Supplementary Table 1: Sensitivity analysis comparing untested and HIV-uninfected population in children < 5 years of age at 6 sentinel sites in South Africa, 2009 –2013

Characteristic	HIV-uninfected (n=1,557)	HIV untested (n=765)	p-value
Demographics			
Age, months; median (IQR)	4.9 (2.4 – 11.3)	5.4 (2.2 – 13.0)	0.15
Female sex	667/1,557 (42.8)	336/765 (43.9)	0.62
Race, black (%)	1,537/1,557 (98.7)	739/761 (97.1)	0.006
Duration of Symptoms; median (days, IQR)	2 (1 – 3)	2 (1 – 3)	0.70
Premature	26/1,556 (1.7)	11/760 (1.5)	0.69
DOB within 10 weeks of start of RSV season (%)	793/1,557 (50.9)	418/765 (54.6)	0.09
RSV CT Value; mean (SD)	25.7 (4.6)	25.1 (5.1)	0.003
Crowding (5+ people in the household)	140/1,534 (9.1)	86/758 (11.4)	0.09
Underlying Conditions			
Underlying illness	56/1,557 (3.6)	16/762 (2.1)	0.05
Whole blood PCR+ S. Pneumo (%)	62/1,134 (5.5)	4/147 (2.7)	0.16
Outcomes			
Primary Outcome (%)	27/1,540 (1.8)	11/737 (1.5)	0.65
Secondary Outcome (%)	555/1538 (36.1)	212/753 (28.2)	<0.001

A sensitivity analysis was performed to comapre HIV-uninfected children with HIV-untested children. Abbreviations: HIV: human immunodeficiency virus.

Supplementary Table 2: RSV coinfection matrix of viral coinfections in RSV-infected HIV-uninfected children aged <5 years at 6 sentinel sites in South Africa, 2009 –2013

	RV N (%)	HMPV N (%)	AdV N (%)	EV N (%)	Infl N (%)	PIV1 N (%)	PIV2 N (%)	PIV 3 N (%)
RV	438[a] (18.9)							
HMPV	10[b]	9 (0.39)						
ADV	117	5	159 (6.8)					
EV	0	1	47	134 (5.8)				
Infl	7	1	8	3	10 (0.43)			
PIV1	2	0	4	2	0	4 (0.17)		
PIV2	5	0	3	2	0	0	2 (0.09)	
PIV3	6	0	4	2	1	0	0	7 (0.30)
Total positive	575 (24.5)[c]	26 (1.1)	347 (14.9)	191 (8.2)	30 (1.3)	12 (0.52)	12 (0.52)	20 (0.86)

a: Exclusive dual infection only, this cell shows RSV-RV positive children. b: This cell shows detection of both RV and HMPV in the RSV-positive population.
c: In this cell total prevalence of rhinovirus-positive children in the population of RSV-positive children; this row shows total prevalence of the virus in the RSV-positive population including all permutations of coinfection. All percentages are given out of the total RSV-positive population of 2,322 children.
Abbreviations: RSV: Respiratory Syncytial Virus, HMPV: human metapneumovirus; RV: rhinovirus; ADV: adenovirus; EV: enterovirus; Infl: influenza; PIV1: parainfluenza type 1; PIV2: parainfluenza type 2; PIV-3: parainfluenza 3.

Supplementary Table 3: Univariate analysis for predictors of disease severity amongst patients with RSV in HIV-uninfected children < 5 years of age at 6 sentinel sites in South Africa, 2009 - 2013

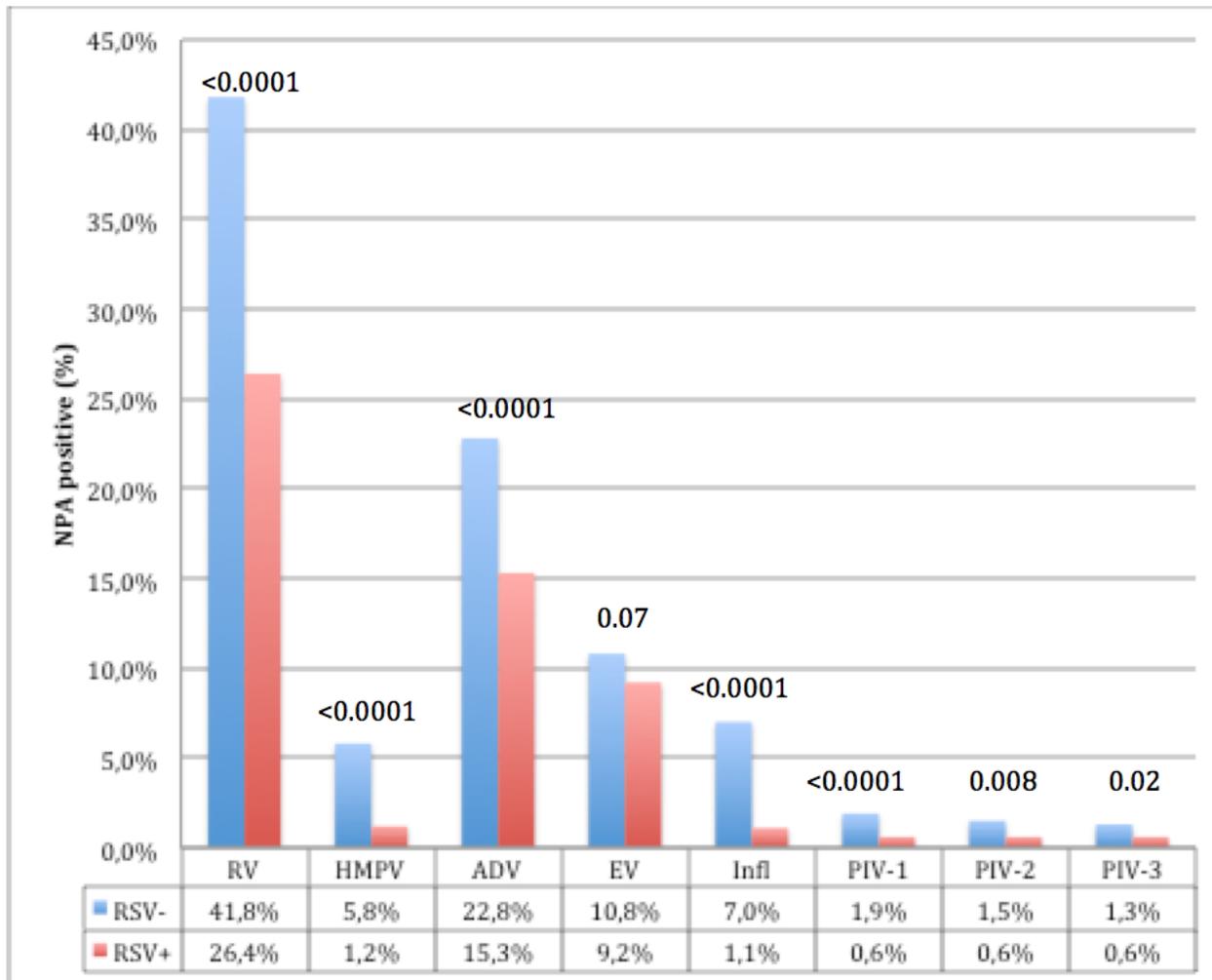| Predictor	Life-threatening disease	p-value	Life-threatening disease, or LOS 5+ days	p-value
Age in months OR (95% CI)	0.94 (0.89–0.99)	0.03 $^{\Psi}$	0.94 (0.92–0.95)	<0.0001 $^{\Psi}$
Sex OR (95% CI)	0.84 (0.44–1.6)	0.60	1.1 (0.95–1.3)	0.17 $^{\Psi}$
Symptom Duration OR (95% CI)	0.98 (0.78–1.2)	0.83	1.1 (1.0–1.1)	0.07 $^{\Psi}$
Prematurity OR (95% CI)	5.6 (1.6–18.9)	0.006 $^{\Psi}$	2.4 (1.2–4.6)	0.009 $^{\Psi}$
DOB within 10 weeks of start of RSV season OR (95% CI)	1.3 (0.66–2.4)	0.48	1.3 (1.1–1.5)	0.006 $^{\Psi}$
RSV Ct value OR (95% CI)	1.0 (0.93–1.1)	1.0	0.98 (0.97–1.0)	0.09 $^{\Psi}$
Crowding OR (95% CI)	0.51 (0.12–2.1)	0.36	1.2 (0.93–1.6)	0.14 $^{\Psi}$
Underlying Illness OR (95% CI)	2.8 (0.85–9.4)	0.09 $^{\Psi}$	1.6 (0.99–2.6)	0.05

All factors with P<0.20 were entered into the multivariate model using the manual forward stepwise procedure. Only age and prematurity with P<0.05 were used in the final multivariate model. Sex, DOB within 10 weeks of start of RSV season, RSV Ct value and crowding were excluded because P>= 0.20 in univariate analysis for primary outcome and RSV Ct value and underlying illness were excluded for secondary outcome. Abbreviations: MV: mechanical ventilation, ICU: Intensive Care Unit, LOS: length of stay. DOB: Date of birth, RSV: respiratory syncytial virus. Ψ P<0.2.

Supplementary Table 4: Primary outcome, univariate and multivariate analyses of RSV viral coinfection and life-threatening disease in HIV-infected children < 5 years of age at 6 sentinel sites in South Africa, 2009 – 2013

Coinfection	Life-Threatening Disease	MV, ICU, Death n/N (%)	OR (95% CI)	p-value OR
Any[a]	No	36/38 (5.3)	1.4	
	Yes	3/41 (7.3)	(0.22 – 9.0)	0.71
HMPV	No	5/77 (6.5)		
	Yes	0/2 (0)		
RV	No	5/65 (7.7)		
	Yes	0/14 (0)		
ADV	No	4/62 (6.5)	0.9	
	Yes	1/17 (5.9)	(0.09–8.7)	0.93
EV	No	4/68 (5.9)	1.6	
	Yes	1/11 (9.1)	(0.16–15.8)	0.70
Infl	No	4/76 (5.3)	9	0.10
	Yes	1/3 (33.3)	(0.67–121.5)	
PIV2	No	5/77 (6.5)		
	Yes	0/2 (0)		

No multivariate analysis was done because P>= 0.20 in univariate analysis for all viral coinfections. PIV1 and PIV 3 were omitted from the table because they were not identified in the HIV-positive population. Outcome data was missing for 3 of 82 HIV-positive children <5 years of age. Abbreviations: MV: mechanical ventilation, ICU: Intensive Care Unit. RSV: Respiratory Syncytial Virus, HMPV: human metapneumovirus; RV: rhinovirus; ADV: adenovirus; EV: enterovirus; Infl: influenza; PIV1: parainfluenza type 1; PIV2: parainfluenza type 2; PIV-3: parainfluenza 3. a: Any viral respiratory coinfection with HMPV, RV, ADV, EV, Infl, PIV1, PIV2, or PIV3.

Supplementary Figure 1: Virus prevalence in the absence or presence of RSV in children < 5 years of age at 6 sentinel sites in South Africa, 2009 - 2013

	RV	HMPV	ADV	EV	Infl	PIV-1	PIV-2	PIV-3
■ RSV-	41,8%	5,8%	22,8%	10,8%	7,0%	1,9%	1,5%	1,3%
■ RSV+	26,4%	1,2%	15,3%	9,2%	1,1%	0,6%	0,6%	0,6%

Supplementary Figure Legend

1. The prevalence of RV, HMPV, ADV, EV, Infl, PIV-1, PIV-2, PIV-3 were measured during the RSV season children with an NPA positive for RSV (RSV+) or negative for RSV (RSV-). Abbreviations: RV: rhinovirus, ADV: adenovirus, EV: enterovirus, Inlf: influenza; PIV-1: parainfluenza 1, PIV-2: parainfluenza 2; PIV-3: parainfluenza 3, RSV: Respiratory syncytial virus, NPA: Nasopharyngeal aspirate, +: positive, -: negative.