Supplementary material to:

Rave N, Sharma AK, Chapagain RH, Shrestha R, Nguyen A, Pecenka C, Shaaban FL, Joshi P, Bont LJ; RSV GOLD III – Health Economics Study Group. Assessing the cost of illness of RSV and non-RSV acute respiratory infections in Nepali children. J Glob Health. 2025;15:04092.

With the RSV GOLD III – Health Economics Study we evaluate costs associated with acute lower respiratory tract infections (LRTIs) in children <2 years old in four developing countries (Ghana, Mozambique, Nepal, and Nigeria), during one local respiratory season. Here, we provide supplementary material related to the study conducted in Nepal.

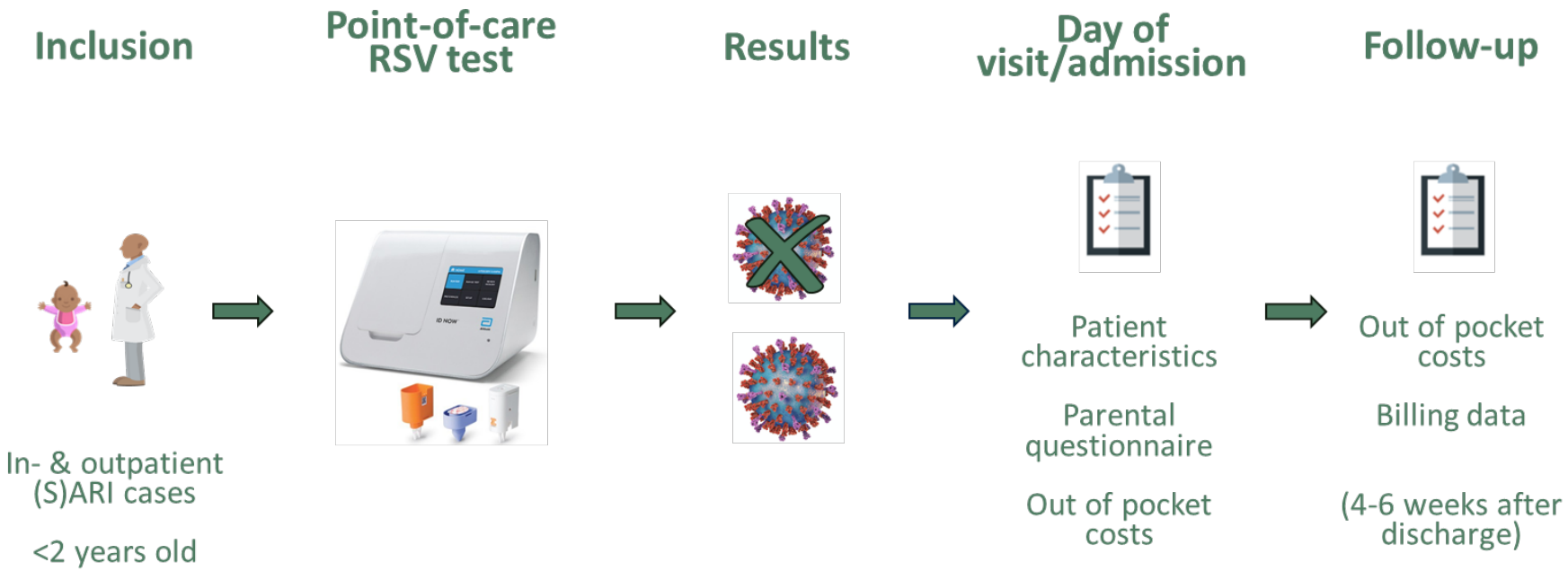

Figure S1. Overview of the clinical process and data collection. RSV – respiratory syncytial virus, (S)ARI – (severe) acute respiratory infection.

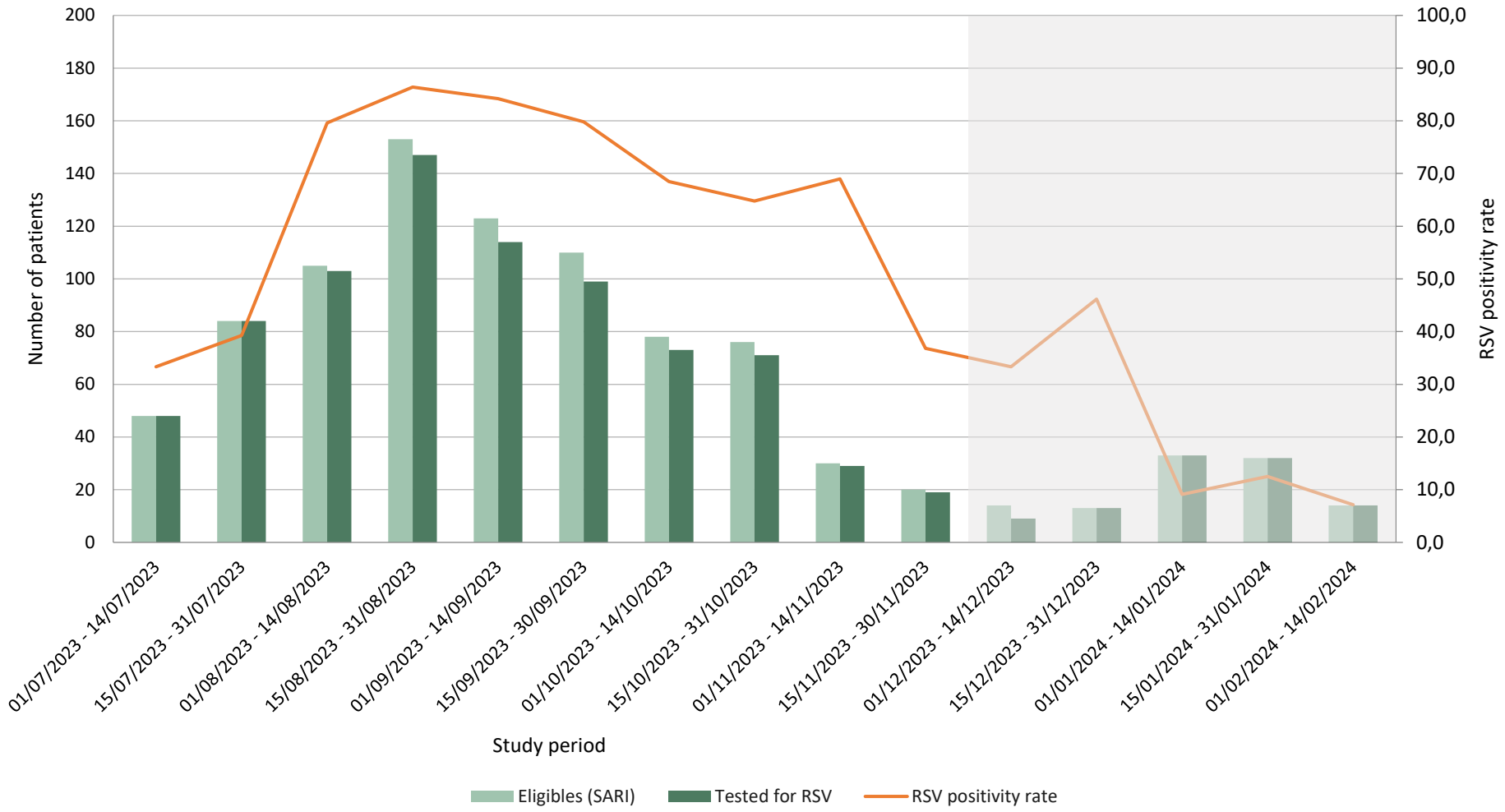

Figure S2. Biweekly numbers of eligible and tested hospitalised children <2 years old, as well as RSV positivity rates, during the original study period and additional testing period. RSV – respiratory syncytial virus, (S)ARI – (severe) acute respiratory infection.

Table S1. RSV testing results for all children <2 years old admitted to the participating hospitals, with testing conducted at two one-week intervals during the study period*

	(S)ARI cases (meet inclusion criteria)		Exclusion (do not meet inclusion criteria)				
	RSV-positive	**RSV-negative**	**RSV-positive**	**RSV-negative**	**Total**	**Overall RSV positivity rate**	**Diagnosis and remarks for excluded children who were RSV-positive by testing**
Week 1							
15th OCT 2023	7	2	5	9	23	52.2%	Bronchiolitis n=2 (excluded as they spent more than three days in emergency); Down syndrome n=1; Very late onset neonatal sepsis n=1; Suspected meningitis n=1
16th OCT 2023	3	2	3	9	17	35.3%	Sepsis n=1; ACHD n=1; Pneumonia n=1 (symptoms of more than 10 days)
17th OCT 2023	4	1	0	4	9	44.4%	N/A
18th OCT 2023	2	1	2	1	6	66.7%	Pneumonia n=1 (referred case from other hospital with long treatment); Pertussis like illness n=1 (admitted after three days of stay in observation ward)
19th OCT 2023	3	3	3	3	12	50.0%	Seizure Disorder n=1; Pneumonia n=1 (referred case from other hospital after long treatment); Pneumonia n=1 (admitted after more than three days of stay in ward)
TOTAL	19	9	13	26	67	47.8%	

Table S1. Continued

Week 2							
5th NOV 2023	4	3	3	11	21	33.3%	Pneumonia n=1; Bronchiolitis n=1; Respiratory distress syndrome n=1 (all referred form anther hospital with at least four days of admission)
6th NOV 2023	3	0	1	0	4	100%	N/A
7th NOV 2023	0	1	2	5	8	25.0%	Pneumonia n=1 (admitted to ward after five days of stay in observation ward)
8th NOV 2023	1	0	1	5	7	28.6%	Bronchiolitis n=1 (referred case from other hospital); Pertussis like illness n=1 (admitted after stay in observation ward for four days)
9th NOV 2023	1	1	0	0	2	50.0%	N/A
TOTAL	9	6	8	23	46	37.0%	

ACHD – acyanotic congenital heart disease, (S)ARI – (severe) acute respiratory illness, RSV – respiratory syncytial virus.
*Values presented as n.

Table S2**.** Demographics and clinical characteristics of RSV-related deaths compared to non-RSV (severe) acute respiratory illness mortality cases*

	Fatal RSV infection	Fatal (S)ARI
Total number of participants	2	10
Age in months, $\bar{X}$ (SD)	4.0 (4.2)	3.2 (2.8)
Female	0 (0.0)	2 (20.0)
Median household size, MD (IQR)	4.5 (4–5)	5.0 (4–5)
Prematurity	1 (50.0)	1 (10.0)
Comorbidity	1 (50.0)	5 (50.0)
Fully vaccinated according to local immunisation schedule and age	1 (50.0)	9 (90.0)
Maternal immunisation	2 (100.0)	10 (100.0)
Presentation upon admission		
Time between onset of symptoms and hospital admission in days, $\bar{X}$ (SD)	2.0 (1.4)	3.1 (2.0)
Fever (temperature >38ºC)	1 (50.0)	5 (50.0)
Oxygen saturation on room air, $\bar{X}$ (SD)	86.5 (0.71)	80.0 (6.36)
Concomitant non-respiratory diagnosis	0 (0.0)	0 (0.0)
Disease management		
Oxygen support	2 (100.0)	6 (60.0)
Non-invasive ventilatory support (CPAP or HFNC)	1 (50.0)	2 (20.0)
Mechanical ventilation	0 (0.0)	5 (50.0)

Table S2. Continued

Systemic corticosteroids administered	0 (0.0)	0 (0.0)
Antibiotics administered	2 (100.0)	9 (90.0)
Disease course, MD (IQR)		
Duration of oxygen support in days	7.0 (2.0–12.0)	2.5 (2.0–4.0)
Duration of non-invasive ventilatory support in days	7.0 (7.0–7.0)	6.0 (3.0–9.0)
Duration of mechanical ventilation in days	N/A	1.0 (1.0–3.0)
Duration of hospital stay in days	11.5 (2.0–21.0)	3.5 (1.0–7.0)

(S)ARI – (severe) acute respiratory illness, CPAP – continuous positive airway pressure, HFNC – high-flow nasal cannula, IQR – interquartile range, MD – median, RSV – respiratory syncytial virus, SD – standard deviation, x̃ – mean.
*Values presented as n (%) unless specified otherwise.

Table S3. Demographics and clinical characteristics of RSV-positive inpatients included during and outside the study period*

	RSV-positive			Non-RSV (S)ARI		
	During study period	**Outside study period**	**P-value**	**During study period**	**Outside study period**	**P-value**
Total number of participants	469	17		177	83	
Age in months, $\bar{X}$ (SD)	6.6 (5.6)	4.2 (5.2)†	0.14	6.5 (6.4)	8.6 (5.9)‡	0.05
Female	187 (39.9)	5 (29.4)	0.39	54 (30.5)	33 (39.8)	0.14
Median household size, MD (IQR)	4.84 (1.7)	5.8 (2.4)	0.05	4.8 (4.6)	5.4 (2.5)	0.05
Prematurity	29 (6.2)	1 (5.9)	0.98	19 (9.7)	6 (7.2)	0.64
Comorbidity	34 (7.2)	2 (11.8)	0.23	30 (17.0)	2 (2.4)	0.001
Fully vaccinated according to local immunisation schedule and age	445 (94.9)	16 (94.1)	0.85	163 (92.6)	81 (97.6)	0.23
Maternal immunisation	467 (99.6)	16 (94.1)	0.005	174 (98.9)	82 (98.8)	0.96
Presentation upon admission						
Time between onset of symptoms and hospital admission in days, $\bar{X}$ (SD)	3.1 (1.6)	3.9 (1.6)	0.05	3.3 (2.0)	3.9 (3.6)	0.02
Fever (temperature >38ºC)	305 (65.0)	10 (58.8)	0.60	116 (65.5)	45 (54.2)	0.08
Oxygen saturation on room air, $\bar{X}$ (SD)	88.4 (5.2)	85.3 (2.5)	0.04	89.9 (5.9)	89.9 (4.3)	0.96
Concomitant non-respiratory diagnosis						
Disease management						
Oxygen support	271 (57.8)	16 (94.1)	0.003	74 (41.8)	38 (45.8)	0.55

Table S3. Continued

Non-invasive ventilatory support (CPAP or HFNC)	131 (27.9)	10 (58.8)	0.006	31 (17.5)	12 (14.5)	0.54
Mechanical ventilation	1 (0.6)	0 (0.0)	0.75	9 (5.1)	1 (1.2)	0.13
Systemic corticosteroids administered	125 (26.7)	8 (47.1)	0.06	30 (17.0)	31 (37.4)	0.00
Antibiotics administered	425 (90.6)	15 (88.2)	0.74	149 (84.2)	78 (94.0)	0.03
Disease course						
Duration of oxygen support in days	2.0 (1.0–3.0)	2.0 (1.0–2.0)	0.68	2.0 (1.0–3.0)	2.0 (1.0–2.0)	0.18
Duration of non-invasive ventilatory support in days	2.0 (1.0–3.0)	2.0 (2.0–3.0)	0.14	2.0 (1.0–3.0)	2.0 (1.0–7.0)	0.23
Duration of mechanical ventilation in days	4.0 (3.0–6.0)	-	N/A	4.0 (1.0–11.0)	3.0 (3.0–3.0)	0.59
Duration of hospital stay in days	4.0 (3.0–6.0)	6.0 (4.0–9.0)	0.004	4.0 (3.0–7.0)	4.0 (4.0–6.0)	0.68

(S)ARI – (severe) acute respiratory illness, CPAP – continuous positive airway pressure, HFNC – high-flow nasal cannula, IQR – interquartile range, MD – median, RSV – respiratory syncytial virus, SD – standard deviation, x̃ – mean.
*Values presented as n (%) unless specified otherwise.
† & ‡ Indicate variables with more than 10% missing observations. Missing data are due to incomplete or missing clinical records. † n=13/17; ‡ n=47/83.

Table S4. Overview of costs (in 2023 USD) per LRTI episode for RSV-positive and non-RSV (severe) acute respiratory illness patients < 2 years old, comparing outpatients and inpatients

	RSV positive (n=532)		RSV negative (n=198)	
	Outpatient (n=63)	**Inpatient (n=469)**	**Outpatient (n=21)**	**Inpatient (n=167)**
Societal costs total				
$\bar{X}$ (95% CI)	43.43 (24.77–62.09)	333.33 (306.05–360.60)	70.09 (20.68–119.51)	432.60 (374.48–490.73)
MD (IQR)	28.30 (24.68–39.46)	270.27 (180.57–408.35)	31.00 (24.88–47.82)	324.23 (205.73–469.28)
Direct medical costs				
$\bar{X}$ (95% CI)	21.61 (20.28–22.94)	136.29 (125.83–146.75)	24.66 (20.11–29.22)	193.98 (160.59–227.36)
MD (IQR)	20.43 (18.92–23.99)	108.99 (84.17–150.28)	19.04 (18.03–26.11)	126.19 (90.02–200.83)
Direct non-medical costs				
$\bar{X}$ (95% CI)	8.32 (3.00–13.65)	67.14 (57.58–76.72)	34.98 (0.00–81.46)	78.81 (65.19–92.42)
MD (IQR)	1.80 (0.84–5.83)	37.60 (20.46–69.56)	7.52 (0.90–13.99)	45.84 (21.79–105.66)
Indirect costs				
$\bar{X}$ (95% CI)	13.50 (0.00–27.20)	132.49 (117.43–147.56)	10.46 (2.24–18.67)	160.92 (132.04–189.80)
MD (IQR)	3.40 (0.63–9.61)	95.70 (48.41–161.12)	2.27 (1.51–7.63)	111.54 (48.41–209.47)
Health system costs total				
$\bar{X}$ (95% CI)	15.78 (15.04–16.52)	58.05 (53.86–80.87)	15.93 (15.26–16.60)	67.91 (59.12–76.71)

Table S4. Continued

MD (IQR)	14.71 (14.71–17.84)	49.08 (36.83–65.70)	14.71 (14.71–17.84)	58.09 (40.17–80.87)
Household costs total				
$\bar{X}$ (95% CI)	18.92 (9.92–27.93)	216.71 (199.33–234.10)	49.86 (1.01–98.72)	293.63 (247.27–339.99)
MD (IQR)	11.00 (7.36–16.79)	171.99 (110.86–263.46)	13.15 (9.88–33.11)	207.82 (128.19–316.14)
Direct medical costs				
$\bar{X}$ (95% CI)	5.83 (4.61–7.05)	78.25 (69.92–86.57)	8.73 (4.45–13.02)	126.06 (96.30–155.82)
MD (IQR)	5.23 (3.03–7.45)	55.74 (34.90–93.73)	4.14 (2.63–8.27)	71.08 (39.41–125.26)
Direct non-medical costs				
$\bar{X}$ (95% CI)	8.32 (2.99–13.65)	67.14 (57.56–76.72)	34.98 (0.00–81.46)	78.81 (65.19–92.42)
MD (IQR)	1.80 (0.84–5.83)	37.60 (20.46–69.56)	7.52 (0.90–13.99)	45.84 (21.79–105.66)
Indirect costs				
$\bar{X}$ (95% CI)	4.77 (1.23–8.32)	72.80 (67.58–78.03)	6.16 (1.50–10.81)	89.48 (76.58–102.37)
MD (IQR)	2.27 (0.44- 4.54)	60.70 (36.69–92.22)	2.27 (1.51–4.54)	66.57 (36.56–115.22)

CI - confidence interval, IQR - interquartile range, MD - median, RSV - respiratory syncytial virus, LRTI - lower respiratory tract infection, $\tilde{x}$ – mean

Table S5. Breakdown of direct medical costs components (in 2023 USD) per ARI episode, according to severity level

	RSV-positive (n=532)			Non-RSV (S)ARI (n=198)		
	Non-severe (n=63)	**Severe (n=441)**	**Life-threatened (n=28)**	**Non-severe (n=21)**	**Severe (n=149)**	**Life-threatened (n=28)**
Medication costs						
$\bar{X}$ (95% CI)	2.57 (2.16–2.98)	13.67 (12.59–14.74)	35.52 (22.82–48.22)	2.89 (1.61–4.17)	16.16 (13.53–18.79)	55.64 (35.01–76.27)
MD (IQR)	2.45 (1.20–3.65)	11.01 (7.38–16.55)	19.53 (13.86–42.97)	2.14 (0.90–3.38)	11.14 (7.98–17.58)	35.37 (16.45–81.37)
Antibiotics						
$\bar{X}$ (95% CI)	0.98 (0.74–1.23)	4.34 (3.76–4.91)	15.52 (6.86–24.18)	1.19 (0.90–1.48)	6.15 (4.26–8.05)	29.15 (13.25–45.05)
MD (IQR)	0.86 (0.61–1.20)	3.37 (2.34–4.70)	6.86 (3.05–13.46)	1.03 (0.95–1.35)	3.38 (2.20–5.08)	8.47 (5.19–43.38)
Steroids						
$\bar{X}$ (95% CI)	0.86 (0.11–1.60)	2.94 (2.49–3.39)	3.92 (1.98–5.86)	0.45 (0.34–0.56)	4.10 (2.45–5.75)	5.09 (1.83–8.34)
MD (IQR)	0.86 (0.36–1.35)	2.29 (1.24–3.23)	3.78 (2.48–6.42)	0.45 (0.38–0.53)	2.48 (1.65–4.14)	4.55 (2.48–5.88)
Bronchodilators						
$\bar{X}$ (95% CI)	0.86 (0.65–1.07)	3.91 (3.47–4.35)	7.47 (3.96–10.99)	1.09 (0.30–1.87)	3.45 (2.97–3.92)	2.95 (2.00 -3.90)
MD (IQR)	0.83 (0.38–1.05)	2.95 (1.70–4.51)	3.61 (2.71–8.12)	0.76 (0.45–1.40)	2.78 (1.68–4.27)	2.89 (1.71–4.28)
Other drugs						
$\bar{X}$ (95% CI)	0.59 (0.41–0.77)	1.66 (1.43–1.89)	6.91 (3.50–10.32)	0.77 (0.48–1.05)	2.21 (1.61–2.82)	8.48 (4.17–12.79)
MD (IQR)	0.30 (0.23–0.83)	1.01 (0.47–1.97)	4.23 (1.85–6.97)	0.69 (0.42–1.17)	0.99 (0.47–2.25)	6.47 (2.79–9.85)

CI - confidence interval, (S)ARI – (severe) acute respiratory illness, IQR - interquartile range, MD - median, RSV - respiratory syncytial virus, LRTI - lower respiratory tract infection, $\tilde{x}$ – mean

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