

Supplemental Table 1: Association of chest radiograph outcome (normal=ref vs. abnormal) with clinical signs, risk factors, and admission diagnoses overall and by site

Variable	Adjusted Odds Ratio ^b										
	Overall	Gambia	Mali	Zambia	Zambia	South	South	Kenya	Thailand	Matlab	Dhaka
				(HIV -)	(HIV +)	Africa	(HIV -)				
Sex (ref=male)	1.16*	0.93*	0.96	0.80	--	1.66**	0.64	1.41*	1.54	1.07	1.29
Severity	0.82	0.92	0.52**	1.36	0.41	1.45*	0.33**	0.43**	1.88	1.29	1.37
Age category (months; ref=1-5)											
1-5 vs 6-11	1.19	1.27	1.10	1.19	1.04	1.20	2.70	1.24	0.62	1.29	1.38
1-5 vs 12-23	1.17	1.40	1.46	1.35	1.48	0.95	3.20	0.97	0.64	1.31	1.28
1-5 vs 24-59	0.84	0.93	0.91	0.64	1.04	0.61	1.10	0.65	0.71	1.94	0.59
Age category (months; ref=1-5), severe											
1-5 vs 6-11	1.36**	1.20	1.58	1.14	0.32	1.54	3.05	2.18*	0.47	1.39	1.42
1-5 vs 12-23	1.38**	1.37	2.09*	1.04	--	1.32	1.00	1.54	0.58	1.51	1.25
1-5 vs 24-59	1.14	1.29	1.69	0.67	0.35	0.68	1.00	1.11	0.72	2.03	0.50
Age category (months; ref=1-5), very severe											
1-5 vs 6-11	0.90	1.99	0.78	1.34	--	0.68	2.36	0.62	2.00	1.40	1.20
1-5 vs 12-23	0.88	1.49	0.94	2.29	0.90	0.48*	0.64	0.73	--	0.35	1.80
1-5 vs 24-59	0.42	0.29	0.37*	0.57	--	0.58	1.00	0.41*	0.67	2.80	1.80
Danger signs											
Head nodding	1.33*	2.78*	1.33	0.83	--	1.09	3.33	1.86*	0.33	--	0.42
Central cyanosis	2.57**	--	4.18**	1.26	0.40	4.62	0.22	0.50	4.40	--	--
Inability to feed/drink	1.28	0.65	1.27	1.12	0.10	1.62	0.72	2.39**	3.44	--	1.06
Vomiting	0.52**	0.44	2.35	--	--	0.56	--	0.43**	0.50	--	--
Lethargy/unconscious	0.99	0.84	0.54*	1.38	0.55	0.70	2.40	1.30	1.20	--	4.45
Convulsions	0.43**	0.16**	0.47*	0.76	0.04*	0.53	0.22	0.28**	0.47	--	2.00
Clinical signs											
Tachypnea ^a	1.51**	2.02**	1.12	1.74**	34.20**	1.03	0.98	2.37**	0.84	1.90	--

Variable	Adjusted Odds Ratio ^b										
	Overall	Gambia	Mali	Zambia (HIV -)	Zambia (HIV +)	South Africa (HIV -)	South Africa (HIV +)	Kenya	Thailand	Matlab	Dhaka
Hypoxemia ^b	2.08**	3.27**	2.28**	3.05**	2.86	1.12	0.31	2.71**	1.68	0.68	1.13
Crackles	1.47**	1.42**	2.24**	0.92	1.07	1.22	1.09	2.00**	1.20	1.73	1.72
Wheeze	0.70**	0.86	0.61*	0.82	1.00	0.55**	0.52	1.06	0.39**	3.35	1.03
Grunting	1.21**	1.40	1.06	0.95	1.00	1.00	0.66	2.01	2.50	3.16	--
Nasal Flaring	1.24**	1.35	1.63*	1.01	1.89	0.86	1.50	1.97**	0.50*	0.91	0.72
Tachycardia ^c	1.10	1.16	1.18	1.03	0.78	0.95	0.56	1.35**	1.02	0.74	2.15
Temperature	1.43**	2.00**	1.26	1.62*	1.83	1.14	--	1.19	1.71	0.51	0.87
Weight-for-age (ref=normal) ^d											
Moderate	1.42**	1.55*	1.09	1.43	1.02	1.74*	0.90	1.32	2.04	1.55	1.54
Severe	1.94**	1.38	3.04**	1.28	4.00	2.42**	1.50	1.59*	2.00	1.81	3.07*
Height-for-age (ref=normal) ^d											
Moderate	1.51**	1.05	2.55**	1.30	0.86	1.20	0.60	1.70*	1.23	2.20*	1.44
Severe	1.36**	0.80	3.07**	1.19	2.57	1.58*	1.17	1.03	3.51	1.32	1.14
Weight-for-height (ref=normal) ^d											
Moderate	1.28*	1.21	1.05	0.80	1.74	1.51	0.52	1.82*	2.67*	1.20	1.42
Severe	1.50**	1.30	2.04**	3.98**	1.11	1.31	1.10	1.27	1.26	1.07	3.87
History											
Died within 30 days	1.74**	1.77	1.64**	1.20	--	--	0.65	1.53	1.18	--	0.58
Antibiotic pretreatment ^e	1.15**	1.30	0.80	1.56	--	1.75**	0.52	0.90	--	0.79	2.12
Hib & PCV vaccination (ref=none) ^f											
Complete Hib, no PCV	1.18	1.79	0.84	--	--	1.72	1.11	0.15	--	--	2.13
Complete PCV	1.02	2.06	0.57	--	--	0.72	--	0.26	--	--	--

Abbreviations: Hib=*Haemophilus influenzae* type b conjugate vaccine; PCV=Pneumococcal conjugate vaccine; HIV=human immunodeficiency virus.

^a Adjusted for age (in months), pneumonia severity, HIV status. Overall model is also adjusted for site (not stratified by HIV status).

^b Tachypnea=respiratory rate \geq 60 breaths per minute for children $<$ 2 months of age, \geq 50 for children 2-11 months, and \geq 40 for children 12-59 months.

^b Hypoxemia=room air pulse-oximetry reading of $<$ 90% if at elevation (Zambia and South Africa) or $<$ 92% at all other sites. If a room air oxygen saturation reading was not available and the child was on supplemental oxygen they were also considered hypoxicemic.

^c Tachycardia=heart rate $>$ 160 beats per minute (bpm) if age 1-11 months, $>$ 150 bpm if age 12-35 months, and $>$ 140 bpm if age 36-59 months.

^d Weight-for-age, height-for-age, and weight-for-height=severe if $<$ -3 z-scores, moderate if between -3 and -2 z-scores below WHO median.

^e Antibiotic pretreatment was defined by having either a positive serum bioassay or documented administration of antibiotics on the day of admission at the referral or study hospital prior to blood culture collection .

^f Vaccine comparison excludes those children too young (<4 months) to have completed a full biologic course of Hib and/or PCV vaccines, as these children by definition are considered to be ‘unvaccinated’ but are not an appropriate comparison group for those who have been vaccinated. Complete vaccination for PCV was defined as 3 or more doses, or 2 doses if there was at least 8 weeks between doses and the child was <9 months of age at enrollment or >12 months of age at the time of the first dose, or 1 or more doses if the age at any of the doses, or age at introduction, was ≥24 months. Complete vaccination for Hib conjugate vaccine was defined as 3 or more doses, or 1 or more doses for a child older than 12 months at first dose.

* p<0.05, ** p<0.01; for binary (no/yes) variables, ‘no’ is the reference category.

Supplemental Table 2: Association of chest radiograph outcome with clinical signs, risk factors, and admission diagnoses among children 1-59 months of age hospitalized with WHO severe or very severe pneumonia

Case characteristic	Normal (ref) vs Abnormal		Other infiltrate only (ref) vs Any consolidation		Normal (ref) vs Any consolidation		Normal (ref) vs Other infiltrate only	
	OR	Adj OR ^a	OR	Adj OR	OR	Adj OR	OR	Adj OR
Severe (ref) vs Very severe	0.89	0.82*	1.59**	1.36**	1.11	0.97	0.70**	0.70**
Danger signs ^b								
Head nodding	1.77**	1.32	1.52*	1.50*	2.12**	1.54*	1.39*	1.05
Central cyanosis	2.68**	2.56**	0.76	0.68	2.37**	2.09*	3.13**	3.17**
Inability to feed/drink	1.15	1.26	1.32	1.56*	1.29	1.49*	0.98	0.99
Vomiting	0.45**	0.53**	0.43*	0.56	0.30**	0.39**	0.68	0.68
Lethargy or unconsciousness	0.83	1.01	1.23	1.42	0.90	1.14	0.73	0.85
Convulsions	0.31**	0.42**	0.62	0.75	0.25**	0.37**	0.40**	0.49**
Clinical signs								
Tachypnea ^c	1.46**	1.53**	1.26	1.46**	1.65**	1.85**	1.30*	1.26*
Hypoxemia ^d	2.31**	2.07**	1.80**	1.13	3.09**	2.21**	1.72**	1.93**
Crackles	1.35**	1.48**	0.86	1.05	1.25**	1.49**	1.46**	1.41**
Wheeze	0.69**	0.71**	0.44**	0.61**	0.44**	0.54**	1.00	0.88
Grunting	1.04	1.21	1.80**	1.35*	1.35**	1.36*	0.75*	1.05
Nasal flaring	1.44**	1.24**	1.99**	1.37**	2.06**	1.46**	1.03	1.06
Tachycardia ^e	1.12	1.10	1.36**	1.15	1.30**	1.17	0.96	1.02
Temperature $\geq 38.5^{\circ}\text{C}$	1.33**	1.46**	1.47**	1.41**	1.59**	1.75**	1.08	1.25
Risk factors								
HIV positive ^f	5.87**	4.52**	3.48**	2.24**	9.37**	6.00**	2.70**	2.54**
Antibiotic pretreatment ^g	1.40**	1.15	1.58**	0.99	1.75**	1.20	1.11	1.14
Weight-for-age (ref=normal)^h								
Moderate	1.46**	1.46**	1.10	1.21	1.53**	1.56**	1.39**	1.35**
Severe	2.18**	1.98**	1.64**	1.45**	2.75**	2.42**	1.67**	1.63**
PCV & Hib Vaccine (ref=none)ⁱ								
Complete Hib, no PCV	1.00	1.24	0.69	0.73	0.83	0.96	1.20	1.59

Case characteristic	Normal (ref) vs Abnormal		Other infiltrate only (ref) vs Any consolidation		Normal (ref) vs Any consolidation		Normal (ref) vs Other infiltrate only	
	OR	Adj OR ^a	OR	Adj OR	OR	Adj OR	OR	Adj OR
Complete PCV	1.04	1.11	0.74	0.59	0.90	0.78	1.21	1.61
Admission diagnoses								
Paraffin ingestion	1.43	1.50	--	--	2.87	2.93	--	--
Meningitis ^j	0.32**	0.34**	0.96	0.64	0.31**	0.28**	0.33**	0.43**
Sepsis	1.02	1.05	1.39	1.15	1.19	1.13	0.85	0.98
Shock ^k	1.07	1.12	1.62**	1.33*	1.34**	1.32*	0.83	0.96
Bronchiolitis	0.79*	0.70**	0.86	0.69*	0.73*	0.61**	0.85	0.83
Asthma	0.59**	0.72*	0.54*	0.81	0.42**	0.63*	0.77	0.77
Gastroenteritis	0.73	0.67*	1.33	1.03	0.84	0.69	0.63*	0.66
Developmental delay	3.70**	4.32**	1.00	0.97	3.70**	4.71**	3.70**	4.56**
Malaria with parasitemia >5000/uL ^l	0.22**	0.29**	1.93	1.71	0.29**	0.37*	0.15**	0.19**

Abbreviations: Hib=*Haemophilus influenzae* type b conjugate vaccine; PCV=Pneumococcal conjugate vaccine; OR=odds ratio; HIV=human immunodeficiency virus, WHO, World Health Organization.

^a Adjusted for age (in months), site (not stratified for HIV status), HIV status, and pneumonia severity (except danger signs and severity models).

^b Danger sign analyses were restricted to very severe cases only.

^c Tachypnea=respiratory rate ≥60 breaths per minute for children <2 months of age, ≥50 for children 2-11 months, and ≥40 for children 12-59 months.

^d Hypoxemia=room air pulse-oximetry reading of <90% if at elevation (Zambia and South Africa) or <92% at all other sites. If a room air oxygen saturation reading was not available and the child was on supplemental oxygen they were also considered hypoxic.

^e Tachycardia=heart rate >160 beats per minute (bpm) if age 1-11 months, >150 bpm if age 12-35 months, and >140 bpm if age 36-59 months.

^f South Africa and Zambia sites only.

^g Antibiotic pretreatment was defined by having either a positive serum bioassay or documented administration of antibiotics on the day of admission at the referral or study hospital prior to blood culture collection.

^h Weight-for-age=severe if <-3 z-scores, moderate if between -3 and -2 z-scores below WHO median.

ⁱ Adjusted models for vaccine use do not include site, as there is little variation in vaccine use within sites making site collinear to vaccine use, and exclude those children too young (<4 months) to have completed a full biologic course of Hib and/or PCV vaccines, as these children by definition are considered to be ‘unvaccinated’ but are not an appropriate comparison group for those who have been vaccinated. Complete vaccination for PCV was defined as 3 or more doses, or 2 doses if there was at least 8 weeks between doses and the child was <9 months of age at enrollment or >12 months of age at the time of the first dose, or 1 or more doses if the age at any of the doses, or age at introduction, was ≥24 months. Complete

vaccination for Hib conjugate vaccine was defined as 3 or more doses, or 1 or more doses for a child older than 12 months at first dose.

^j Meningitis defined as an admission diagnosis of meningitis or a bulging fontanelle if age <18 months.

^k Shock defined as capillary refill time of >3sec, or cool peripheries, or weak pulse with tachycardia.

^l Malaria analyses restricted to sites with endemic disease (Gambia, Mali, Kenya, and Zambia).

* p<0.05, ** p<0.01; for binary (no/yes) variables, ‘no’ is the reference category.

Supplemental Table 3: Distribution of signs and pneumonia risk factors by chest radiograph (CXR) findings among children 1-59 months of age hospitalized with WHO severe or very severe pneumonia, excluding cases with wheeze^a

	N	All CXRs			Abnormal CXRs		
		Normal	Abnormal	p-value ^b	Any consolidation	Other infiltrate only	p-value ^b
		1016 (43.1)	1342 (56.9)	--	752 (56.0)	590 (44.0)	--
Clinical and risk factor findings (column %)							
Total (row %)	2358						
Age category							
<i>1-5 months</i>	1006	434 (42.7)	572 (42.6)	<.001	334 (44.4)	238 (40.3)	.16
<i>6-11 months</i>	533	202 (19.9)	331 (24.7)		188 (25.0)	143 (24.2)	
<i>12-23 months</i>	503	213 (21.0)	290 (21.6)		146 (19.4)	144 (24.4)	
<i>24-59 months</i>	316	167 (16.4)	149 (11.1)		84 (11.2)	65 (11.0)	
Pneumonia severity				<.001			.02
<i>Severe</i>	1520	607 (59.7)	913 (68.0)		491 (65.3)	422 (71.5)	
<i>Very severe</i>	838	409 (40.3)	429 (32.0)		261 (34.7)	168 (28.5)	
HIV positive ^c	168	23 (2.3)	145 (10.8)	<.001	114 (15.2)	31 (5.3)	<.001
Head nodding	350	128 (12.6)	222 (16.5)	.008	154 (20.5)	68 (11.5)	<.001
Central cyanosis	65	18 (1.8)	47 (3.5)	.01	26 (3.5)	21 (3.6)	.92
Hypoxemia ^d	919	277 (27.3)	642 (47.9)	<.001	400 (53.3)	242 (41.0)	<.001
Convulsions	227	161 (15.8)	66 (4.9)	<.001	32 (4.3)	34 (5.8)	.20
Lethargy	321	172 (16.9)	149 (11.1)	<.001	93 (12.4)	56 (9.5)	.10
Difficulty feeding	193	85 (8.4)	108 (8.1)	.78	70 (9.3)	38 (6.4)	.05
Vomiting	93	62 (6.1)	31 (2.3)	<.001	13 (1.7)	18 (3.1)	.11
Tachypnea ^e	1868	764 (75.8)	1104 (83.4)	<.001	637 (85.8)	467 (80.2)	.007
Crackles	1421	552 (54.3)	869 (64.8)	<.001	482 (64.1)	387 (65.7)	.54
Grunting	489	212 (20.9)	277 (20.7)	0.9	181 (24.2)	96 (16.4)	<.001
Nasal flaring	1515	591 (58.2)	924 (69.0)	<.001	550 (73.3)	374 (63.4)	<.001
Tachycardia ^f	1296	547 (54.0)	749 (55.9)	.35	439 (58.5)	310 (52.6)	.03
Temperature $\geq 38.5^{\circ}\text{C}$	539	210 (20.7)	329 (24.5)	.03	194 (25.8)	135 (22.9)	.22
Weight-for-age ^g				<.001			.004
<i>Normal</i>	1493	701 (69.3)	792 (59.4)		417 (55.7)	375 (64.1)	
<i>Moderate</i>	438	178 (17.6)	260 (19.5)		152 (20.3)	108 (18.5)	

	Severe	N 415	All CXRs			Abnormal CXRs		
			Normal	Abnormal	p-value ^b	Any consolidation	Other infiltrate only	p-value ^b
Vaccine status ^h					0.60	180 (24.0)	102 (17.4)	.001
<i>None</i>	143	58 (11.2)	85 (13.1)			50 (14.5)	35 (11.6)	
<i>Complete Hib, no PCV</i>	225	101 (19.4)	124 (19.2)			83 (24.1)	41 (13.6)	
<i>Complete PCV</i>	798	360 (69.4)	438 (67.7)			212 (61.5)	226 (74.8)	
Antibiotic pretreatment ⁱ	953	367 (38.4)	586 (46.2)	<.001		360 (50.3)	226 (40.9)	<.001
Died within 30 days	196	66 (7.4)	130 (11.2)	.003		98 (15.3)	32 (6.2)	<.001

Abbreviations: Hib=*Haemophilus influenzae* type b conjugate vaccine; PCV=Pneumococcal conjugate vaccine; HIV=human immunodeficiency virus, WHO, World Health Organization.

^a Restricted to cases with an interpretable chest x-ray finding (n=2358).

^b P-value obtained from Pearson chi-square.

^c South Africa and Zambia sites only.

^d Hypoxemia=room air pulse-oximetry reading of <90% if at elevation (Zambia and South Africa) or <92% at all other sites. If a room air oxygen saturation reading was not available and the child was on supplemental oxygen they were also considered hypoxic.

^e Tachypnea=respiratory rate ≥60 breaths per minute for children <2 months of age, ≥50 for children 2-11 months, and ≥40 for children 12-59 months.

^f Tachycardia=heart rate >160 beats per minute (bpm) if age 1-11 months, >150 bpm if age 12-35 months, and >140 bpm if age 36-59 months.

^g Weight-for-age=severe if <-3 z-scores, moderate if between -3 and -2 z-scores below WHO median.

^h Vaccine comparison excludes those children too young (<4 months) to have completed a full biologic course of Hib and/or PCV vaccines, as these children by definition are considered to be ‘unvaccinated’ but are not an appropriate comparison group for those who have been vaccinated. Complete vaccination for PCV was defined as 3 or more doses, or 2 doses if there was at least 8 weeks between doses and the child was <9 months of age at enrollment or >12 months of age at the time of the first dose, or 1 or more doses if the age at any of the doses, or age at introduction, was ≥24 months. Complete vaccination for Hib conjugate vaccine was defined as 3 or more doses, or 1 or more doses for a child older than 12 months at first dose.

ⁱ Antibiotic pretreatment was defined by having either a positive serum bioassay or documented administration of antibiotics on the day of admission at the referral or study hospital prior to blood culture collection.

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