

Supplementary Material

Supplementary Table 1: Sequence information of primers and probes used to detect viruses.

Virus	PCR protocol	Gene	Primer/probe	Sequence (5'-3')
AdV	PCR	Hexon	Forward primer	CAACACCTAYGASTACATGAA
			Reverse primer	KATGGGGTARAGCATGTT
EV/RhV	RT-PCR	5'UTR	Forward primer	CAAGCACTCTGTTCCC
			Reverse primer	CACGGACACCCAAAGTAGT
hMPV	RT-qPCR	N	Forward primer	CATATAAGCATGCTATATTAAAAGAGTCTCA
			Reverse primer	CCTATYTCTGCAGCATATTGTAATCA G
			Probe	FAM-CAACHGCAGTRACA CYTCATCATTRCA-BHQ1
IFV-A H1N1pdm	RT-qPCR	HA	Forward primer	AGAAAAGAATGTAACAGTAACACACTCTGT
			Reverse primer	TGTTTCCACAATGTARGACCAT
			Probe	FAM-CAGCCAGCAATRTTRCATTACC-MGB
IFV-A H3N2	RT-qPCR	HA	Forward primer	CTATTGGACAATAGTAAAACCGGGRGA
			Reverse primer	GTCATTGGGRATGCTTCATTGG
			Probe	FAM-AAGTAACCCCKAGGAGCAATTAG-MGB
IFV-B	RT-qPCR	NS	Forward primer	GGAGCAACCAATGCCAC
			Reverse primer	GTKTAGGCGGTCTGACCAG
			Probe	FAM-ATAAACTTGAAGCAGGAAT-MGB
PIV-1	RT-PCR	HN	Forward primer	CCG GTAATTCTCATACCTATG
			Reverse primer	CCTTGGAGCGGAGTTGTTAAG
PIV-2	RT-PCR	HN	Forward primer	AACAATCTGCTGCAGCATT
			Reverse primer	ATGTCAGACAATGGGCAAAT
PIV-3	RT-PCR	HN	Forward primer	CTCGAGGTTGTCAGGATATAG
			Reverse primer	CTTTGGGAGTTAACACAGTT
PIV-4	RT-PCR	P	Forward primer	CCTGAACGGTTGCAYTCAGG
			Reverse primer	TTGCATCAAGAACATGAGTCCT
RSV	RT-qPCR	N	Forward primer	GCTCTTAGCAAAGTCAAGTTRAATGATACA
			Reverse primer	GTTTYTGACATCATAATTRGGAGT
			Probe	VIC-CTRTCATCCAGCAAATAYACYATCCAACGKAGYACAGG-MGB

Supplementary Table 2: Demographic and biological characteristics of children with preceding infections and matched controls.

Part 1

		AdV	97%		EV-D68	87%		EVs other than D68	92%		hMPV	91%	
		"children with preceding infection"	matched "children with preceding infection"	matched controls	"children with preceding infection"	matched "children with preceding infection"	matched controls	"children with preceding infection"	matched "children with preceding infection"	matched controls	"children with preceding infection"	matched "children with preceding infection"	matched controls
Total number		91	88	88	46	40	40	52	48	48	128	116	116
Gender	Female	46 (51%)	44 (50%)	47 (53%)	22 (48%)	19 (48%)	18 (45%)	20 (38%)	18 (38%)	20 (42%)	61 (48%)	53 (46%)	58 (50%)
	Male	45 (49%)	44 (50%)	41 (47%)	24 (52%)	21 (53%)	22 (55%)	32 (62%)	30 (63%)	28 (58%)	67 (52%)	63 (54%)	58 (50%)
Age	0–5M	5 (5%)	5 (6%)	4 (5%)	5 (11%)	0 (0%)	2 (5%)	5 (10%)	2 (4%)	2 (4%)	18 (14%)	11 (9%)	12 (10%)
	6–11M	19 (21%)	18 (20%)	14 (16%)	9 (20%)	9 (23%)	7 (18%)	12 (23%)	11 (23%)	9 (19%)	23 (18%)	23 (20%)	19 (16%)
	1Y	31 (34%)	30 (34%)	33 (38%)	13 (28%)	12 (30%)	10 (25%)	11 (21%)	11 (23%)	14 (29%)	34 (27%)	32 (28%)	35 (30%)
	2Y	11 (12%)	11 (13%)	13 (15%)	12 (26%)	12 (30%)	14 (35%)	10 (19%)	10 (21%)	9 (19%)	20 (16%)	20 (17%)	17 (15%)
	3Y	11 (12%)	11 (13%)	13 (15%)	7 (15%)	7 (18%)	7 (18%)	8 (15%)	8 (17%)	8 (17%)	19 (15%)	17 (15%)	23 (20%)
	4Y	14 (15%)	13 (15%)	11 (13%)	0 (0%)	0 (0%)	0 (0%)	6 (12%)	6 (13%)	6 (13%)	14 (11%)	13 (11%)	10 (9%)
Height-for-age Z-score	≥ -2	54 (59%)	53 (60%)	53 (60%)	28 (61%)	22 (55%)	26 (65%)	36 (69%)	32 (67%)	31 (65%)	92 (72%)	83 (72%)	84 (72%)
	< -2	37 (41%)	35 (40%)	35 (40%)	18 (39%)	18 (45%)	14 (35%)	16 (31%)	16 (33%)	17 (35%)	36 (28%)	33 (28%)	32 (28%)
Low birth weight	<2,500 g	9 (13%)	8 (12%)	5 (6%)	8 (20%)	7 (20%)	4 (11%)	5 (12%)	5 (13%)	2 (4%)	18 (17%)	13 (14%)	8 (7%)
Socioeconomic status score	37–93	20 (22%)	20 (23%)	24 (27%)	13 (28%)	11 (28%)	10 (25%)	15 (29%)	15 (31%)	14 (29%)	34 (27%)	28 (24%)	29 (25%)
	25–36	37 (41%)	36 (41%)	32 (36%)	13 (28%)	11 (28%)	13 (33%)	16 (31%)	14 (29%)	14 (29%)	44 (34%)	40 (34%)	39 (34%)
	0–24	34 (37%)	20 (23%)	32 (36%)	20 (43%)	11 (28%)	17 (43%)	21 (40%)	15 (31%)	20 (42%)	50 (39%)	28 (24%)	48 (41%)

Percentage values next to the virus name show the success rate of matching.

Part 2

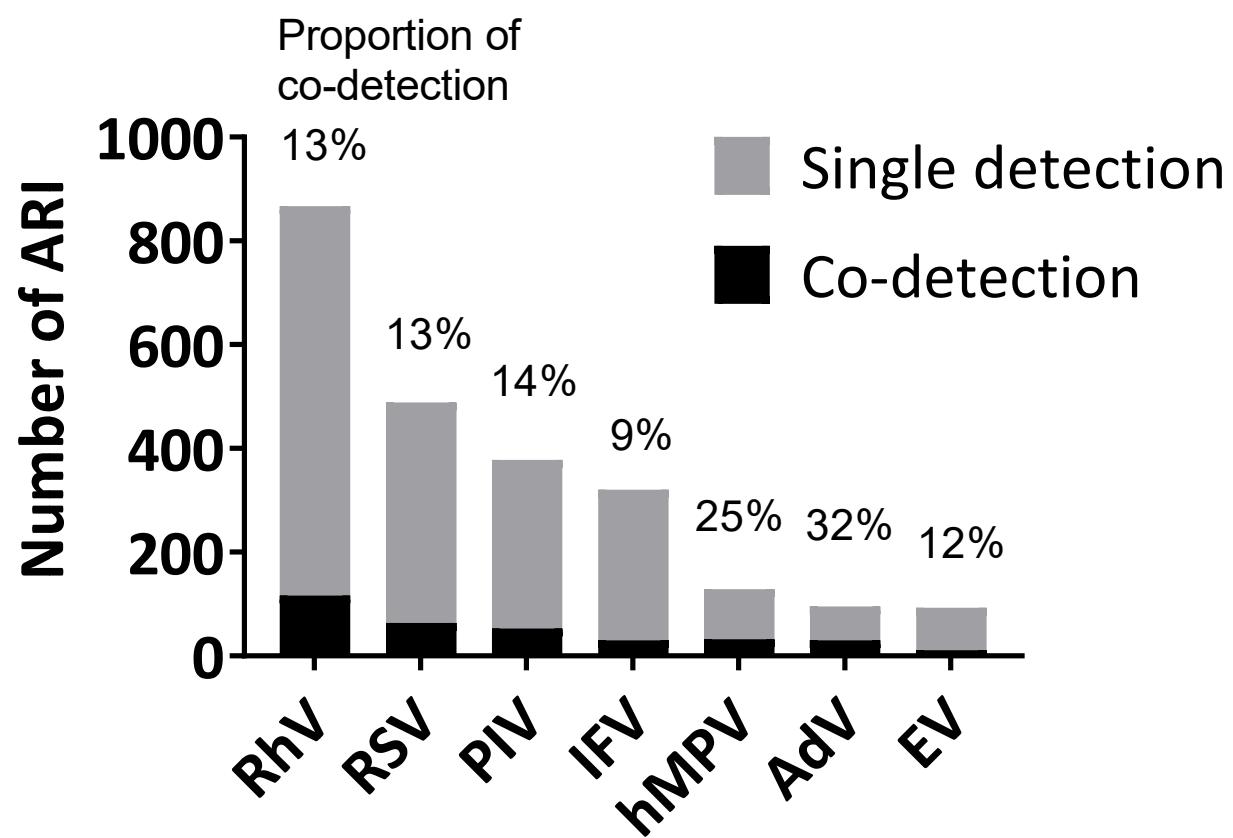
		IFV-A "children with preceding infection"	95% matched "children with preceding infection"		IFV-B "children with preceding infection"	88% matched "children with preceding infection"		PIV-1 "children with preceding infection"	93% matched "children with preceding infection"		PIV-2 "children with preceding infection"	90% matched "children with preceding infection"	
Total number		199	189	189	131	115	115	148	138	138	42	38	38
Gender	Female	77 (39%)	73 (39%)	75 (40%)	53 (40%)	50 (43%)	50 (43%)	63 (43%)	58 (42%)	56 (41%)	26 (62%)	24 (63%)	23 (61%)
	Male	122 (61%)	116 (61%)	114 (60%)	78 (60%)	65 (57%)	65 (57%)	85 (57%)	80 (58%)	82 (59%)	16 (38%)	14 (37%)	15 (39%)
Age	0–5M	7 (4%)	5 (3%)	1 (1%)	9 (7%)	5 (4%)	2 (2%)	8 (5%)	4 (3%)	6 (4%)	3 (7%)	1 (3%)	2 (5%)
	6–11M	28 (14%)	25 (13%)	32 (17%)	16 (12%)	14 (12%)	14 (12%)	26 (18%)	23 (17%)	20 (14%)	7 (17%)	6 (16%)	3 (8%)
	1Y	41 (21%)	41 (22%)	36 (19%)	19 (15%)	17 (15%)	22 (19%)	42 (28%)	41 (30%)	45 (33%)	8 (19%)	8 (21%)	14 (37%)
	2Y	53 (27%)	52 (28%)	55 (29%)	28 (21%)	26 (23%)	24 (21%)	34 (23%)	32 (23%)	29 (21%)	13 (31%)	12 (32%)	8 (21%)
	3Y	39 (20%)	37 (20%)	35 (19%)	26 (20%)	23 (20%)	27 (23%)	20 (14%)	20 (14%)	21 (15%)	5 (12%)	5 (13%)	7 (18%)
	4Y	31 (16%)	29 (15%)	30 (16%)	33 (25%)	30 (26%)	26 (23%)	18 (12%)	18 (13%)	17 (12%)	6 (14%)	6 (16%)	4 (11%)
Height-for-age Z-score	≥ -2	131 (66%)	123 (65%)	127 (67%)	84 (64%)	70 (61%)	72 (63%)	107 (72%)	100 (72%)	97 (70%)	19 (45%)	17 (45%)	23 (61%)
	< -2	68 (34%)	66 (35%)	62 (33%)	47 (36%)	45 (39%)	43 (37%)	41 (28%)	38 (28%)	41 (30%)	23 (55%)	21 (55%)	15 (39%)
Low birth weight	<2,500 g	20 (13%)	19 (13%)	19 (11%)	13 (14%)	10 (12%)	13 (12%)	27 (22%)	24 (21%)	9 (7%)	7 (19%)	6 (18%)	7 (19%)
Socioeconomic status score	37–93	41 (21%)	39 (21%)	36 (19%)	32 (24%)	28 (24%)	34 (30%)	47 (32%)	40 (29%)	40 (29%)	4 (10%)	4 (11%)	4 (11%)
	25–36	72 (36%)	68 (36%)	68 (36%)	46 (35%)	39 (34%)	38 (33%)	52 (35%)	50 (36%)	48 (35%)	19 (45%)	17 (45%)	18 (47%)
	0–24	86 (43%)	39 (21%)	85 (45%)	53 (40%)	28 (24%)	43 (37%)	49 (33%)	40 (29%)	50 (36%)	19 (45%)	4 (11%)	16 (42%)

Part 3

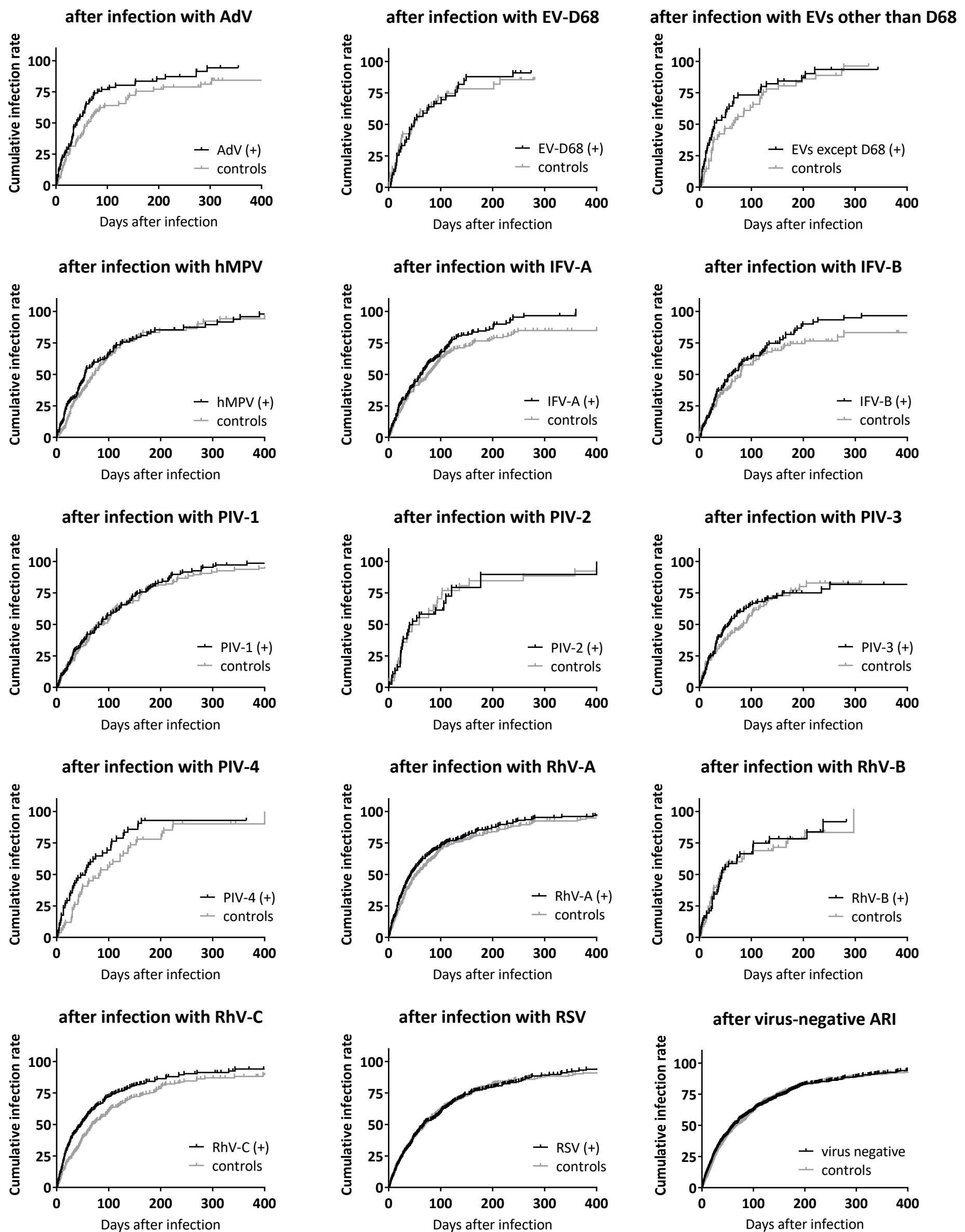
		PIV-3	90%		PIV-4	93%		RhV-A	83%		RhV-B	94%	
		"children with preceding infection"	matched "children with preceding infection"	matched controls	"children with preceding infection"	matched "children with preceding infection"	matched controls	"children with preceding infection"	matched "children with preceding infection"	matched controls	"children with preceding infection"	matched "children with preceding infection"	matched controls
Total number		136	122	122	55	51	51	408	338	338	62	58	58
Gender	Female	68 (50%)	60 (49%)	56 (46%)	35 (64%)	32 (63%)	32 (63%)	190 (47%)	155 (46%)	153 (45%)	31 (50%)	28 (48%)	26 (45%)
	Male	68 (50%)	62 (51%)	66 (54%)	20 (36%)	19 (37%)	19 (37%)	218 (53%)	183 (54%)	185 (55%)	31 (50%)	30 (52%)	32 (55%)
Age	0–5M	16 (12%)	9 (7%)	9 (7%)	3 (5%)	2 (4%)	3 (6%)	96 (24%)	58 (17%)	49 (14%)	17 (27%)	13 (22%)	11 (19%)
	6–11M	24 (18%)	21 (17%)	24 (20%)	6 (11%)	4 (8%)	3 (6%)	89 (22%)	74 (22%)	78 (23%)	14 (23%)	14 (24%)	15 (26%)
	1Y	44 (32%)	41 (34%)	35 (29%)	19 (35%)	19 (37%)	17 (33%)	94 (23%)	85 (25%)	90 (27%)	11 (18%)	11 (19%)	10 (17%)
	2Y	23 (17%)	23 (19%)	23 (19%)	7 (13%)	7 (14%)	9 (18%)	56 (14%)	53 (16%)	56 (17%)	7 (11%)	7 (12%)	10 (17%)
	3Y	15 (11%)	14 (11%)	18 (15%)	16 (29%)	16 (31%)	12 (24%)	45 (11%)	42 (12%)	38 (11%)	5 (8%)	5 (9%)	4 (7%)
	4Y	14 (10%)	14 (11%)	13 (11%)	4 (7%)	3 (6%)	7 (14%)	28 (7%)	26 (8%)	27 (8%)	8 (13%)	8 (14%)	8 (14%)
Height-for-age Z-score	≥ -2	79 (58%)	72 (59%)	79 (65%)	40 (73%)	37 (73%)	38 (75%)	266 (65%)	220 (65%)	221 (65%)	43 (69%)	40 (69%)	42 (72%)
	< -2	57 (42%)	50 (41%)	43 (35%)	15 (27%)	14 (27%)	13 (25%)	142 (35%)	118 (35%)	117 (35%)	19 (31%)	18 (31%)	16 (28%)
Low birth weight	<2,500 g	14 (13%)	11 (11%)	10 (9%)	4 (9%)	3 (7%)	1 (2%)	54 (16%)	35 (13%)	26 (8%)	5 (9%)	5 (10%)	6 (11%)
Socioeconomic status score	37–93	40 (29%)	34 (28%)	35 (29%)	12 (22%)	10 (20%)	11 (22%)	114 (28%)	91 (27%)	98 (29%)	11 (18%)	9 (16%)	10 (17%)
	25–36	53 (39%)	49 (40%)	52 (43%)	26 (47%)	24 (47%)	22 (43%)	138 (34%)	110 (33%)	109 (32%)	24 (39%)	23 (40%)	23 (40%)
	0–24	43 (32%)	34 (28%)	35 (29%)	17 (31%)	10 (20%)	18 (35%)	156 (38%)	91 (27%)	131 (39%)	27 (44%)	9 (16%)	25 (43%)

Part 4

		RhV-C	87%		RSV	90%	
		"children with preceding infection"	matched "children with preceding infection"	matched controls	"children with preceding infection"	matched "children with preceding infection"	matched controls
Total number		324	281	281	479	430	430
Gender	Female	149 (46%)	138 (49%)	135 (48%)	245 (51%)	221 (51%)	221 (51%)
	Male	175 (54%)	143 (51%)	146 (52%)	234 (49%)	209 (49%)	209 (49%)
Age	0–5M	47 (15%)	28 (10%)	24 (9%)	71 (15%)	45 (10%)	43 (10%)
	6–11M	69 (21%)	56 (20%)	55 (20%)	74 (15%)	65 (15%)	70 (16%)
	1Y	88 (27%)	83 (30%)	83 (30%)	155 (32%)	146 (34%)	146 (34%)
	2Y	58 (18%)	54 (19%)	57 (20%)	78 (16%)	77 (18%)	73 (17%)
	3Y	29 (9%)	28 (10%)	29 (10%)	53 (11%)	51 (12%)	55 (13%)
	4Y	33 (10%)	32 (11%)	33 (12%)	48 (10%)	46 (11%)	43 (10%)
Height-for-age Z-score	≥ -2	224 (69%)	195 (69%)	198 (70%)	334 (70%)	302 (70%)	307 (71%)
	< -2	100 (31%)	86 (31%)	83 (30%)	145 (30%)	128 (30%)	123 (29%)
Low birth weight	<2,500 g	31 (11%)	22 (9%)	20 (8%)	46 (12%)	32 (9%)	31 (8%)
Socioeconomic status score	37–93	83 (26%)	74 (26%)	79 (28%)	132 (28%)	118 (27%)	117 (27%)
	25–36	122 (38%)	107 (38%)	105 (37%)	184 (38%)	160 (37%)	159 (37%)
	0–24	119 (37%)	74 (26%)	97 (35%)	163 (34%)	118 (27%)	154 (36%)

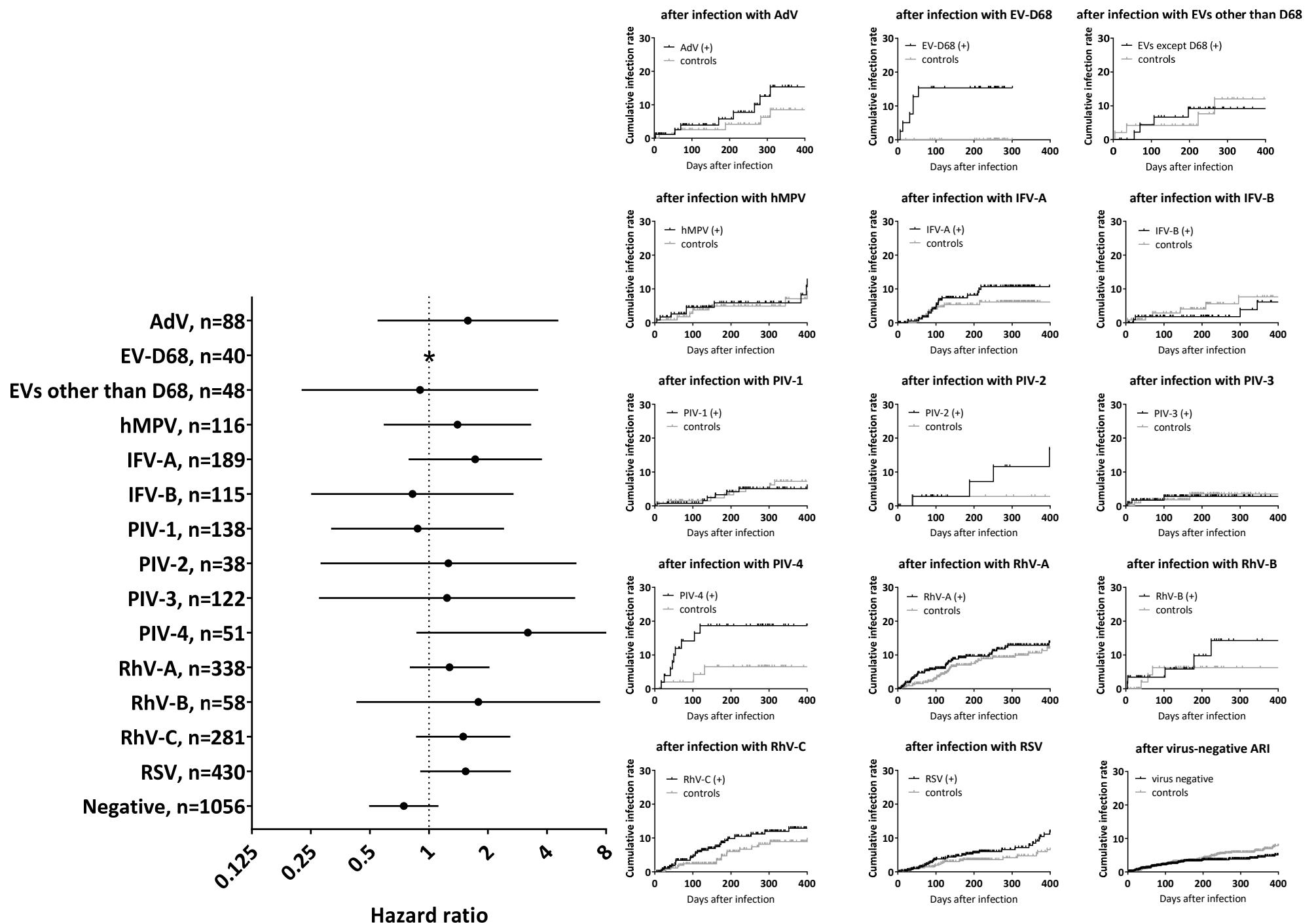


Supplementary Figure 1: Number of virus-positive ARIs detected in this study.



Supplementary Figure 2: Preceding viral infections and subsequent ARIs; Kaplan–Meier curves for all viruses.

Cumulative infection rates by Kaplan–Meier curves are shown for subsequent ARIs after preceding infections and ARIs in matched controls during the corresponding period.

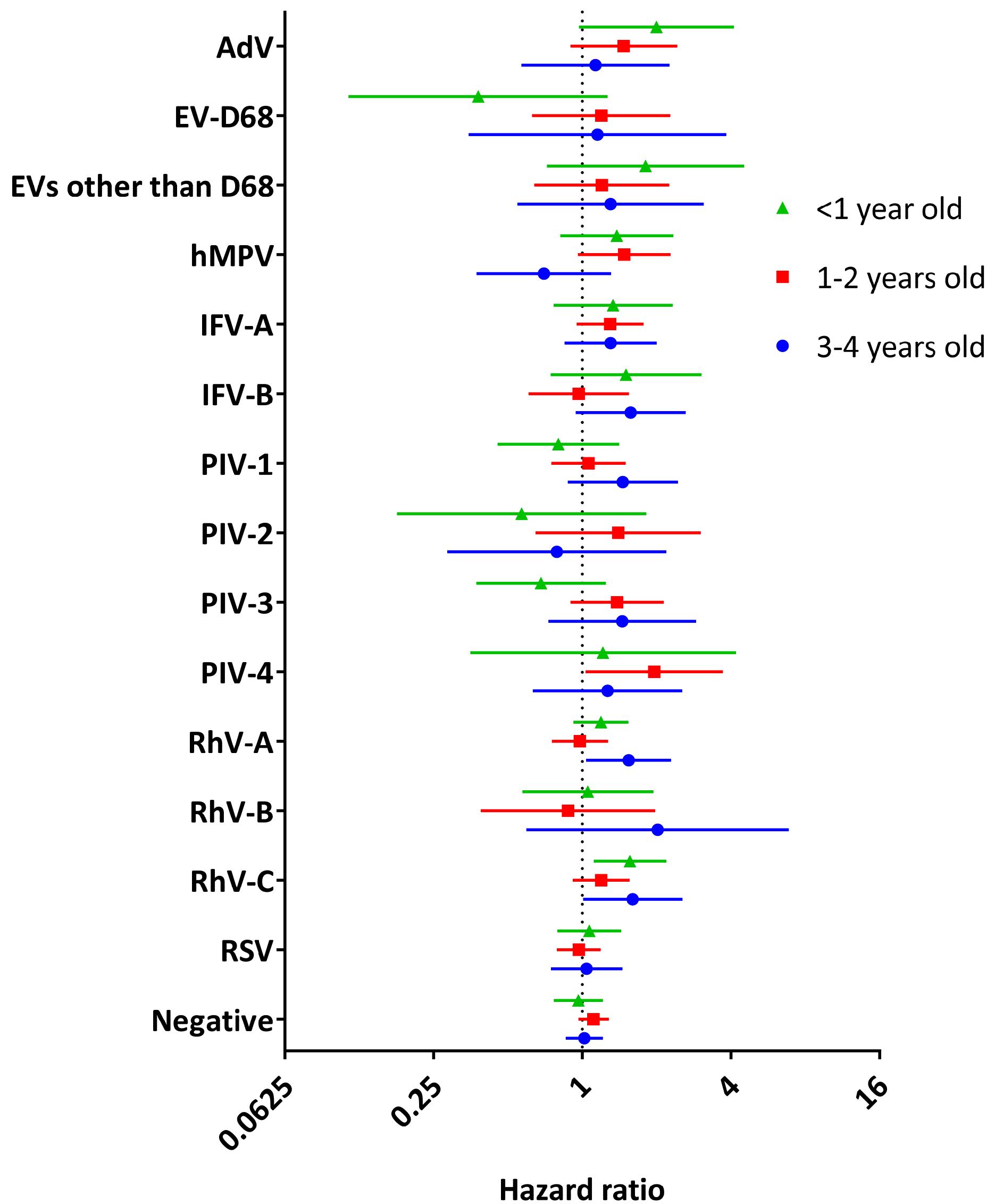


Supplementary Figure 3: Preceding viral infections and subsequent severe ARIs.

(A) Hazard ratios and 95% confidence intervals determined using Cox proportional hazards regression analysis are shown for subsequent severe ARIs after preceding infections compared with the first severe ARIs during the corresponding time for matched controls. A log scale was used for hazard ratios.

Cumulative infection rates by Kaplan-Meier curves are shown for subsequent severe ARIs after preceding infections and severe ARIs in matched controls during the corresponding period.

*: not calculated because of the limited number of events.



Supplementary Figure 4: Preceding viral infections and subsequent ARIs by age group.

Hazard ratios and 95% confidence intervals determined using Cox proportional hazards regression analysis by age group are shown for all subsequent ARIs after preceding infections compared with the first ARIs during the corresponding time for matched controls. A log scale was used for hazard ratios.