (1.18-6.91)	0.02						
12-23 months (n=883)	65 (7.4)	35 (8.2)	25 (6.8)	33 (2.7)	14 (4.2)	19 (2.1)	2.73 (1.77 – 4.21)	<0.0001	1.18 (0.69-2.04)	0.55	2.65 (1.26-5.57)	0.01						
24-59 months (n=540)	28 (5.2)	15 (7.0)	10 (3.8)	21 (2.3)	9 (3.7)	14 (1.8)	2.37 (1.34 – 4.17)	0.003	1.96 (0.85-4.50)	0.11	3.12 (1.22-7.96)	0.02						

Abbreviations: CXR, chest X-ray; RTI, respiratory tract illness, defined as having any of the following: (1) cough, (2) rhinorrhea, or (3) fever or sore throat and one or more of following: the ear discharge, wheeze or difficulty breathing.

All 95% CIs and p values are adjusted for age in months and study site.

*Test of differences in association across subgroups (e.g., across sites or age groups).

Table S2. Association between hMPV detection and demographic and microbiologic characteristics among CXR-positive pneumonia cases and community controls with respiratory tract illness

Characteristics, <i>n</i> (%)	CXR-positive cases				Community controls with respiratory tract illness			
	hMPV A/B positive (<i>n</i> = 147)	hMPV A/B negative (<i>n</i> = 1578)	Adjusted odds ratio (95% CI) ^a	<i>p</i> value ^a	hMPV A/B positive (<i>n</i> = 45)	hMPV A/B negative (<i>n</i> = 1135)	Adjusted odds ratio (95% CI) ^a	<i>p</i> value ^a
Demographic								
Site				0.08				0.17
Kenya	25 (17.0)	257 (16.3)	Reference		9 (20.0)	201 (17.7)	Reference	
Gambia	19 (12.9)	254 (16.1)	0.77 (0.41 – 1.43)		8 (17.8)	148 (13.0)	1.21 (0.46 – 3.20)	
Mali	23 (15.7)	216 (13.7)	1.10 (0.60 – 1.99)		7 (15.6)	291 (25.6)	0.54 (0.20 – 1.47)	
Zambia	26 (17.7)	160 (10.1)	1.67 (0.93 – 3.02)		5 (11.1)	47 (4.1)	2.37 (0.76 – 7.42)	
South Africa	31 (21.1)	397 (25.2)	0.80 (0.46 – 1.40)		1 (2.2)	44 (3.9)	0.51 (0.06 – 4.11)	
Thailand	4 (2.7)	94 (6.0)	0.44 (0.15 – 1.29)		6 (13.3)	244 (21.5)	0.55 (0.19 – 1.59)	
Bangladesh	19 (12.9)	200 (12.6)	0.98 (0.52 – 1.82)		9 (20.0)	160 (14.1)	1.26 (0.49 – 3.24)	
Age group				0.25				0.62
28 days-2 months	25 (17.0)	313 (19.8)	Reference		0 (0.0)	62 (5.5)	Reference	
2-5 months	26 (17.7)	310 (19.6)	1.07 (0.59 – 1.92)		12 (26.7)	220 (19.4)	0.37 (0.04 – 3.27)	
6-11 months	46 (31.3)	366 (23.2)	1.60 (0.86 – 2.97)		10 (22.2)	296 (26.1)	0.30 (0.04 – 2.11)	
12-23 months	35 (23.8)	391 (24.8)	1.10 (0.43 – 2.81)		14 (31.1)	322 (28.4)	0.52 (0.12 – 2.28)	
24-59 months	15 (10.2)	198 (12.6)	0.88 (0.14 – 5.53)		9 (20.0)	235 (20.7)	-	
Female	70 (47.6)	683 (43.3)	1.20 (0.85 – 1.69)	0.29	23 (51.1)	566 (49.87)	1.07 (0.59 – 1.94)	0.83
Underweight ^b	56 (38.1)	637 (40.4)	0.90 (0.63 – 1.28)	0.56	6 (13.3)	175 (15.4)	0.74 (0.30 – 1.79)	0.50
Day care attendance	23 (15.7)	240 (15.3)	0.99 (0.53 – 1.85)	0.98	6 (13.3)	321 (28.3)	0.45 (0.13 – 1.52)	0.20
Smoker in household	42 (28.6)	569 (36.2)	0.76 (0.51 – 1.13)	0.18	21 (46.7)	428 (37.8)	1.50 (0.80 – 2.84)	0.21
Never breastfed	11 (7.5)	168 (10.7)	0.74 (0.37 – 1.46)	0.39	1 (2.2)	23 (2.0)	1.50 (0.17 – 13.59)	0.72
Premature birth ^c	18 (12.5)	198 (12.8)	1.09 (0.64 – 1.87)	0.75	3 (6.7)	92 (8.2)	0.81 (0.24 – 2.75)	0.74
Low birth weight ^d	31 (21.2)	342 (21.9)	0.98 (0.64 – 1.50)	0.94	7 (15.6)	139 (12.3)	1.19 (0.52 – 2.76)	0.68
Premature birth ^c or low birth weight ^d	36 (24.7)	403 (25.7)	0.98 (0.65 – 1.47)	0.92	8 (17.8)	198 (17.5)	0.96 (0.43 – 2.11)	0.91
HEU ^e	19 (34.6)	192 (36.0)	1.03 (0.76 – 1.38)	0.86	2 (33.3)	14 (15.6)	2.37 (0.83 – 6.78)	0.11
Prior antibiotics	70 (47.6)	727 (46.1)	1.33 (0.97-1.82)	0.08	0 (0.0)	26 (2.3)	1.05 (0.41-2.66)	0.92
DTP vaccine (≥ 1 dose)	123 (83.7)	1260 (79.8)	1.47 (0.85-2.53)	0.17	44 (97.8)	1069 (94.2)	2.21 (0.29-16.86)	0.44
PCV vaccine (≥ 1 dose)	77 (52.4)	852 (54.0)	1.08 (0.64-1.82)	0.77	21 (46.7)	549 (48.4)	0.86 (0.26-2.81)	0.80
Microbiologic Findings								
<u>Microbiologically confirmed</u>								
hMPV (in lung aspirates) ^f	1 (0.7)	0 (0.0)	--	--	N/A	N/A	N/A	N/A

Any viruses (in lung aspirates, other than hMPV) ^g	2 (1.4)	0 (0.0)	--	--	N/A	N/A	N/A	N/A
Any non-contaminant bacteria ^h	9 (6.2)	71 (4.5)	1.37 (0.66 – 2.83)	0.40	N/A	N/A	N/A	N/A
Blood culture positivity	6 (4.1)	50 (3.2)	1.26 (0.53 – 3.01)	0.61	N/A	N/A	N/A	N/A
Any invasive specimen positivity ^h	8 (5.4)	61 (3.9)	1.37 (0.64-2.95)	0.42				
<i>S. pneumoniae</i> ^h	2 (1.4)	28 (1.8)	0.76 (0.18 – 3.28)	0.72	N/A	N/A	N/A	N/A
<i>H. influenzae</i> ^h	2 (1.4)	13 (0.8)	1.61 (0.36 – 7.27)	0.54	N/A	N/A	N/A	N/A
<u><i>S. pneumoniae</i> LytA PCR in whole blood</u>								
Any positivity	9 (6.1)	115 (7.3)	0.81 (0.40 – 1.64)	0.55	2 (4.4)	61 (5.4)	0.75 (0.17 – 3.20)	0.69
Positivity >2.2 log ₁₀ copies/mL	7 (4.8)	81 (5.1)	0.90 (0.41 – 2.01)	0.80	1 (2.2)	38 (3.3)	0.62 (0.08 – 4.70)	0.64
<u>Detection in NP/OP</u>								
Any organism positive (other than hMPV)	142 (96.6)	1529 (96.9)	0.99 (0.39 – 2.55)	0.99	45 (100.0)	1108 (97.6)	--	--
Restricted to high density for <i>S. pneumoniae</i> and <i>H. influenzae</i> ⁱ	95 (64.6)	1375 (87.1)	0.28 (0.19 – 0.40)	<0.0001	24 (53.3)	873 (76.9)	0.34 (0.18 – 0.63)	0.001
<u>Viral detection in NP/OP:</u>								
Any NP viral positive (other than HMPV)	44 (29.9)	1205 (76.4)	0.13 (0.09 – 0.19)	<0.0001	15 (33.3)	700 (61.7)	0.30 (0.16 – 0.56)	<0.0001
Respiratory Syncytial Virus	6 (4.1)	500 (31.7)	0.09 (0.04 – 0.20)	<0.0001	1 (2.2)	53 (4.7)	0.47 (0.06 – 3.51)	0.46
Adenovirus	7 (4.8)	162 (10.3)	0.45 (0.21 – 0.98)	0.04	2 (4.4)	175 (15.4)	0.29 (0.07 – 1.21)	0.09
Human Bocavirus	10 (6.8)	225 (14.3)	0.43 (0.22 – 0.84)	0.013	7 (15.6)	170 (15.0)	1.00 (0.44 – 2.30)	0.99
Human Rhinovirus	9 (6.1)	351 (22.2)	0.22 (0.11 – 0.44)	<0.0001	8 (17.8)	290 (25.6)	0.60 (0.27 – 1.31)	0.20
Parainfluenza virus	6 (4.1)	202 (12.8)	0.29 (0.12 – 0.66)	0.003	2 (4.4)	92 (8.1)	0.51 (0.12 – 2.14)	0.35
Human Coronavirus	8 (5.4)	117 (7.4)	0.71 (0.34 – 1.49)	0.37	4 (8.9)	116 (10.2)	0.88 (0.31 – 2.53)	0.81
Influenza virus	4 (2.7)	85 (5.4)	0.48 (0.17 – 1.34)	0.16	0 (0.0)	41 (3.6)	--	--
<u>Bacterial detection in NP/OP:</u>								
Any bacteria positive	136 (92.5)	1412 (89.5)	1.45 (0.76 – 2.75)	0.26	44 (97.8)	1064 (93.7)	2.40 (0.32 – 18.03)	0.40
restricted to high density for <i>S. pneumoniae</i> and <i>H. influenzae</i> ⁱ	77 (52.4)	782 (49.6)	1.13 (0.80 – 1.61)	0.49	14 (31.1)	477 (42.0)	0.63 (0.32 – 1.22)	0.17
<i>S. pneumoniae</i>	118 (80.3)	1199 (76.0)	1.28 (0.83 – 1.97)	0.26	43 (95.6)	968 (85.3)	3.26 (0.76 – 13.91)	0.11
<i>S. pneumoniae</i> >6.9 log ₁₀ copies/mL	19 (12.9)	216 (13.7)	0.94 (0.56 – 1.57)	0.80	1 (2.2)	113 (10.0)	0.22 (0.03 – 1.67)	0.14
<i>H. influenzae</i>	99 (67.4)	898 (56.9)	1.61 (1.12 – 2.32)	0.01	25 (55.6)	673 (59.3)	0.85 (0.45 – 1.58)	0.60
<i>H. influenzae</i> > 5.9 log ₁₀ copies/mL	48 (32.7)	459 (29.1)	1.23 (0.85 – 1.79)	0.27	6 (13.3)	325 (28.6)	0.38 (0.16 – 0.92)	0.03
<i>S. aureus</i>	25 (17.0)	242 (15.3)	1.11 (0.70 – 1.77)	0.65	2 (4.4)	112 (9.9)	0.38 (0.09 – 1.60)	0.19
<i>B. pertussis</i>	1 (0.7)	15 (1.0)	0.67 (0.09 – 5.21)	0.71	0 (0.0)	4 (0.4)	N/A	N/A
<i>C. pneumoniae</i>	1 (0.7)	20 (1.3)	0.57 (0.08 – 4.27)	0.58	1 (2.2)	14 (1.2)	1.99 (0.25 – 15.82)	0.52

<i>M. pneumoniae</i>	2 (1.4)	20 (1.3)	1.35 (0.31 – 5.92)	0.69	6 (5.2)	46 (1.0)	14.55 (4.54 – 46.66)	<0.0001
<i>Salmonella</i> species	2 (1.4)	15 (1.0)	1.43 (0.32 – 6.42)	0.64	0 (0.0)	6 (0.5)	N/A	N/A
Fungi detection in NP/OP								
<i>P. jirovecii</i>	10 (6.8)	142 (9.0)	0.69 (0.35 – 1.37)	0.29	1 (2.2)	67 (5.9)	0.34 (0.05 – 2.57)	0.30
<i>P. jirovecii</i> > 4 log ₁₀ copies/mL	4 (2.7)	70 (4.4)	0.56 (0.20 -1.58)	0.28	0 (0.0)	20 (1.8)	--	--

CXR: Chest X-ray; HEU: HIV-exposed but uninfected; N/A: not applicable; '--', not estimable

^a Adjusted for age in months and study site

^b Underweight defined as weight for age <-2SD of the median age-sex specific WHO reference

^c Premature birth defined as gestational age <37 weeks

^d Birth weight <2.5 kg

^e HEU refers to children exposed to HIV but uninfected, defined as having undetectable viral load and HIV seronegative with a positive maternal history. Positive maternal status based on self-report was accepted, except for seronegative children < 7 months of age where documented positive maternal status was required. Analyses were limited to Zambia and South Africa, which were sites with high HIV prevalence.

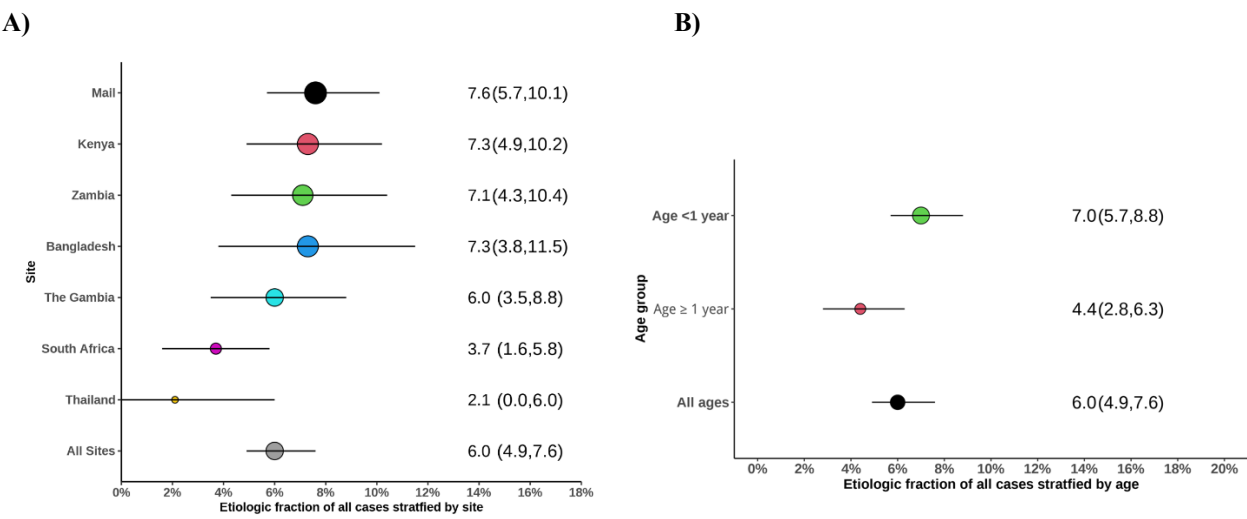
^f One case (aged 6 months) had hMPV detected and two other bacteria co-detected, *Haemophilus influenzae* and *Moraxella catarrhalis* in lung aspirates.

^g One case (aged 9 months) had Adenovirus detected and another case (aged 7 months) had Cytomegalovirus detected in lung aspirates.

^h Detected by culture of blood; by PCR or culture of lung aspirate; or by PCR, culture, or pneumococcal antigen detection (BinaxNOW) of pleural fluid

ⁱ Restricting to high density for *S. pneumoniae* (>6.9 log₁₀ copies/mL) and *H. influenzae* (> 5.9 log₁₀ copies/mL)

Figure S1. Etiological fraction of hMPV among all cases, (A) by site and (B) age



Description of symbols: Line represents the 95% credible interval. The size of the circle is scaled based on the ratio of the estimated etiological fraction to its standard error, meaning given two identical etiological fraction estimates, the estimate with a larger symbol is more informed by the data than the priors.

Table S3. Clinical and laboratory characteristics among cases with high ($\geq 80\%$) etiologic fraction (EF) attributed to hMPV or RSV and cases negative for both hMPV and RSV

Restricting hMPV-positive cases to those with high etiologic probability excludes those with bacteria detected in sterile specimens, including the case where both bacteria and hMPV were detected in the lung aspirate specimen, i.e., excludes some hMPV-bacterial co-infection. Cases with high EF for hMPV and RSV were positive in NP/OP specimen for that pathogen; cases positive for both hMPV and RSV were excluded.

Characteristics, n (%)	hMPV EF $\geq 80\%$ & RSV- [A] (n = 111)	RSV EF $\geq 80\%$ & hMPV- [B] (n=931)	hMPV- & RSV- [C] (n=2596)	A vs B adjusted odds ratio (95% CI) ^a	p value ^a	A vs C adjusted odds ratio (95% CI) ^a	p value ^a
Clinical							
Tachypnea ^b	96 (86.5)	779 (84.4)	2090 (81.0)	1.21 (0.67, 2.29)	0.54	1.75 (1.01, 3.21)	0.06
Rhinorrhea	53 (47.7)	443 (47.7)	1112 (42.9)	0.56 (0.35, 0.89)	0.01	1.21 (0.79, 1.84)	0.38
Cough	73 (65.8)	713 (76.6)	1730 (66.6)	0.77 (0.5, 1.11)	0.22	1.20 (0.89, 1.51)	0.16
Fever ^c	43 (38.7)	262 (28.1)	777 (29.9)	1.28 (0.82, 2)	0.27	1.27 (0.84, 1.91)	0.26
Diarrhea	16 (14.4)	124 (13.3)	405 (15.6)	1.31 (0.9, 1.98)	0.15	1.16 (0.74, 1.64)	0.45
Wheeze	25 (22.7)	368 (39.7)	845 (32.7)	0.51 (0.27, 0.91)	0.03	0.98 (0.53, 1.7)	0.94
Stridor	2 (1.8)	7 (0.8)	84 (3.2)	3.8 (0.44, 32.61)	0.19	0.66 (0.11, 2.24)	0.57
Nasal flaring	69 (62.2)	562 (60.4)	1494 (57.6)	0.91 (0.57, 1.48)	0.70	1.22 (0.79, 1.92)	0.37
Grunting	33 (30.0)	161 (17.3)	458 (17.7)	0.85 (0.49, 1.45)	0.56	1.02 (0.6, 1.7)	0.95
Chest wall retraction	110 (99.1)	915 (98.3)	2310 (89.0)	1.64 (0.27, 31.49)	0.65	13.98 (3.05, 248.03)	0.01
Tachycardia ^d	53 (47.7)	480 (51.7)	1304 (50.3)	0.68 (0.45, 1.04)	0.07	0.82 (0.55, 1.21)	0.31
Very severe pneumonia	32 (28.8)	242 (26.0)	902 (34.7)	0.8 (0.49, 1.29)	0.37	0.55 (0.35, 0.85)	0.01
Vomiting	4 (3.6)	13 (1.4)	89 (3.4)	2.02 (0.53, 6.36)	0.25	0.94 (0.28, 2.41)	0.91
Inability to feed	9 (8.1)	66 (7.1)	209 (8.1)	0.65 (0.29, 1.33)	0.27	0.58 (0.26, 1.12)	0.13
Lethargy	9 (8.2)	40 (4.3)	325 (12.5)	1.46 (0.62, 3.15)	0.36	0.5 (0.23, 0.96)	0.05
Multiple convulsions	5 (4.5)	12 (1.3)	211 (8.1)	2.43 (0.71, 7.48)	0.13	0.5 (0.17, 1.15)	0.14
Nodding	20 (18.0)	188 (20.2)	397 (15.3)	0.67 (0.37, 1.14)	0.15	1.06 (0.61, 1.75)	0.84
Cyanosis	2 (1.8)	9 (1.0)	64 (2.5)	1.24 (0.18, 5.38)	0.79	0.43 (0.07, 1.43)	0.25
Hypoxaemia ^c	38 (34.2)	349 (37.6)	900 (34.7)	1.03 (0.64, 1.64)	0.89	1.1 (0.71, 1.69)	0.67
Supplemental O2	38 (34.5)	400 (43.1)	1064 (41.3)	1.31 (0.81, 2.09)	0.27	1.21 (0.77, 1.89)	0.41
Outcomes							

Mortality within 30 days of admission	3 (2.9)	18 (2.1)	248 (10.4)	0.85 (0.19, 2.72)	0.80	0.14 (0.03, 0.39)	0.001
Hospital stay > 3 days ^f	69 (62.2)	521 (56.3)	1441 (55.6)	1.59 (1.02, 2.48)	0.04	1.32 (0.87, 2)	0.19
Hospital duration (median, IQR)	4.0 (3.0, 7.0)	4.0 (3.0, 6.0)	4.0 (3.0, 7.0)	1.08 (1.03, 1.13)	0.002	0.98 (0.94, 1.02)	0.39
Radiographic Findings^g							
Abnormal CXR ^h	59 (53.2)	450 (48.3)	1078 (41.5)	1.5 (0.99, 2.29)	0.06	1.82 (1.24, 2.7)	0.003
Consolidation	27 (24.3)	185 (19.9)	538 (20.7)	1.55 (0.93, 2.52)	0.08	1.31 (0.81, 2.04)	0.25
Other infiltrates	32 (28.8)	265 (28.5)	540 (20.8)	1.16 (0.72, 1.83)	0.53	1.8 (1.15, 2.77)	0.01
Laboratory Findings							
Leukocytosis ⁱ	34 (32.4)	260 (30.8)	1206 (48.6)	1.35 (0.83, 2.16)	0.22	0.67 (0.43, 1.03)	0.07
Leukopenia	4 (3.6)	27 (2.9)	63 (2.4)	0.67 (0.22-2.04)	0.48	0.94 (0.33-2.69)	0.91
CRP (mg/mL)					0.48		0.62
<5	27 (24.3)	262 (28.1)	629 (24.2)	Reference		Reference	
5-<10	13 (11.7)	107 (11.5)	286 (11.0)	1.34 (0.64-2.80)		1.20 (0.60-2.40)	
10-<20	7 (6.3)	113 (12.1)	319 (12.3)	0.60 (0.24-1.45)		0.62 (0.26-1.46)	
20-<40	16 (14.4)	124 (13.3)	351 (13.5)	1.16 (0.57-2.36)		1.25 (0.65-2.40)	
40-<60	8 (7.2)	53 (6.0)	168 (6.5)	1.30 (0.50-3.34)		1.35 (0.59-3.10)	
>=60	25 (22.5)	95 (10.2)	468 (18.0)	2.04 (1.07-3.89)		1.29 (0.72-2.32)	
CRP >=40mg/mL	33 (34.4)	150 (19.8)	636 (28.6)	1.83 (1.11, 2.99)	0.02	1.28 (0.81, 1.99)	0.29
Prior antibiotics	54 (48.6)	431 (46.3)	1141 (44.0)	0.93 (0.63, 1.36)	0.71	0.89 (0.61, 1.28)	0.54
Microbiologic Findings in NP/OP							
Any NP viral positive (other than RSV and HMPV)	30 (27.0)	306 (32.9)	1663 (64.1)	0.74 (0.46, 1.16)	0.20	0.21 (0.13, 0.32)	<0.0001
Any NP/OP bacteria positive ^j	45 (40.5)	444 (47.7)	1206 (46.5)	0.75 (0.49, 1.15)	0.20	0.7 (0.46, 1.05)	0.08
<i>S. pneumoniae</i> >6.9 log ₁₀ copies/mL	13 (11.7)	117 (12.6)	317 (12.2)	0.77 (0.39, 1.43)	0.42	0.75 (0.39, 1.33)	0.35
<i>H. influenzae</i> >5.9 log ₁₀ copies/mL	30 (27.0)	239 (25.7)	690 (26.6)	1.06 (0.65, 1.69)	0.82	0.99 (0.62, 1.53)	0.95

CXR: Chest X-ray; CRP: C-reactive protein

a Adjusted for study sites and age in months

b Tachypnea defined as respiratory rate ≥60 breaths/minute if aged <2 months, respiratory rate ≥50 breaths/minute if aged 2-12 months, respiration rate ≥40 breaths/minute if aged >12 months

c Fever defined as measured temperature ≥38°C or reported history of fever

d Tachycardia defined as heart rate >160 beats per minute (bpm) if aged <11 months, heart rate >150 bpm if aged 12-35 months, heart rate >140 bpm if aged 36-59 months

e Children were considered to have hypoxaemia if: 1) a room air pulse-oximetry reading indicated oxygen saturation <90% at the two sites at elevation (Zambia and South Africa) or <92% at all other sites, or 2) supplemental oxygen used if a room air oxygen saturation reading was not available.

f Excluding cases with inpatient mortality

g Excluding missing or uninterpretable CXRs

h Defined as findings of consolidation or other infiltrates on chest radiographs

i Leukocytosis defined as white blood cell count >15 000 cells/uL if age <12 months, or >13 000 cells/uL if age >12 months

j Restricting to high density for *S. pneumoniae* (>6.9 log₁₀ copies/mL) and *H. influenzae* (> 5.9 log₁₀ copies/mL)

Table S4. Clinical and laboratory characteristics among CXR-positive cases: hMPV-positive compared to RSV-positive and cases negative for both hMPV and RSV
Excludes n=12 cases positive for both hMPV and RSV.

Characteristics, n (%)	CXR-positive cases						
	HMPV-positive [A] (n=141)	RSV-positive [B] (n=500)	Negative for HMPV & RSV [C] (n=1078)	A vs B adjusted odds ratio (95% CI) ^a	p value ^a	A vs C adjusted odds ratio (95% CI) ^a	p value ^a
Clinical							
Tachypnea ^b	122 (86.5)	420 (84.0)	908 (84.2)	0.94 (0.53-1.69)	0.85	1.14 (0.67-1.95)	0.62
Rhinorrhea	60 (42.6)	208 (41.6)	453 (42.0)	0.84 (0.54-1.30)	0.43	1.10 (0.74-1.63)	0.62
Cough	103 (73.0)	380 (76.0)	780 (72.4)	0.86 (0.54-1.37)	0.53	1.13 (0.75-1.70)	0.57
Fever ^c	67 (47.5)	163 (32.6)	342 (31.7)	1.54 (1.00-2.37)	0.05	1.93 (1.30-2.85)	0.001
Diarrhea	15 (10.6)	69 (13.8)	157 (14.6)	0.71 (0.38-1.33)	0.28	0.65 (0.37-1.17)	0.15
Wheeze	35 (24.8)	172 (34.4)	337 (31.3)	0.56 (0.32-0.97)	0.04	0.74 (0.44-1.26)	0.27
Stridor	2 (1.4)	3 (0.6)	29 (2.7)	1.66 (0.25-11.22)	0.60	0.59 (0.14-2.52)	0.48
Nasal flaring	85 (60.3)	300 (60.0)	657 (60.9)	1.14 (0.72-1.81)	0.57	0.96 (0.63-1.45)	0.85
Grunting	27 (19.1)	70 (14.0)	186 (17.3)	1.05 (0.59-1.89)	0.86	0.95 (0.56-1.63)	0.86
Chest wall retraction	136 (96.5)	491 (98.2)	1014 (94.1)	0.47 (0.14-1.54)	0.21	1.68 (0.66-4.30)	0.28
Tachycardia ^d	78 (55.3)	253 (50.6)	553 (51.3)	1.23 (0.82-1.85)	0.31	1.10 (0.76-1.58)	0.62
Very severe pneumonia	43 (30.5)	125 (25.0)	335 (31.1)	1.32 (0.84-2.06)	0.23	0.93 (0.63-1.38)	0.71
Vomiting	7 (5.0)	6 (1.2)	21 (1.9)	4.57 (1.43-14.56)	0.01	2.88 (1.18-7.05)	0.02
Inability to feed	13 (9.2)	30 (6.0)	76 (7.1)	1.59 (0.78-3.27)	0.20	1.24 (0.66-2.32)	0.51
Lethargy	13 (9.2)	28 (5.6)	110 (10.2)	1.34 (0.65-2.77)	0.43	0.82 (0.44-1.52)	0.52
Multiple convulsions	5 (3.5)	10 (2.0)	39 (3.6)	1.22 (0.83-3.85)	0.74	0.92 (0.35-2.40)	0.86
Nodding	26 (18.4)	90 (18.0)	177 (16.4)	1.20 (0.71-2.03)	0.50	1.21 (0.75-1.94)	0.43
Cyanosis	3 (2.1)	4 (0.8)	32 (3.0)	4.20 (0.85-20.71)	0.08	0.69 (0.20-2.33)	0.55
Hypoxaemia ^e	69 (48.9)	217 (43.4)	440 (40.8)	1.47 (0.92-2.33)	0.10	1.53 (1.03-2.27)	0.04
Supplemental O2	72 (51.1)	249 (49.8)	532 (49.4)	1.52 (0.94-2.46)	0.09	1.19 (0.76-1.86)	0.45
Radiographic Findings ^f							
Abnormal CXR ^g	NA	NA	NA	NA		NA	
Consolidation	67 (47.5)	209 (41.8)	538 (49.9)	1.28 (0.86-1.91)	0.23	0.85 (0.59-1.23)	0.39
Other infiltrates	74 (52.5)	291 (58.2)	540 (50.1)	0.78 (0.52-1.17)	0.23	1.18 (0.81-1.70)	0.39
Laboratory Findings							
Leukocytosis ^h	59 (41.8)	165 (33.0)	549 (50.9)	1.41 (0.93-2.13)	0.11	0.74 (0.51-1.07)	0.11
Leukopenia	2 (1.4)	13 (2.6)	22 (2.0)	0.36 (0.07-1.71)	0.20	0.66 (0.15-2.87)	0.58
CRP (mg/mL)					0.01		0.03
<5	28 (19.9)	113 (22.6)	221 (20.5)	Reference		Reference	
5-<10	7 (5.0)	51 (10.2)	99 (9.2)	0.57 (0.23-1.42)		0.56 (0.24-1.34)	
10-<20	17 (12.1)	17 (3.4)	125 (11.6)	1.31 (0.64-2.68)		1.19 (0.62-2.27)	
20-<40	12 (8.5)	12 (2.4)	158 (14.7)	0.73 (0.34-1.57)		0.64 (0.31-1.32)	
40-<60	17 (12.1)	17 (3.4)	73 (6.8)	2.05 (0.97-4.34)		2.01 (1.02-3.95)	
≥60	43 (30.5)	43 (8.6)	262 (24.3)	1.89 (1.03-3.45)		1.34 (0.78-2.31)	
CRP ≥ 40mg/mL	60 (42.6)	115 (23.0)	335 (31.1)	2.10 (1.35-32.7)	0.001	1.70 (1.14-2.54)	0.009

Prior antibiotics	66 (46.8)	245 (49.0)	482 (44.7)	1.49 (1.05-2.12)	0.03	1.34 (0.96-1.87)	0.09
Microbiologic Findings in NP/OP							
Any organism positive (other than hMPV and RSV)	137 (97.2)	462 (92.4)	1045 (96.9)	2.79 (0.96-8.11)	0.06	1.14 (0.39-3.31)	0.81
Any NP viral positive (other than RSV and HMPV)	38 (27.0)	167 (33.4)	705 (65.4)	0.67 (0.44-1.04)	0.07	0.20 (0.13-0.29)	<0.0001
Any NP/OP bacteria positive i	74 (52.5)	243 (48.6)	539 (50.0)	1.29 (0.86-1.93)	0.22	1.10 (0.77-1.59)	0.60
<i>S. pneumoniae</i> >6.9 log ₁₀ copies/mL	19 (13.5)	66 (13.2)	150 (13.9)	1.12 (0.62-2.02)	0.70	0.98 (0.58-1.66)	0.94
<i>H. influenzae</i> >5.9 log ₁₀ copies/mL	46 (32.6)	140 (28.0)	319 (29.6)	1.35 (0.88-2.08)	0.17	1.18 (0.80-1.74)	0.40
Microbiologically confirmed infection in sterile specimen							
Any pathogen	9 (6.4)	5 (1.0)	66 (6.1)	6.25 (1.94-20.18)	0.002	1.03 (0.50-2.13)	0.94
Any bacteria	8 (5.7)	5 (1.0)	56 (5.2)	5.23 (1.58-17.32)	0.007	1.04 (0.48-2.24)	0.92
Outcomes							
Hospital stay >3 days ^j	94 (66.7)	308 (61.6)	683 (63.4)	1.34 (0.86-2.08)	0.20	1.19 (0.80-1.79)	0.39
Hospital duration (median, IQR)	4.0 (3.0-7.0)	5.0 (3.0-7.0)	4.0 (3.0-8.0)	1.03 (0.99-1.07)	0.19	0.85 (0.65-1.10)	0.21
Mortality within 30 days of admission	6 (4.3) ¹	14 (2.8)	94 (8.7)	1.20 (0.43-3.33)	0.73	0.42 (0.18-0.99)	0.048

CXR: Chest X-ray; CRP: C-reactive protein

^a Adjusted for study sites and age in months

^b Tachypnea defined as respiratory rate ≥60 breaths/minute if aged <2 months, respiratory rate ≥50 breaths/minute if aged 2-12 months, respiration rate ≥40 breaths/minute if aged >12 months

^c Fever defined as measured temperature ≥38°C or reported history of fever

^d Tachycardia defined as heart rate >160 beats per minute (bpm) if aged <11 months, heart rate >150 bpm if aged 12-35 months, heart rate >140 bpm if aged 36-59 months

^e Children were considered to have hypoxaemia if: 1) a room air pulse-oximetry reading indicated oxygen saturation <90% at the two sites at elevation (Zambia and South Africa) or <92% at all other sites, or 2) supplemental oxygen used if a room air oxygen saturation reading was not available.

^f Excluding missing or uninterpretable CXRs

^g Defined as findings of consolidation or other infiltrates on chest radiographs

^h Leukocytosis defined as white blood cell count >15 000 cells/uL if age <12 months, or >13 000 cells/uL if age >12 months

ⁱ Restricting to high density for *S. pneumoniae* (>6.9 log₁₀ copies/mL) and *H. influenzae* (> 5.9 log₁₀ copies/mL)

^j Excluding cases with inpatient mortality

¹ See Supplemental Table 10 for characteristics of hMPV-positive cases that died

Table S5. Characteristics of hMPV-positive cases that died (n=10)

		Demographics			Risk Factors										Microbiological Findings (other than HMPV)						Etiological Fraction		Clinical Findings																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																												
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0=No or negative test, blank=missing

HEU = HIV exposed uninfected

¹ >2.2 log₁₀ copies/mL

² Restricted to high density for *S. pneumoniae* and *H. influenzae*

³ >4 log₁₀ copies/mL

Table S6. Comparison of clinical and laboratory findings by probability of hMPV as single cause, estimated using PERCH Integrated Analysis (PIA), among hMPV-positive cases

Probability is estimated assuming a single-cause model, therefore non-zero probability <100% reflects shared probability with other pathogens. 100% etiology is only assigned to pathogens detected in sterile specimens (e.g., blood culture, lung aspirate PCR or culture, pleural fluid PCR, culture or BinaxNow). For example, the etiologic probability of hMPV for a case with lung aspirate specimen positive for hMPV, *Haemophilus influenzae* and *Moraxella catarrhalis* would be 33.3% because the model assumes only one pathogen is the cause. Conversely, cases positive in NP/OP for both RSV and hMPV are assigned higher probability for RSV because the association of RSV detection with case status is stronger than it is for hMPV. A case with bacteria detected in blood and hMPV detected in NP/OP would have 0% probability of hMPV etiology and 100% attributed to the bacteria detected in blood culture.

to the bacteria detected in blood culture.					
Characteristics, <i>n</i> (%)	hMPV Etiology Probability among hMPV+ Cases			p value (Unadjusted)	p value (low-med vs high adjusted for age and site)
	Low	Middle	High		
	(EF<50%) (<i>n</i> = 66)	(50%≤EF<80%) (<i>n</i> = 90)	(EF≥80%) (<i>n</i> = 111)		
Demographic					
Site				<0.0001	<0.0001
Kenya	7 (10.6%)	11 (12.2%)	28 (25.2%)		
Gambia	8 (12.1%)	17 (18.9%)	15 (13.5%)		
Mali	0 (0.0%)	1 (1.1%)	40 (36.0%)		
Zambia	14 (21.2%)	10 (11.1%)	17 (15.3%)		
South Africa	25 (37.9%)	27 (30.0%)	0 (0.0%)		
Thailand	3 (4.5%)	5 (5.6%)	0 (0.0%)		
Bangladesh	9 (13.6%)	19 (21.1%)	11 (9.9%)		
Age group				<0.0001	0.07
28 days-5 months	14 (21.2%)	29 (32.2%)	53 (47.7%)		
6-11 months	7 (10.6%)	27 (30.0%)	44 (39.6%)		
12-23 months	35 (53.0%)	22 (24.4%)	8 (7.2%)		
24-59 months	10 (15.2%)	12 (13.3%)	6 (5.4%)		
Female	38 (57.6%)	38 (42.2%)	42 (37.8%)	0.03	0.54
Underweight ^a	22 (33.3%)	28 (31.1%)	34 (30.6%)	>0.9	0.64
Day care attendance	5 (7.6%)	9 (10.2%)	23 (20.7%)	0.02	0.87
Smoker in household	23 (34.8%)	30 (33.7%)	29 (26.1%)	0.34	0.30
Never breastfed	7 (10.6%)	11 (12.5%)	3 (2.7%)	0.03	0.18
Premature birth ^b	9 (13.8%)	15 (17.6%)	9 (8.3%)	0.14	0.20
Low birth weight ^c	12 (18.2%)	16 (18.6%)	28 (25.5%)	0.40	0.12
Premature ^b or low birth weight ^c	13 (19.7%)	22 (25.6%)	31 (28.2%)	0.50	0.45
HEU ^d	13 (20.0%)	16 (18.6%)	4 (4.1%)	0.42	0.37
Prior antibiotics	33 (50.0%)	44 (48.9%)	54 (48.6%)	>0.9	0.10
Clinical					
Tachypnea ^f	58 (87.9%)	74 (82.2%)	96 (86.5%)	0.55	0.08
Rhinorrhea	20 (30.3%)	38 (42.2%)	53 (47.7%)	0.07	0.84
Cough	55 (83.3%)	71 (78.9%)	73 (65.8%)	0.02	0.78
Fever ^g	28 (42.4%)	31 (34.4%)	43 (38.7%)	0.59	0.83
Diarrhea	9 (13.6%)	5 (5.6%)	16 (14.4%)	0.22	0.30

Wheeze	20 (30.3%)	34 (37.8%)	25 (22.5%)	0.07	0.85
Stridor	2 (3.0%)	0 (0.0%)	2 (1.8%)	0.29	0.69
Nasal flaring	38 (57.6%)	48 (53.3%)	69 (62.2%)	0.45	0.36
Grunting	8 (12.1%)	7 (7.8%)	33 (29.7%)	<0.0001	0.61
Chest wall retraction	63 (95.5%)	84 (93.3%)	110 (99.1%)	0.04	0.86
Tachycardia ^h	37 (56.1%)	43 (47.8%)	53 (47.7%)	0.50	0.04
Very severe pneumonia	18 (27.3%)	22 (24.4%)	32 (28.8%)	0.78	0.24
Vomiting	2 (3.0%)	5 (5.6%)	4 (3.6%)	0.69	>0.9
Inability to feed	3 (4.5%)	7 (7.8%)	9 (8.1%)	0.64	0.21
Lethargy	7 (10.6%)	8 (8.9%)	9 (8.1%)	0.86	>0.9
Multiple convulsions	5 (7.6%)	2 (2.2%)	5 (4.5%)	0.28	0.55
Nodding	9 (13.6%)	10 (11.1%)	20 (18.0%)	0.37	0.37
Cyanosis	2 (3.0%)	2 (2.2%)	2 (1.8%)	0.87	0.24
Hypoxaemia ⁱ	34 (51.5%)	35 (38.9%)	38 (34.2%)	0.07	0.02
Supplemental Oxygen	39 (59.1%)	41 (45.6%)	38 (34.2%)	0.006	0.42
Radiographic Findings ^j					
Abnormal CXR ^k	41 (62.1%)	47 (52.2%)	59 (53.2%)	0.41	0.56
Consolidation	20 (30.3%)	21 (23.3%)	27 (24.3%)	0.58	0.34
Other infiltrates	21 (31.8%)	26 (28.9%)	32 (28.8%)	0.90	0.79
Laboratory Findings					
Leukocytosis ^l	27 (40.9%)	33 (36.7%)	34 (30.6%)	0.39	0.06
Leukopenia	1 (1.5%)	1 (1.1%)	4 (3.6%)	0.45	0.36
CRP (mg/mL)					
<5	10 (15.2%)	26 (28.9%)	27 (24.3%)	0.14	>0.9
5-<10	3 (4.5%)	10 (11.1%)	13 (11.7%)		
10-<20	10 (15.2%)	12 (13.3%)	7 (6.3%)		
20-<40	7 (10.6%)	9 (10.0%)	15 (13.5%)		
40-<60	4 (6.1%)	9 (10.0%)	7 (6.3%)		
>=60	22 (33.3%)	16 (17.8%)	25 (22.5%)		
CRP >= 40mg/mL	26 (39.4%)	25 (27.8%)	33 (29.7%)	0.21	>0.9
Outcomes					
Hospital stay >3 days ^m	3 (4.5%)	4 (4.4%)	2 (1.8%)	0.48	0.29
Hospital duration (median, IQR)	5.0 (3.0-7.0)	4.0 (3.0-6.0)	4.0 (3.0-7.0)	0.62	0.64
Mortality ≤30 days of admission ⁿ	3 (4.5%)	4 (4.4%)	3 (2.7%)	0.70	0.57
Microbiologic Findings					
Any organism positive (other than hMPV) in NP/OP	65 (98.5%)	87 (96.7%)	108 (97.3%)	0.78	0.30
Restricted to high density for <i>S. pneumoniae</i> and <i>H. influenzae</i> ^e	57 (86.4%)	71 (78.9%)	74 (66.7%)	0.009	0.001

Viral detection in NP/OP:

Any NP viral positive (other than HMPV)	44 (66.7%)	49 (54.4%)	52 (46.8%)	0.04	0.004
Respiratory Syncytial Virus	12 (18.2%)	0 (0.0%)	0 (0.0%)	<0.0001	NA
Adenovirus	7 (10.6%)	5 (5.6%)	6 (5.4%)	0.35	0.22
Human Bocavirus	7 (10.6%)	7 (7.8%)	10 (9.0%)	0.83	0.39
Human Rhinovirus	10 (15.2%)	9 (10.0%)	8 (7.2%)	0.24	0.03
Parainfluenza virus	3 (4.5%)	8 (8.9%)	0 (0.0%)	0.007	NA
Human Coronavirus	1 (1.5%)	3 (3.3%)	6 (5.4%)	0.41	0.73
Influenza virus	2 (3.0%)	3 (3.3%)	3 (2.7%)	>0.9	0.46
<u>Bacterial detection in NP/OP:</u>					
Any bacteria positive	62 (93.9%)	86 (95.6%)	104 (93.7%)	0.84	0.73
Restricted to high density for <i>S. pneumoniae</i> and <i>H. influenzae</i>	37 (56.1%)	56 (62.2%)	45 (40.5%)	0.007	0.001
<i>S. pneumoniae</i>	53 (80.3%)	70 (77.8%)	97 (87.4%)	0.18	0.34
<i>S. pneumoniae</i> >6.9 log ₁₀ copies/mL	13 (19.7%)	10 (11.1%)	13 (11.7%)	0.23	0.11
<i>H. influenzae</i>	42 (63.6%)	54 (60.0%)	70 (63.1%)	0.87	0.51
<i>H. influenzae</i> >5.9 log ₁₀ copies/mL	22 (33.3%)	35 (38.9%)	30 (27.0%)	0.20	0.20
<i>S. aureus</i>	14 (21.2%)	19 (21.1%)	15 (13.5%)	0.28	0.02
<i>B. pertussis</i>	0 (0.0%)	0 (0.0%)	1 (0.9%)	0.49	NA
<i>C. pneumoniae</i>	0 (0.0%)	1 (1.1%)	0 (0.0%)	0.37	NA
<i>M. pneumoniae</i>	2 (3.0%)	1 (1.1%)	1 (0.9%)	0.49	0.47
<i>Salmonella</i> species	2 (3.0%)	0 (0.0%)	1 (0.9%)	0.20	0.77
Fungal detection in NP/OP					
<i>P. jirovecii</i>	8 (12.1%)	4 (4.4%)	4 (3.6%)	0.05	0.01
<i>P. jirovecii</i> > 4 log ₁₀ copies/mL	6 (9.1%)	3 (3.3%)	0 (0.0%)	0.005	NA
<i>S. pneumoniae</i> PCR positive in whole blood					
Any positivity	8 (12.7%)	4 (4.8%)	2 (2.0%)	0.02	0.52
Positivity >2.2 log ₁₀ copies/mL	6 (9.5%)	4 (4.8%)	2 (2.0%)	0.10	0.57
Microbiologically confirmed non-contaminant bacterial infection^c					
Any invasive specimen positivity ^c	9 (13.6%)	0 (0.0%)	1 (0.9%)	<0.0001	0.13
Blood culture positivity	7 (10.6%)	0 (0.0%)	0 (0.0%)	<0.0001	NA
<i>S. pneumoniae</i> ^c	2 (3.0%)	0 (0.0%)	0 (0.0%)	0.046	NA
<i>H. influenzae</i> ^c	2 (3.0%)	0 (0.0%)	0 (0.0%)	0.046	NA

CXR: Chest X-ray; HEU: HIV-exposed but uninfected; CRP: C-reactive protein

^a Underweight defined as weight for age <-2SD of the median age-sex specific WHO reference;

^b Premature birth defined as gestational age <37 weeks;

^c Birth weight <2.5 kg;

^d HEU defined as HIV-uninfected but HIV-exposed. Undetectable viral load, HIV seronegative in the child with a positive maternal history. Positive maternal status based on self-report was accepted, except for seronegative children < 7 months of age where documented positive maternal status was required. Analyses were limited to Zambia and South Africa;

- ^e Detected by culture of blood; by PCR or culture of lung aspirate; or by PCR, culture, or pneumococcal antigen detection (BinaxNOW) of pleural fluid. By definition, etiology for other pathogens is set to 0% probability for microbiologically-confirmed cases.
- ^f Tachypnea defined as respiratory rate ≥ 60 breaths/minute if aged <2 months, respiratory rate ≥ 50 breaths/minute if aged 2-12 months, respiration rate ≥ 40 breaths/minute if aged >12 months
- ^g Fever defined as measured temperature $\geq 38^{\circ}\text{C}$ or reported history of fever
- ^h Tachycardia defined as heart rate >160 beats per minute (bpm) if aged <11 months, heart rate >150 bpm if aged 12-35 months, heart rate >140 bpm if aged 36-59 months
- ⁱ Children were considered to have hypoxaemia if: 1) a room air pulse-oximetry reading indicated oxygen saturation <90% at the two sites at elevation (Zambia and South Africa) or <92% at all other sites, or 2) supplemental oxygen used if a room air oxygen saturation reading was not available.
- ^j Excluding missing or uninterpretable CXRs
- ^k Defined as findings of consolidation or other infiltrates on chest radiographs
- ^l Leukocytosis defined as white blood cell count >15 000 cells/uL if age <12 months, or >13 000 cells/uL if age >12 months
- ^m Excluding cases with inpatient mortality
- ⁿ See Supplemental Table 10 for characteristics of hMPV-positive cases that died

Table S7. Latent Class Analysis of clinical findings among hMPV-positive and RSV-positive cases

Classes are ordered by percent with wheeze.

A. All hMPV-positive cases (n=267)

	Class 1	Class 2	Class 3	Class 4	Class 5	Class 6
Proportion in each class	12%	31%	4%	10%	19%	23%
cough	1.00	0.82	0.68	1.00	0.69	0.46
fever	0.06	0.21	0.00	0.00	0.68	0.55
CXR consolidation	0.00	0.09	1.00	0.48	0.52	0.12
CRP $\geq$ 40 mg/mL	0.27	0.00	0.18	0.67	1.00	0.05
Leukocytosis	1.00	0.00	1.00	0.00	0.42	0.42
Wheeze	0.73	0.65	0.34	0.23	0.00	0.00

Rhinorrhea added to list of clinical findings

	Class 1	Class 2	Class 3	Class 4	Class 5	Class 6
Proportion in each class	8%	3%	36%	12%	27%	14%
Rhinorrhea	0.59	0.39	0.58	0.16	0.45	0.18
cough	1.00	0.84	0.80	0.80	0.75	0.41
fever	0.00	0.16	0.21	0.00	0.51	0.76
CXR consolidation	0.05	0.47	0.09	0.43	0.47	0.13
CRP $\geq$ 40 mg/mL	0.17	1.00	0.00	0.00	1.00	0.00
Leukocytosis	1.00	0.53	0.00	0.68	0.36	0.50
Wheeze	1.00	1.00	0.57	0.14	0.00	0.00

B. All RSV-positive cases (n=1035)

	Class 1	Class 2	Class 3	Class 4	Class 5	Class 6
Proportion in each class	5%	37%	15%	23%	10%	10%
cough	0.76	0.92	0.88	0.56	0.99	0.54
fever	0.00	0.01	0.98	0.19	0.17	0.58
CXR consolidation	0.29	0.11	0.16	0.17	0.61	0.38
CRP $\geq$ 40 mg/mL	0.39	0.02	0.19	0.18	0.41	0.64
Leukocytosis	0.66	0.21	0.31	0.13	0.39	0.65
Wheeze	0.98	0.70	0.50	0.05	0.00	0.00

C. CXR-positive hMPV-positive cases (n=179)

	Class 1	Class 2	Class 3	Class 4	Class 5	Class 6
Proportion in each class	18%	14%	13%	6%	27%	23%
cough	0.943	1.000	0.682	0.000	0.818	0.589
fever	0.210	0.000	0.000	1.000	0.651	0.617
CXR consolidation	0.187	0.606	1.000	1.000	0.568	0.000
CRP $\geq$ 40 mg/mL	0.000	0.615	0.213	0.519	1.000	0.000
Leukocytosis	0.342	0.000	0.662	0.499	0.351	0.452
Wheeze	1.000	0.313	0.241	0.000	0.000	0.000

D. CXR-positive hMPV-positive cases with hMPV etiologic probability* $\geq 80\%$ (n=76)

	Class 1	Class 2	Class 3	Class 4	Class 5	Class 6
Proportion in each class	17%	11%	23%	13%	16%	20%
Cough	1.000	1.000	1.000	0.830	0.603	0.000
fever	0.000	1.000	0.000	0.414	1.000	0.444
CXR consolidation	0.375	0.000	0.621	1.000	0.471	0.222
CRP ≥ 40 mg/mL	0.000	0.000	0.526	1.000	1.000	0.000
Leukocytosis	0.250	0.200	0.474	0.000	0.397	0.556
Wheeze	1.000	0.200	0.000	0.000	0.000	0.000

*Estimated using PERCH Integrated Analysis (PIA)

Table S8. Characteristics and etiologic probability among hMPV-positive cases, by presence of CXR consolidation or leukocytosis and/or wheeze

	CXR consolidation or leukocytosis* without wheeze (n=100, 39.8%)	Wheeze without CXR consolidation or leukocytosis (n=40, 15.9%)	Both CXR consolidation or leukocytosis & wheeze (n=32, 12.7%)	No CXR consolidation, leukocytosis or wheeze (n=79, 31.5%)	p value (unadj.)	p value (adj. for age & site)	Total (n=251, 100%)
Cough	69 (69.0%)	33 (82.5%)	29 (90.6%)	55 (69.6%)	0.04	0.92	186 (74.1%)
Fever	49 (49.0%)	10 (25.0%)	5 (15.6%)	31 (39.2%)	0.002	0.21	95 (37.8%)
CRP $\geq$ 40 mg/L	44 (53.7%)	2 (5.1%)	11 (35.5%)	22 (30.1%)	<0.0001	0.005	79 (35.1%)
Very severe	31 (31.0%)	8 (20.0%)	6 (18.8%)	24 (30.4%)	0.35	0.82	69 (27.5%)
Mortality $\leq$ 30 days of admission	9 (10.1%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0.01	0.10	10 (4.5%)
RSV positive	2 (2.0%)	1 (2.5%)	2 (6.3%)	7 (8.9%)	0.16	0.02	12 (4.8%)
Probability of hMPV etiology**							
<25%	9 (9.0%)	5 (12.5%)	3 (9.4%)	13 (16.5%)	0.14	0.37	30 (12.0%)
25% $\leq$ – <50%	18 (18.0%)	5 (12.5%)	7 (21.9%)	4 (5.1%)			34 (13.5%)
50% $\leq$ – <80%	31 (31.0%)	15 (37.5%)	15 (46.9%)	22 (27.8%)			83 (33.1%)
$\geq$ 80%	42 (42.0%)	15 (37.5%)	7 (21.9%)	40 (50.6%)			104 (41.4%)
Probability of RSV etiology							
<50%	98 (98.0%)	39 (97.5%)	30 (93.8%)	72 (91.1%)	0.16	0.02	239 (95.2%)
50% $\leq$ – <80%	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			0 (0.0%)
$\geq$ 80%	2 (2.0%)	1 (2.5%)	2 (6.3%)	7 (8.9%)			12 (4.8%)
Probability of bacterial etiology							
<25%	82 (82.0%)	38 (95.0%)	31 (96.9%)	72 (91.1%)	0.13	0.36	223 (88.8%)
25% $\leq$ – <50%	10 (10.0%)	2 (5.0%)	0 (0.0%)	4 (5.1%)			16 (6.4%)
50% $\leq$ – <80%	5 (5.0%)	0 (0.0%)	1 (3.1%)	0 (0.0%)			6 (2.4%)
$\geq$ 80%	3 (3.0%)	0 (0.0%)	0 (0.0%)	3 (3.8%)			6 (2.4%)
Probability of hMPV etiology plus probability of bacterial etiology							
<25%	3 (3.0%)	5 (13.5%)	3 (11.1%)	7 (9.3%)	0.004	0.03	18 (7.6%)
25% $\leq$ – <50%	1 (1.0%)	3 (7.5%)	5 (15.6%)	4 (5.1%)			13 (5.2%)
50% $\leq$ – <80%	30 (30.0%)	13 (32.5%)	14 (43.8%)	19 (24.1%)			76 (30.3%)
$\geq$ 80%	66 (66.0%)	19 (47.5%)	10 (31.3%)	49 (62.0%)			144 (57.4%)

*Leukocytosis defined as white blood cell count >15 000 cells/uL if age <12 months, or >13 000 cells/uL if age >12 months

**Etiologic fraction is the proportion of etiology attributed to the pathogen in an individual case. If a child's etiology has probability distributed across pathogens. When there is evidence for only one pathogen, a higher probability due to that pathogen is assigned but is <100% unless confirmed with invasive specimen (e.g., blood culture positive) to allow for false-negative test results for other pathogens. If more than one pathogen is detected in invasive specimens (e.g., pleural fluid PCR identified two pathogens), the etiology probability is split between them equally.

Table S9. Association of clinical findings with hMPV detection among controls

Clinical Findings	hMPV positive (n = 115)	hMPV negative (n = 4861)	Odds ratio (95% CI)	p value	Adjusted odds ratio ^a (95% CI)	p value ^a
Respiratory tract illness ^b	45 (39.1)	1135 (23.4)	2.11 (1.41 – 3.13)	<0.0001	2.81 (1.86 – 4.22)	<0.0001
Rhinorrhea	31 (27.0)	820 (16.9)	1.81 (1.15 – 2.79)	0.005	2.57 (1.62 – 4.08)	<0.0001
Cough	27 (23.5)	394 (8.2)	3.45 (2.13 – 5.45)	<0.0001	4.12 (2.59 – 6.57)	<0.0001
Fever ^c	1 (0.9)	26 (0.5)	1.63 (0.04 – 10.1)	0.63	1.74 (0.23 – 13.1)	0.59
Tachypnea ^d	14 (12.4)	549 (11.4)	1.10 (0.58 – 1.96)	0.73	1.18 (0.67 – 2.11)	0.56
Diarrhea	5 (4.4)	90 (1.9)	2.40 (0.75 – 5.98)	0.054	2.81 (1.10 – 7.13)	0.03

^a Adjusted for study sites and age in months.

^b Meets any of the following criteria: (1) cough, (2) rhinorrhea, or (3) fever or sore throat and one or more of following: ear discharge, wheeze or difficulty breathing.

^c Temperature $\geq 38^{\circ}\text{C}$ or reported history of fever.

^d Respiratory rate ≥ 60 breaths/minute if aged <2 months, ≥ 50 breaths/minute if aged 2-12 months, or ≥ 40 breaths/minute if aged >12 months.