

Supplementary Table S1: Number of co-infections for different respiratory viruses in included studies

	Study name	Sample size	No. RVIs found	No Co-infects	Flu A	RSV	RV	AdV	hMPV	hBoV	hCoV	PIV	Highest Co-infection	Severity
1	Richard et al., ³⁰	180	173	44	5	36	22	0	8	0	5	0	14	↑
2	Cilla et al., ²¹	315	226	61	7	34	9	1	8	37	8	16	14	↑
3	Huguenin et al., ¹⁹	152	138	85	1	54	10	30	15	28	1	17	26	↓
4	Franz et al., ²²	404	315	127	1	29	30	19	2	19	6	5	14	↑
5	Drews et al., ²⁵	4,336	1339	67	30	21	23	12	0	0	22	12	10	↑
6	Martin et al., ²⁰	893	563	103	25	55	0	59	18	0	30	25	24	↓
7	Boivin et al., ²³	265	164	23	21	22	0	3	12	0	0	0	18	↑
8	Camargo et al., ³⁵	159	104	9	9	2	2	4	2	0	0	0	4	↓
9	Venter et al., ²⁹	610	510	279	11	70	95	20	20	26	22	15	?	↓
10	O'Callaghani-Gordo et al., ²⁶	333	185	30	11	0	21	17	6	0	0	3	9	↑
11	Rhedin et al., ⁴³	502	309	45	12	1	30	11	1	18	11	9	9	↓
12	Marcone et al., ²⁷	620	476	61	3	31	48	0	12	0	0	5	30	↑
13	Kouni et al., ²⁴	611	397	161	37	112	31	14	4	5	0	46	29	↑
14	Echneque et al., ³²	1,192	666	49	24	13	28	13	1	0	1	8	17	↑
15	Libster et al., ³⁸	251	251	47	47	10	10	7	6	0	1	8	10	↑

Notes: RVIs - respiratory virus infections, RSV - respiratory syncytial virus, RV - rhino virus, hMPV – human metapneumovirus, hCoV - human coronavirus, Flu A/B - influenza A or B, AdV - adenovirus, PIV1-4 - parainfluenza virus types 1 to 4. ↑ Study reported increased risk associated with co-infections, ↓ study found co-infections reduced severity, ? – number not given. In bold is the co-infection pair that was found to be the most predominant by the study and the actual number of such co-infection is provided in column “Highest Co-infection”. The number of studies in this table is less than the number of studies included in the review because some of the included studies did not give details of the number of specific viruses involved in co-infections.

Supplementary Table S2: Influenza virus single and multiple infections and disease severity

Study name	Test	Age	Primary virus	Co-infection	Admission to GW		Admission to ICU		Bronchiolitis		Pneumonia	
					OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Venter et al., ²⁹	RT-PCR Direct IF ELISA	<5 yrs	Flu A	RSV A/B, RV, AdV, hMPV, hCOV, hBOV, PIV1-3	1.31 (0.19 – 9.10)	0.73						
Singleton et al., ²⁸	QRT-PCR	<3 yrs	Flu A/B	RSV A/B, RV, AdV, hMPV, hCOV, hBOV, PIV1-3	1.01 (0.21 – 4.96)	0.99			0.43 (0.18-1.0)	0.05*	0.77 (0.32 – 1.9)	0.56
Boivin et al., ²³	RT-PCR	<3 yrs	Flu A	RSV A/B, AdV, hMPV, PIV1-4					4.69 (1.38 – 15.95)	0.01*	0.73 (0.25 – 2.11)	0.56
Do et al., ³¹	RT-PCR	<13 yrs	Flu A	RSV A/B, RV, AdV, hMPV, hCOV 229E, NL63, OC43, hBOV, PIV1-3			1.88 (0.22 – 15.9)	0.56				
Camargo et al., ³⁵	RT-PCR	Children & adults	Flu A	Flu A, RSV			0.70 (0.07 – 7.2)	0.77				
Libster et al., ³⁸	RT-PCR	<18 yrs	Flu A	RSV A/B, AdV, PIV1-4			1.43 (0.67 – 3.10)	0.36				
Rhedin et al., ⁴³	RT-PCR	<17 yrs	Flu A	RSV A/B, RV, AdV, hMPV, hCOV, hBOV, PIV1-3			1.38 (0.26 – 7.32)	0.71				
Echenique et al., ³²	RT-PCR	Children & adults	Flu A	RSV A/B, RV, AdV, hMPV, hCOV, hBOV, PIV1-3			1.72 (0.65 – 4.57)	0.27				

Notes: RSV - respiratory syncytial virus, RV - rhino virus, hMPV – human metapneumovirus, hCoV - human coronavirus, Flu A/B - influenza A or B, AdV - adenovirus, PIV1-3 - parainfluenza virus types 1 to 3, EV – Enterovirus, HI: Hemagglutination inhibition assay, . ICU - intensive care unit. IF- Immunofluorescence test. RT-PCR - Real time polymerase chain reaction. All odds ratios were calculated with single viral infections as the baseline. * Statistically significant at $p < 0.05$.