**Supplemental Table 1. Listing of non-pneumococcal blood culture positive cases who were pneumococcal PCR positive in whole blood**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Case No.** | **Site** | **Blood Culture** **Organism** | **Pneumococcal Load (log10 copies/ml)** | **Induced sputum culture organism** | **Induced sputum PCR organism** | **NP/OP PCR organism** | **NP culture results** |  |  |
| **Whole Blood**  | **NP/OP**  |  |  |
| 1 | Gambia | *Candida* species | 4.06 | 5.50 | MCAT PNEU | CMV MCAT PNEU RHINO | CMV MCAT PNEU | PNEU |  |  |
| 2 | Gambia | *Acinetobacter* species | 2.69 | 4.12 |   | HMPV A/B PNEU PVEV | CMV HINF PNEU |   |  |  |
| 3 | Gambia | *Neisseria meningitidis* | 3.55 | 6.38 | HINF MCAT PNEU SAUR | COR43 HINF HMPV A/B MCAT PNEU | CMV COR43 HINF MCAT PNEU | PNEU |  |  |
| 4 | Gambia | *Escherichia coli* | 3.22 | NA | NA  |   | NA   |   |  |  |
| 5 | Kenya | *Haemophilus influenzae* | 3.18 | 6.92 |   | HINF MCAT PNEU | HINF MCAT PNEU | PNEU |  |  |
| 6 | Kenya | *Pseudomonas aeruginosa* | 1.80 | 4.58 |  NA  |   | MCAT PNEU | PNEU |  |  |
| 7 | Kenya | *Salmonella* species; *Streptococcus* Group A (*S. pyogenes*) | 2.33 | 5.70 |  NA  |   | HBOV PNEU RHINO |   |  |  |
| 8 | Mali | *Salmonella* species | 2.04 | 6.00 |  NA  |   | HINF MCAT PNEU SAUR |   |  |  |
| 9 | Mali | *Pseudomonas aeruginosa* | 4.94 | 7.80 |   | ADENO CMV HINF MCAT PNEU SAUR | ADENO CMV HINF HMPV A/B MCAT PNEU SAUR |   |  |  |
| 10 | South Africa | *Staphylococcus aureus* | 3.89 | 6.96 | SAUR | ADENO CMV HBOV HINF MCAT PARA3 PNEU SAUR | CMV HBOV HINF MCAT PNEU SAUR | PNEU |  |  |
| 11 | Zambia | *Haemophilus influenzae* | 2.63 | 6.16 | HINF |   | ADENO CMV HBOV HINF MCAT PNEU |   |  |  |
| 12 | Zambia | *Klebsiella pneumoniae* | 2.81  | 6.73 | NA | NA | CMV HBOV HINF MCAT PARA 4 PNEU RHINO |  |  |  |

Abbreviations: ADENO = adenovirus; CMV = cytomegalovirus; COR = Coronavirus; HBOV = human bocavirus; HINF = *Haemophilus influenzae*; HMPV = human metapneumovirus; MCAT = *Moraxella catarrhalis*; NA = specimen results not available; NP/OP = nasopharyngeal/oropharyngeal; PARA = parainfluenza; PCR = polymerase chain reaction; PNEU = *Streptococcus pneumoniae*; PV/EV = parechovirus/enterovirus; RHINO = rhinovirus; SAUR = *Staphylococcus aureus*.

**Supplemental Figure 1. Whole blood pneumococcal PCR load among cases and controls by site**

|  |  |
| --- | --- |
|  |  |
|   |  |
|  |  |

Description of figures: diamonds = group means; horizontal lines through boxes = group medians; boxes extend to the 25th and 75th percentiles; whiskers extend to minimum and maximum; log density is the pneumococcal density (log10 copies/ml) calculated by PCR for the *lyt*A gene on whole blood specimens among PCR-positive children.

Abbreviations and definitions: PCR = polymerase chain reaction; MCPP = microbiologically confirmed pneumococcal pneumonia, defined as pneumococcus isolated from culture of blood, lung aspirate, pleural fluid, PCR of lung aspirate or pleural fluid, or detection of *S. pneumoniae* antigen in pleural fluid on Binax Now; Confirmed non-pneumococcal cases = confirmed for a non-pneumococcal pathogen defined as non-MCPP and culture positive in blood, lung aspirate or pleural fluid for a non-contaminant pathogen; Non-confirmed cases defined as cases without isolation of bacteria from culture of blood, lung aspirate or pleural fluid, or PCR of lung aspirate or pleural fluid; CXR+ defined as radiographic evidence of pneumonia (consolidation and/or other infiltrates); Non-RTI controls = controls without respiratory tract illness.

**Supplemental Figure 2. Distribution of pneumococcal PCR loada in whole blood by case-control group, HIV and prior antibiotic use**

|  |  |  |
| --- | --- | --- |
| 1. **MCPP cases by HIV status**

 | 1. **Controls by HIV status**

 | 1. **Non-Confirmed cases by HIV status**
 |
| 1. **MCPP cases by prior antibiotic use**

 | 1. **Controls by prior antibiotic use**

 | 1. **Non- Confirmed cases by prior antibiotic use**

 |

Abbreviations: PCR = polymerase chain reaction; MCPP = microbiologically confirmed pneumococcal pneumonia; HIV = human immunodeficiency virus.

a Pneumococcal load calculated by PCR for the *lyt*A gene (expressed as log10 copies/ml) on whole blood specimens among PCR-positive children.

Definitions: MCPP defined as isolation of pneumococcus from blood culture, culture or PCR of lung aspirate or pleural fluid, or BinaxNOW antigen detection on pleural fluid. Non-confirmed cases defined as cases without isolation of bacteria from culture of blood, lung aspirate or pleural fluid, or PCR of lung aspirate or pleural fluid. Prior antibiotic use defined as serum bioassay positive (cases and controls), antibiotic administration at the referral facility or antibiotic administration prior to whole blood specimen collection at the study facility (cases only).

**Supplemental Table 2: Median pneumococcal PCR load (103 copies/ml) in whole blood among PCR positive controls by characteristic and respiratory tract illness (RTI) status**

| **Characteristic** | **RTI controlsN=1181** | **Non-RTI controlsN=3806** |
| --- | --- | --- |
| **N PCR+** | **Median (IQR) loada** | **N PCR+** | **Median (IQR) load** |
| **Overall** | 70 | 0.23 (0.12,0.64)b | 203 | 0.18 (0.1,0.43) |
| **PERCH sites** |  | p=0.24 |  | p=0.22 |
|  **Kenya** | 18 | 0.28 (0.16,0.61) | 30 | 0.22 (0.12,0.35) |
|  **The Gambia** | 11 | 0.2 (0.13,0.99) | 36 | 0.23 (0.13,0.45) |
|  **Mali** | 16 | 0.42 (0.07,0.73) | 22 | 0.39 (0.12,1.5) |
|  **Zambia** | 9 | 0.16 (0.12,0.27) | 22 | 0.24 (0.09,0.42) |
|  **South Africa** | 8 | 0.24 (0.11,1.95) | 90 | 0.15 (0.09,0.32) |
|  **Thailand** | 4 | 0.16 (0.05,0.56) | 1 | 0.92 (0.92,0.92) |
|  **Bangladesh** | 4 | 0.08 (0.06,0.11) | 2 | 0.1 (0.09,0.1) |
| **Age** |  | **P=.38** |  | **P=.71** |
|  **1-5 months** | 15 | 0.51 (0.16,0.75) | 73 | 0.17 (0.11,0.38) |
|  **6-11 months** | 23 | 0.18 (0.1,0.38) | 49 | 0.22 (0.12,0.42) |
|  **12-23 months** | 16 | 0.17 (0.13,0.28) | 48 | 0.16 (0.11,0.36) |
|  **24-59 months** | 16 | 0.38 (0.11,1.43) | 33 | 0.19 (0.09,0.8) |
| **HIV infected** |  | **P=.86** |  | **P=.96** |
|  **Yesc** | 7 | 0.18 (0.12,0.38) | 12 | 0.15 (0.1,0.59) |
|  **No** | 52 | 0.21 (0.12,0.83) | 172 | 0.18 (0.11,0.38) |
| **Prior antibioticsd** |  | **P=.18** |  | **P=.86** |
|  **Yes** | 3 | 0.61 (0.19,13.31) | 6 | 0.22 (0.05,0.57) |
|  **No** | 66 | 0.23 (0.12,0.64) | 187 | 0.18 (0.11,0.43) |
| **Pneumococcal NP/OP PCR load >6.9 log10 copies/ml** |  | **P=.02** |  | **P=.96** |
|  **Yes** | 7 | 0.85 (0.27,2.53) | 20 | 0.16 (0.11,0.61) |
|  **No** | 62 | 0.18\ (0.11,0.58) | 181 | 0.18 (0.11,0.42) |

Abbreviations: PCR = polymerase chain reaction for *lyt*A gene; NP/OP = nasopharyngeal, oropharyngeal swab specimen; IQR = interquartile range.

All p-values obtained by Kruskal-Wallis test; p-values in cell represent comparison within control stratum for the characteristic.

a Median load is among children with PCR-positive whole blood specimens.

b Compared to Non-RTI controls: p=.32.

c Controls were enriched for HIV+ due to matching on HIV status at the two sites (South Africa and Zambia) with high HIV prevalence among cases.

d Prior antibiotics defined as serum bioassay positive.

**Supplemental Table 3: Median pneumococcal PCR load (103 copies/ml) in whole blood among positives by case/control group and HIV status, among the four sites that had at least one PCR-positive HIV-positive case**

|  | **MCPP casesa** | **Non-Confirmed casesb** | **Non-Confirmed CXR+ casesc** | **Confirmed non-pneumococcal casesd** | **All controlse** |
| --- | --- | --- | --- | --- | --- |
|  | **N PCR+** | **Median (IQR) loadf(103 copies/ml)** | **N PCR+** | **Median (IQR) load(103 copies/ml)** | **N PCR+** | **Median (IQR) load****(103 copies/ml)** | **N PCR+** | **Median (IQR) load(103 copies/ml)** | **N PCR+** | **Median (IQR) load(103 copies/ml)** |
| **The Gambia** |  |  |  | p=.84 |  | p=.39 |  |  |  |  |
| **HIV-positive** | 0 | -- | 1 | 0.29(0.29,0.29) | 1 | 0.29(0.29,0.29) | 0 | -- | 0 | -- |
| **HIV-negativeg** | 6 | 2.18(0.63,8.8) | 44 | 0.2(0.11,0.46) | 18 | 0.24(0.11,0.5) | 4 | 2.61(1.08,7.46) | 47 | 0.23(0.13,0.52) |
| **Mali** |  | p=.59 |  | p=.09 |  | p=.09 |  |  |  | p=0.249 |
| **HIV-positive** | 6 | 3.17(0.53,12.11) | 2 | 28.71(25.58,31.83) | 2 | 28.71(25.58,31.83) | 1 | 86.21(86.21,86.21) | 0 | -- |
| **HIV-negative** | 10 | 1.7(0.73,96.8) | 42 | 0.6(0.22,3.17) | 16 | 0.55(0.1,1.88) | 1 | 0.11(0.11,0.11) | 13 | 0.64(0.2,1.16) |
| **Zambia** |  | p=.66 |  | p=.92 |  | p=.78 |  |  |  | p=.64 |
| **HIV-positive** | 3 | 7.08(1.06,126.82) | 9 | 0.3(0.17,0.31) | 5 | 0.3(0.3,0.31) | 1 | 2.81(2.81,2.81) | 7 | 0.16(0.11,0.38) |
| **HIV-negative** | 1 | 70.9(70.9,70.9) | 28 | 0.27(0.14,1.29) | 17 | 0.41(0.14,1.36) | 1 | 0.43(0.43,0.43) | 24 | 0.2(0.12,0.4) |
| **South Africa** |  | p=.66 |  | p=.41 |  | p=.25 |  |  |  | p=.50 |
| **HIV-positive** | 1 | 1.91(1.91,1.91) | 12 | 0.48(0.15,8.97) | 11 | 0.48(0.17,16.99) | 1 | 7.83(7.83,7.83) | 12 | 0.17(0.11,0.59) |
| **HIV-negative** | 3 | 7.72(1.81,33.55) | 54 | 0.26(0.16,0.89) | 33 | 0.28(0.16,0.86) | 0 | -- | 86 | 0.15(0.09,0.32) |

Abbreviations: PCR = polymerase chain reaction for *lyt*A gene; IQR = interquartile range; MCPP = microbiologically confirmed pneumococcal pneumonia; HIV = human immunodeficiency virus.

All p-values obtained from Kruskal-Wallis test comparing HIV-positive to HIV-negative.

a MCPP defined as isolation of pneumococcus from blood culture, culture or PCR of lung aspirate or pleural fluid, or BinaxNOW antigen detection on pleural fluid.

b Non-confirmed cases defined as cases without isolation of bacteria from culture of blood, lung aspirate or pleural fluid, or PCR of lung aspirate or pleural fluid.

c CXR+ defined as radiographic evidence of pneumonia (consolidation and/or other infiltrates).

d Confirmed non-pneumococcal bacterial case was defined as a case with any non-pneumococcal bacterial pathogen detected by blood culture, by lung aspirate culture or PCR, or by pleural fluid culture or PCR.

e Controls were matched on HIV status at the two sites (South Africa and Zambia) with high HIV prevalence.

f Median load = median whole blood *lyt*A density (103 copies/ml) among children with PCR-positive whole blood specimens.

gHIV-negative includes children with unknown HIV status.

**Supplemental Table 4a: Proportion of children with pneumococcal whole blood PCR load ≥ 2.2 log10 copies/ml by characteristics common for both cases and controls.**

|  | **MCPP casesa** | **Non-Confirmed casesb** | **Non-Confirmed** **CXR+ casesc** | **Confirmed non-pneumococcal cased** | **All controls** | **RTI controls** | **Non-RTI controls** |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Total N** | **N (%)** | **Total N** | **N (%)** | **Total N** | **N (%)** | **Total N** | **N (%)** | **Total N** | **N (%)** | **Total N** | **N (%)** | **Total N** | **N (%)** |
| **Overall** | 56 | 35 (62.5) | 3832 | 166 (4.3) | 1745 | 91 (5.2) | 107 | 10 (9.3) | 4987 | 154 (3.1) | 1181 | 43 (3.6) | 3806 | 111 (2.9) |
| **Age** |  | p=.48 |  | p=.34 |  | p=.66 |  | p=.32 |  | p=.59 |  | p=.91 |  | p=.46 |
|  **1-5 months** | 11 | 7 (63.6) | 1570 | 69 (4.4) | 690 | 41 (5.9) | 43 | 2 (4.7) | 1534 | 48 (3.1) | 280 | 11 (3.9) | 1254 | 37 (3.0) |
|  **6-11 months** | 14 | 10 (71.4) | 869 | 45 (5.2) | 424 | 20 (4.7) | 27 | 3 (11.1) | 1195 | 43 (3.6) | 309 | 12 (3.9) | 886 | 31 (3.5) |
|  **12-23 months** | 17 | 8 (47.1) | 854 | 35 (4.1) | 420 | 22 (5.2) | 22 | 2 (9.1) | 1218 | 36 (3.0) | 335 | 10 (3.0) | 883 | 26 (2.9) |
|  **24-59 months** | 14 | 10 (71.4) | 539 | 17 (3.2) | 211 | 8 (3.8) | 15 | 3 (20.0) | 1040 | 27 (2.6) | 257 | 10 (3.9) | 783 | 17 (2.2) |
| **Gender** |  | **p=.03** |  | p=.87 |  | p=.28 |  | p=.52 |  | p=.51 |  | p > .99 |  | p=.50 |
|  **Male** | 29 | 14 (48.3) | 2218 | 95 (4.3) | 981 | 46 (4.7) | 44 | 3 (6.8) | 2495 | 73 (2.9) | 589 | 21 (3.6) | 1906 | 52 (2.7) |
|  **Female** | 27 | 21 (77.8) | 1614 | 71 (4.4) | 764 | 45 (5.9) | 63 | 7 (11.1) | 2491 | 81 (3.3) | 592 | 22 (3.7) | 1899 | 59 (3.1) |
| **HIV infected** |  | p=.50 |  | **p < .01** |  | **p < .01** |  | p=.12 |  | p=.15 |  | p=.09 |  | p=.47 |
|  **Yese** | 13 | 10 (76.9) | 211 | 19 (9.0) | 144 | 17 (11.8) | 14 | 3 (21.4) | 208 | 10 (4.8) | 47 | 4 (8.5) | 161 | 6 (3.7) |
|  **No** | 36 | 22 (61.1) | 3299 | 130 (3.9) | 1470 | 66 (4.5) | 83 | 6 (7.2) | 4224 | 127 (3.0) | 943 | 32 (3.4) | 3281 | 95 (2.9) |
| **At least 1 dose of PCVf** |  | p=.17 |  | p=.11 |  | **p=.04** |  | p > .99 |  | p=.27 |  | p=.83 |  | p=.14 |
|  **Yes** | 37 | 21 (56.8) | 1949 | 95 (4.9) | 917 | 48 (5.2) | 49 | 4 (8.2) | 2447 | 112 (4.6) | 547 | 29 (5.3) | 1900 | 83 (4.4) |
|  **No** | 11 | 9 (81.8) | 574 | 38 (6.6) | 253 | 23 (9.1) | 20 | 1 (5.0) | 473 | 16 (3.4) | 126 | 7 (5.6) | 347 | 9 (2.6) |
| **Prior antibiotic use** |  | p > .99 |  | p=.32 |  | **p < .01** |  | p=.32 |  | p=.09 |  | p=.12 |  | p=.30 |
|  **Yesg** | 14 | 9 (64.3) | 1504 | 72 (4.8) | 722 | 50 (6.9) | 52 | 3 (5.8) | 111 | 7 (6.3) | 31 | 3 (9.7) | 80 | 4 (5.0) |
|  **No** | 40 | 24 (60.0) | 2166 | 88 (4.1) | 944 | 37 (3.9) | 51 | 6 (11.8) | 4582 | 141 (3.1) | 1072 | 40 (3.7) | 3510 | 101 (2.9) |
| **Pneumococcal NP/OP PCR load >6.9 log10 copies/ml** |  | p=.07 |  | **p < .01** |  | **p < .01** |  | p=.69 |  | p=.17 |  | p=.18 |  | p=.46 |
|  **Yes** | 36 | 26 (72.2) | 457 | 37 (8.1) | 231 | 25 (10.8) | 27 | 3 (11.1) | 392 | 17 (4.3) | 117 | 7 (6.0) | 275 | 10 (3.6) |
|  **No** | 18 | 8 (44.4) | 3306 | 127 (3.8) | 1481 | 65 (4.4) | 77 | 6 (7.8) | 4490 | 135 (3.0) | 1041 | 35 (3.4) | 3449 | 100 (2.9) |
| **Any virus NP/OP PCR+** |  | p=.29 |  | p=.13 |  | p=.11 |  | p > .99 |  | p > .99 |  | p=.19 |  | p=.56 |
|  **Yesh** | 51 | 31 (60.8) | 3353 | 140 (4.2) | 1538 | 76 (4.9) | 87 | 8 (9.2) | 3853 | 120 (3.1) | 974 | 32 (3.3) | 2879 | 88 (3.1) |
|  **No** | 3 | 3 (100) | 414 | 24 (5.8) | 175 | 14 (8.0) | 17 | 1 (5.9) | 1034 | 32 (3.1) | 185 | 10 (5.4) | 849 | 22 (2.6) |
| **RSV A/B NP/OP PCR+** |  | p=.29 |  | **p < .01** |  | p=.22 |  | p > .99 |  | p=.32 |  | p=.70 |  | p=.33 |
|  **Yes** | 4 | 4 (100) | 912 | 25 (2.7) | 449 | 18 (4.0) | 5 | 0 (0) | 137 | 6 (4.4) | 50 | 2 (4.0) | 87 | 4 (4.6) |
|  **No** | 50 | 30 (60.0) | 2830 | 138 (4.9) | 1251 | 71 (5.7) | 99 | 9 (9.1) | 4748 | 146 (3.1) | 1108 | 40 (3.6) | 3640 | 106 (2.9) |

Percent = row percent. Denominator includes all those below the 2.2 log10 copies/ml WB pneumococcal PCR threshold, including those without pneumococcus detected in the blood.

Abbreviations: PCR = polymerase chain reaction; MCPP = microbiologically confirmed pneumococcal pneumonia; RTI = respiratory tract illness; NP/OP = nasopharyngeal, oropharyngeal; PCV = pneumococcal conjugate vaccine; RSV = respiratory syncytial viruses A and B; HIV = human immunodeficiency virus; CXR = chest x-ray.

All p-values were obtained by Fisher’s exact or chi-square test and are for comparisons of strata within characteristic for the corresponding case/control group column.

a MCPP defined as isolation of pneumococcus from blood culture, culture or PCR of lung aspirate or pleural fluid, or BinaxNOW antigen detection on pleural fluid.

b Non-confirmed cases defined as cases without isolation of bacteria from culture of blood, lung aspirate or pleural fluid, or PCR of lung aspirate or pleural fluid.

c CXR+ defined as radiographic evidence of pneumonia (consolidation and/or other infiltrates).

d Confirmed non-pneumococcal bacterial case was defined as a case with any non-pneumococcal bacterial pathogen detected by blood culture, by lung aspirate culture or PCR, or by pleural fluid culture or PCR.

e Controls were matched on HIV status at the two sites (South Africa and Zambia) with high HIV prevalence.

f Restricted to PCV-using sites (Kenya, Gambia, Mali and South Africa).

gPrior antibiotic use defined as serum bioassay positive (cases and controls), antibiotic administration at the referral facility or antibiotic administration prior to whole blood specimen collection at the study facility (cases only).

h Virus co-infection defined as positive for any virus tested by PCR of the nasopharyngeal/oropharyngeal specimen (viruses tested for included: influenza A, B and C; parainfluenza 1, 2, 3 and 4; coronaviruses NL63, 229E, OC43 and HKU1; human metapneumoviruses A and B; human rhinovirus; RSV A and B; adenovirus; enterovirus, parechovirus; bocavirus; cytomegalovirus).

**Supplemental Table 4b: Proportion of cases with pneumococcal whole blood PCR load ≥2.2 log10copies/ml by case-only clinical characteristics**

|  | **MCPP casesaN=56** | **Non-Confirmed casesbN=3832** | **Non-Confirmed** **CXR+ casescN=1745** | **Confirmed non-pneumococcal casedN=107** |
| --- | --- | --- | --- | --- |
|  | **Total N** | **N (%)** | **Total N** | **N (%)** | **Total N** | **N (%)** | **Total N** | **N (%)** |
| **Very severe pneumonia** |  | p=.28 |  | **p=.04** |  | **p < .01** |  | p=.75 |
|  **Yes** | 32 | 22 (68.8) | 1213 | 65 (5.4) | 506 | 38 (7.5) | 50 | 4 (8.0) |
|  **No** | 24 | 13 (54.2) | 2619 | 101 (3.9) | 1239 | 53 (4.3) | 57 | 6 (10.5) |
| **CXR+** |  | p=.07 |  | **p < .01** |  | -- |  | p=.48 |
|  **Yes** | 38 | 20 (52.6) | 1745 | 91 (5.2) | 1745 | 91 (5.2) | 55 | 8 (14.5) |
|  **No** | 6 | 6 (100) | 1525 | 48 (3.1) | 0 | 0 (0) | 29 | 2 (6.9) |
| **CXR consolidation** |  | p=.51 |  | **p < .01** |  | **p < .01** |  | p=.75 |
|  **Yes** | 31 | 17 (54.8) | 853 | 66 (7.7) | 853 | 66 (7.7) | 38 | 5 (13.2) |
|  **No** | 13 | 9 (69.2) | 2417 | 73 (3.0) | 892 | 25 (2.8) | 46 | 5 (10.9) |
| **Hypoxemia** |  | **p=.01** |  | **p < .01** |  | p=.28 |  | p=.20 |
|  **Yes** | 23 | 19 (82.6) | 1446 | 80 (5.5) | 782 | 46 (5.9) | 54 | 3 (5.6) |
|  **No** | 33 | 16 (48.5) | 2377 | 86 (3.6) | 960 | 45 (4.7) | 52 | 7 (13.5) |
| **CRP ≥40mg/L** |  | p=.25 |  | **p < .01** |  | **p < .01** |  | p=.67 |
|  **Yes** | 40 | 25 (62.5) | 873 | 69 (7.9) | 515 | 44 (8.5) | 64 | 5 (7.8) |
|  **No** | 8 | 3 (37.5) | 2456 | 70 (2.9) | 1018 | 34 (3.3) | 27 | 1 (3.7) |
| **WBC >15/mm3** |  | p=.26 |  | p=.28 |  | p > .99 |  | p=.19 |
|  **Yes** | 27 | 14 (51.9) | 1383 | 53 (3.8) | 699 | 37 (5.3) | 42 | 2 (4.8) |
|  **No** | 27 | 19 (70.4) | 2277 | 105 (4.6) | 962 | 50 (5.2) | 61 | 8 (13.1) |
| **Died** |  | p=.21 |  | p=.22 |  | p=.67 |  | p=.18 |
|  **Yes** | 14 | 11 (78.6) | 283 | 16 (5.7) | 124 | 7 (5.6) | 38 | 6 (15.8) |
|  **No** | 36 | 21 (58.3) | 3147 | 130 (4.1) | 1417 | 69 (4.9) | 59 | 4 (6.8) |

Abbreviations: PCR = polymerase chain reaction; MCPP = microbiologically confirmed pneumococcal pneumonia; CXR+ = chest radiograph positive; CRP = C-reactive protein; WBC = white blood cell.

Percent = row percent. Denominator includes all those below the threshold, including those without pneumococcus detected in the blood.

All p-values were obtained by Fisher’s exact or chi-square test and are for comparisons of strata within characteristic for the corresponding case/control group column.

a MCPP defined as isolation of pneumococcus from blood culture, culture or PCR of lung aspirate or pleural fluid, or BinaxNOW antigen detection on pleural fluid.

b Non-confirmed cases defined as cases without isolation of bacteria from culture of blood, lung aspirate or pleural fluid, or PCR of lung aspirate or pleural fluid.

c CXR+ defined as radiographic evidence of pneumonia (consolidation and/or other infiltrates).

d Confirmed non-pneumococcal bacterial case was defined as a case with any non-pneumococcal bacterial pathogen detected by blood culture, by lung aspirate culture or PCR, or by pleural fluid culture or PCR.

**Supplemental Table 5: Number of children with whole blood pneumococcal PCR data, by site and case and control group**

|  |  |  |
| --- | --- | --- |
|  | **Cases** | **Controls** |
| **Site** | **MCPPa** | **Non-Confirmedb** | **Non-Confirmed CXR+c** | **Non-Confirmed CXR-AC** | **All** | **RTI** | **Non-RTI** |
| **All Sites** | 56 | 3832 | 1745 | 853 | 4987 | 1181 | 3806 |
| **Kenya** | 4 | 556 | 239 | 98 | 751 | 189 | 562 |
| **The Gambia** | 16 | 570 | 253 | 85 | 608 | 150 | 458 |
| **Mali** | 24 | 619 | 230 | 128 | 715 | 296 | 419 |
| **Zambia** | 7 | 494 | 221 | 155 | 603 | 96 | 507 |
| **South Africa** | 5 | 885 | 500 | 290 | 963 | 53 | 910 |
| **Bangladesh** | 0 | 490 | 206 | 56 | 725 | 153 | 572 |
| **Thailand** | 0 | 218 | 96 | 41 | 622 | 244 | 378 |

Abbreviations: PCR = polymerase chain reaction for *lyt*A gene; MCPP = microbiologically confirmed pneumococcal pneumonia; RTI = respiratory tract illness; CXR = chest radiograph; AC, alveolar consolidation.

a MCPP defined as isolation of pneumococcus from blood culture, culture or PCR of lung aspirate or pleural fluid, or BinaxNOW antigen detection on pleural fluid.

b Non-confirmed cases defined as cases without isolation of bacteria from culture of blood, lung aspirate or pleural fluid, or PCR of lung aspirate or pleural fluid.

c CXR+ defined as radiographic evidence of pneumonia (consolidation and/or other infiltrates).

Denominators used in Figure 2b.

**Acknowledgements:**

***PERCH Expert Group.*** William C. Blackwelder, Harry Campbell, John A. Crump, Adegoke Falade, Menno D. de Jong, Claudio Lanata, Kim Mulholland, Shamim Qazi, Cynthia G. Whitney.

***Pneumonia Methods Working Group.*** Robert E Black, Zulfiqar A Bhutta, Harry Campbell, Thomas Cherian, Derrick W Crook, Menno D de Jong, Scott F Dowell, Stephen M Graham, Keith P Klugman, Claudio F Lanata, Shabir A Madhi, Paul Martin, James P Nataro, Franco M Piazza, Shamim A Qazi, and Heather J Zar.

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