

Supplementary material

Case-fatality and sequelae following bacterial meningitis in South Africa, 2016 through 2020

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Case-fatality and sequelae following bacterial meningitis

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Case-fatality and sequelae following bacterial meningitis

Table S_A: Risk factors for death following pneumococcal meningitis in South Africa, 2016-2020, n=1199

| | In hospital Outcome | | | | | Univariate analysis | | | Multivariable analysis | | |
|--|---------------------|---------|------|---------|------------|--------------------------|-----------|------------|--------------------------|-----------|--------|
| | ALIVE | % | DIED | % | Odds Ratio | 95% confidence intervals | p-value | Odds Ratio | 95% confidence intervals | p-value | |
| | 1199 | 712 | 59 | 487 | 41 | | | | | | |
| Sex | | | | | | | | | | | |
| female | 602/1199 | 357/602 | 59 | 245/602 | 41 | Reference | | | | | |
| male | 597/1199 | 355/597 | 59 | 242/597 | 41 | 0.99 | 0.79-1.25 | 0.955 | | | |
| Age category | | | | | | | | | | | |
| less than 5 years | 246/1199 | 182/246 | 74 | 64/246 | 26 | Reference | | | | | |
| 5 years and older | 953/1199 | 530/953 | 56 | 423/953 | 44 | 2.27 | 1.66-3.10 | <0.001 | | | |
| HIV | | | | | | | | | | | |
| negative | 295/1199 | 224/295 | 76 | 71/295 | 24 | Reference | | | Reference | | |
| positive | 669/1199 | 389/669 | 58 | 280/669 | 42 | 2.27 | 1.67-3.09 | <0.001 | 2.40 | 1.64-3.50 | <0.001 |
| not done | 235/1199 | 99/235 | 42 | 136/235 | 58 | 4.33 | 2.99-6.29 | <0.001 | 4.22 | 2.59-6.88 | <0.001 |
| HIV category with CD4 count value | | | | | | | | | | | |
| HIV negative | 295/835 | 224/295 | 76 | 71/295 | 24 | Reference | | | | | |
| HIV positive CD4 ≥200cells/μL | 190/835 | 133/190 | 70 | 57/190 | 30 | 1.35 | 0.90-2.04 | 0.149 | | | |
| HIV positive CD4 <200cells/μL* | 350/835 | 204/350 | 58 | 146/350 | 42 | 2.24 | 1.61-3.18 | <0.001 | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | | | |
|--|----------|---------|----|---------|----|-----------|------------|--------|-----------|-----------|--------|
| GCS category | | | | | | | | | | | |
| GCS of 15 (alert) | 344/992 | 292/344 | 85 | 52/344 | 15 | Reference | | | | | |
| GCS <15 | 648/992 | 312/648 | 48 | 336/648 | 52 | 6.05 | 4.34-8.44 | <0.001 | 6.28 | 4.41-8.95 | <0.001 |
| Pitt Bacteraemia Score on admission | | | | | | | | | | | |
| 0 (mild) | 185/878 | 156/185 | 84 | 29/185 | 16 | Reference | | | | | |
| 1-3 (moderate) | 586/878 | 344/586 | 59 | 242/586 | 41 | 3.78 | 2.46-5.81 | <0.001 | | | |
| 4-12 (severe) | 107/878 | 25/107 | 23 | 82/107 | 77 | 17.64 | 9.70-32.09 | <0.001 | | | |
| Underlying illness | | | | | | | | | | | |
| no | 990/1199 | 627/990 | 63 | 363/990 | 37 | Reference | | | Reference | | |
| yes | 209/1199 | 85/209 | 41 | 124/209 | 59 | 2.52 | 1.86-3.42 | <0.001 | 2.79 | 1.94-4.02 | <0.001 |
| Specimen type | | | | | | | | | | | |
| Cerebrospinal fluid | 954/1199 | 575/954 | 60 | 379/954 | 40 | Reference | | | | | |
| Blood | 242/1199 | 135/242 | 56 | 107/242 | 44 | 1.2 | 0.90-1.60 | 0.205 | | | |
| Other | 3/1199 | 2/3 | 67 | 1/3 | 33 | 0.76 | 0.07-8.40 | 0.822 | | | |
| Serotype category | | | | | | | | | | | |
| PCV7 | 113/1197 | 69/113 | 61 | 44/113 | 39 | Reference | | | | | |
| PCV13 add | 118/1197 | 64/118 | 54 | 54/118 | 46 | 1.32 | 0.78-2.23 | 0.295 | | | |
| non PCV | 718/1197 | 423/718 | 59 | 295/718 | 41 | 1.09 | 0.73-1.64 | 0.666 | | | |
| Not-typed | 248/1197 | 154/248 | 62 | 94/248 | 38 | 0.96 | 0.61-1.51 | 0.851 | | | |
| Vaccine serotype | | | | | | | | | | | |
| no | 719/951 | 424/719 | 59 | 295/719 | 41 | Reference | | | | | |
| yes | 232/951 | 134/232 | 58 | 98/232 | 42 | 1.05 | 0.78-1.42 | 0.744 | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | | | |
|---|----------|---------|----|---------|----|-----------|-----------|-----------|------|-----------|-------|
| Resistant organism | | | | | | | | | | | |
| no | 577/762 | 332/577 | 58 | 245/577 | 42 | Reference | | | | | |
| yes | 185/762 | 93/185 | 50 | 92/185 | 50 | 1.34 | 0.96-1.87 | 0.084 | | | |
| Appropriate empiric therapy initiated within 24hrs | | | | | | | | | | | |
| no | 393/1199 | 251/393 | 64 | 142/393 | 36 | Reference | | | | | |
| yes | 806/1199 | 461/806 | 57 | 345/806 | 43 | 1.32 | 1.03-1.70 | 0.027 | | | |
| Directed therapy initiated | | | | | | | | | | | |
| no | 313/1199 | 158/313 | 50 | 155/313 | 50 | Reference | | Reference | | | |
| yes | 886/1199 | 554/886 | 63 | 332/886 | 37 | 0.61 | 0.47-0.79 | <0.001 | 0.63 | 0.45-0.88 | 0.008 |

*HIV-infected children <5 years of age and with CD4 T lymphocyte percentage <15% were included in the group “HIV positive CD4 <200cells/ μ L”

irrespective of their CD4 T lymphocyte count. GCS: Glasgow Coma Scale. Underlying illness: chronic lung, renal, heart or liver disease; previous cerebrovascular accident; previous head injury; connective tissue disease; asplenia (functional/anatomical); previous malignancy; solid organ transplant; diabetes; chromosomal abnormality; complement deficiency; or current immunosuppressive therapy. Serotype category: PCV pneumococcal conjugate vaccine, PCV7 – 4, 6B, 9V, 14, 18C, 19F and 23F, PCV13 additional – 1, 3, 5, 6A, 7F and 19A, non PCV – serotypes not in the 13-valent PCV, Not-typed – episodes where the pneumococcus was not serotyped. Vaccine serotype: pneumococcal serotype present in 13-valent PCV. Resistant organism: organism was not susceptible to penicillin (minimum inhibitory concentration >0.6 μ g/ml). Appropriate empiric therapy initiated within 24hours: intravenous third generation cephalosporin. Directed antibiotic therapy initiated: antibiotics given which are appropriate to susceptibility profile of the organism.

Case-fatality and sequelae following bacterial meningitis

Table S_B: Risk factors for death following meningococcal meningitis in South Africa, 2016-2020, n=137

| | | In hospital Outcome | | | | Univariate analysis | | | Multivariable analysis | | |
|--|--------|---------------------|----|-------|----|---------------------|--------------------------|---------|------------------------|--------------------------|---------|
| | | ALIVE | % | DIED | % | Odds Ratio | 95% confidence intervals | p-value | Odds Ratio | 95% confidence intervals | p-value |
| | 137 | 118 | 86 | 19 | 14 | | | | | | |
| Sex | | | | | | | | | | | |
| female | 67/137 | 56/67 | 84 | 11/67 | 16 | Reference | | | | | |
| male | 70/137 | 62/70 | 89 | 8/70 | 11 | 0.66 | 0.25-1.75 | 0.401 | | | |
| Age category | | | | | | | | | | | |
| less than 5 years | 59/137 | 54/59 | 92 | 5/59 | 8 | Reference | | | | | |
| 5 years and older | 78/137 | 64/78 | 82 | 14/78 | 18 | 2.36 | 0.80-6.98 | 0.12 | | | |
| HIV | | | | | | | | | | | |
| negative | 86/137 | 82/86 | 95 | 4/86 | 5 | Reference | | | Reference | | |
| positive | 25/137 | 19/25 | 76 | 6/25 | 24 | 6.47 | 1.66-25.22 | 0.007 | 7.42 | 1.02-54.02 | 0.048 |
| not done | 26/137 | 17/26 | 65 | 9/26 | 35 | 10.85 | 2.99-39.36 | <0.001 | 15.81 | 1.91-131.17 | 0.011 |
| HIV category with CD4 count value | | | | | | | | | | | |
| HIV negative | 86/105 | 82/86 | 95 | 4/86 | 5 | Reference | | | | | |
| HIV positive CD4 ≥200cells/μL | 11/105 | 10/11 | 91 | 1/11 | 9 | 2.05 | 0.21-20.19 | 0.539 | | | |
| HIV positive CD4 <200cells/μL* | 8/105 | 5/8 | 63 | 3/8 | 38 | 12.30 | 2.14-70.65 | 0.005 | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | | | |
|--|---------|---------|-----|--------|----|-----------|-------------|--------|-----------|-------------|-------|
| GCS category | | | | | | | | | | | |
| GCS of 15 (alert) | 67/112 | 65/67 | 97 | 2/67 | 3 | Reference | | | Reference | | |
| GCS <15 | 45/112 | 33/45 | 73 | 12/45 | 27 | 11.82 | 2.50-55.93 | 0.002 | 20.85 | 2.87-151.65 | 0.003 |
| Pitt Bacteraemia Score on admission | | | | | | | | | | | |
| 0 (mild) | 35/87 | 34/35 | 97 | 1/35 | 3 | Reference | | | | | |
| 1-3 (moderate) | 46/87 | 42/46 | 91 | 4/46 | 9 | 3.24 | 0.35-30.34 | 0.303 | | | |
| 4-12 (severe) | 6/87 | 2/6 | 33 | 4/6 | 67 | 68 | 4.98-928.89 | 0.002 | | | |
| Underlying illness | | | | | | | | | | | |
| no | 126/137 | 113/126 | 90 | 13/126 | 10 | Reference | | | Reference | | |
| yes | 11/137 | 5/11 | 45 | 6/11 | 55 | 10.43 | 2.79-38.98 | <0.001 | 26.51 | 1.94-362.96 | 0.014 |
| Specimen type | | | | | | | | | | | |
| Cerebrospinal fluid | 107/137 | 95/107 | 89 | 12/107 | 11 | Reference | | | | | |
| Blood | 30/137 | 23/30 | 77 | 7/30 | 23 | 2.41 | 0.85-6.80 | 0.097 | | | |
| Serogroup category | | | | | | | | | | | |
| B | 51/111 | 48/51 | 94 | 3/51 | 6 | Reference | | | | | |
| ACWY | 59/111 | 48/59 | 81 | 11/59 | 19 | 3.67 | 0.96-13.97 | 0.057 | | | |
| other | 1/111 | 1/1 | 100 | 0/1 | 0 | . | | | | | |
| Vaccine serogroup | | | | | | | | | | | |
| no | 53/112 | 50/53 | 94 | 3/53 | 6 | Reference | | | | | |
| yes | 59/112 | 48/59 | 81 | 11/59 | 19 | 3.82 | 1.00-14.54 | 0.049 | | | |
| Resistant organism | | | | | | | | | | | |
| no | 57/62 | 51/57 | 89 | 6/57 | 11 | Reference | | | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | | | | |
|---|---------|---------|-----|--------|----|-----------|-----------|-------|-----------|-----------|-------|--|
| yes | 5/62 | 5/5 | 100 | 0/5 | 0 | . | | | | | | |
| Appropriate empiric therapy initiated within 24hrs | | | | | | | | | | | | |
| no | 41/137 | 34/41 | 83 | 7/41 | 16 | Reference | | | | | | |
| yes | 96/137 | 84/96 | 88 | 12/96 | 13 | 0.69 | 0.25-1.91 | 0.480 | | | | |
| Directed therapy initiated | | | | | | | | | | | | |
| no | 15/137 | 10/15 | 67 | 5/15 | 33 | Reference | | | Reference | | | |
| yes | 122/137 | 108/122 | 89 | 14/122 | 11 | 0.26 | 0.08-0.89 | 0.029 | 0.04 | 0.00-0.37 | 0.005 | |

*HIV-infected children <5 years of age and with CD4 T lymphocyte percentage <15% were included in the group “HIV positive CD4 <200cells/ μ L” irrespective of their CD4 T lymphocyte count.

GCS: Glasgow Coma Scale. Underlying illness: chronic lung, renal, heart or liver disease; previous cerebrovascular accident; previous head injury; connective tissue disease; asplenia (functional/anatomical); previous malignancy; solid organ transplant; diabetes; chromosomal abnormality; complement deficiency; or current immunosuppressive therapy. Vaccine serogroup: meningococcal serogroup present in quadrivalent meningococcal conjugate vaccine (A, C, W or Y). Resistant organism: organism was not susceptible to penicillin. Appropriate empiric therapy initiated within 24hours: intravenous third generation cephalosporin. Directed antibiotic therapy initiated: antibiotics given which are appropriate to susceptibility profile of the organism.

Case-fatality and sequelae following bacterial meningitis

Table S_C: Risk factors for death following *Haemophilus influenzae* meningitis in South Africa, 2016-2020, n=119

| | In hospital Outcome | | | | | Univariate analysis | | | Multivariable analysis | | |
|---|---------------------|-------|------|-------|----|---------------------|--------------------------|---------|------------------------|--------------------------|---------|
| | ALIVE | % | DIED | % | | Odds Ratio | 95% confidence intervals | p-value | Odds Ratio | 95% confidence intervals | p-value |
| | 119 | 91 | 76 | 28 | 24 | | | | | | |
| Sex | | | | | | | | | | | |
| female | 57/119 | 44/57 | 77 | 13/57 | 23 | Reference | | | | | |
| male | 62/119 | 47/62 | 76 | 15/62 | 24 | 1.08 | 0.46-2.52 | 0.859 | | | |
| Age category | | | | | | | | | | | |
| less than 5 years | 71/119 | 54/71 | 76 | 17/71 | 24 | Reference | | | | | |
| 5 years and older | 48/119 | 37/48 | 77 | 11/48 | 23 | 0.94 | 0.40-2.25 | 0.897 | | | |
| HIV | | | | | | | | | | | |
| negative | 67/119 | 52/67 | 78 | 15/67 | 22 | Reference | | | Reference | | |
| positive | 29/119 | 25/29 | 86 | 4/29 | 14 | 0.55 | 0.17-1.84 | 0.336 | 0.66 | 0.14-3.13 | 0.603 |
| not done | 23/119 | 14/23 | 61 | 9/23 | 39 | 2.23 | 0.81-6.15 | 0.122 | 1.47 | 0.29-7.29 | 0.64 |
| HIV category with CD4 count values | | | | | | | | | | | |
| HIV negative | 67/93 | 52/67 | 78 | 15/67 | 22 | Reference | | | | | |
| HIV positive CD4 ≥200cells/μL | 11/93 | 11/11 | 100 | 0/11 | 0 | . | | | | | |
| HIV positive CD4 <200cells/μL* | 15/93 | 13/15 | 87 | 2/15 | 13 | 0.53 | 0.11-2.63 | 0.440 | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | | | |
|--|---------|--------|-----|--------|----|-----------|------------|-------|-----------|------------|-------|
| GCS category | | | | | | | | | | | |
| GCS of 15 (alert) | 72/92 | 65/72 | 90 | 7/72 | 10 | Reference | | | Reference | | |
| GCS <15 | 20/92 | 11/20 | 55 | 9/20 | 45 | 7.6 | 2.34-24.64 | 0.001 | 7.32 | 2.10-25.53 | 0.002 |
| Pitt Bacteraemia Score on admission | | | | | | | | | | | |
| 0 (mild) | 27/67 | 27/27 | 100 | 0/27 | 0 | . | | | | | |
| 1-3 (moderate) | 35/67 | 26/35 | 74 | 9/25 | 26 | Reference | | | | | |
| 4-12 (severe) | 5/67 | 2/5 | 40 | 3/5 | 60 | 4.33 | 0.62-30.25 | 0.139 | | | |
| Underlying illness | | | | | | | | | | | |
| no | 100/119 | 80/100 | 80 | 20/100 | 20 | Reference | | | Reference | | |
| yes | 19/119 | 11/19 | 58 | 8/19 | 42 | 2.91 | 1.03-8.18 | 0.043 | 1.98 | 0.43-9.05 | 0.377 |
| Specimen type | | | | | | | | | | | |
| Cerebrospinal fluid | 86/119 | 66/86 | 77 | 20/86 | 23 | Reference | | | | | |
| Blood | 32/119 | 24/32 | 75 | 8/32 | 25 | 1.1 | 0.43-2.83 | 0.843 | | | |
| Other | 1/119 | 1/1 | 100 | 0/1 | 0 | 1 | . | | | | |
| Serotype category | | | | | | | | | | | |
| Non-typeable | 27/88 | 19/27 | 70 | 8/27 | 30 | 2.53 | 0.58-11.05 | 0.218 | | | |
| a,c,d,e,f | 21/88 | 18/21 | 86 | 3/21 | 14 | Reference | | | | | |
| b | 40/88 | 32/40 | 80 | 8/40 | 20 | 1.5 | 0.35-6.38 | 0.583 | | | |
| Vaccine serotype | | | | | | | | | | | |
| no | 48/88 | 37/48 | 77 | 11/48 | 23 | Reference | | | | | |
| yes | 40/88 | 32/40 | 80 | 8/40 | 20 | 0.84 | 0.30-2.35 | 0.741 | | | |
| Resistant organism | | | | | | | | | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | | | |
|---|--------|-------|----|-------|----|-----------|-----------|-------|-----------|-----------|-------|
| no | 42/55 | 30/42 | 71 | 12/42 | 29 | Reference | | | | | |
| yes | 13/55 | 12/13 | 92 | 1/13 | 8 | 0.21 | 0.02-1.78 | 0.152 | | | |
| Appropriate empiric therapy initiated within 24hrs | | | | | | | | | | | |
| no | 54/119 | 38/54 | 70 | 16/54 | 30 | Reference | | | | | |
| yes | 65/119 | 53/65 | 82 | 12/65 | 18 | 0.54 | 0.23-1.27 | 0.156 | | | |
| Directed therapy initiated | | | | | | | | | | | |
| no | 25/119 | 13/25 | 52 | 12/25 | 48 | Reference | | | Reference | | |
| yes | 94/119 | 78/94 | 83 | 16/94 | 17 | 0.22 | 0.09-0.56 | 0.002 | 0.33 | 0.08-1.34 | 0.122 |

*HIV-infected children <5 years of age and with CD4 T lymphocyte percentage <15% were included in the group “HIV positive CD4 <200cells/ μ L” irrespective of their CD4 T lymphocyte count.

GCS: Glasgow Coma Scale. Underlying illness: chronic lung, renal, heart or liver disease; previous cerebrovascular accident; previous head injury; connective tissue disease; asplenia (functional/anatomical); previous malignancy; solid organ transplant; diabetes; chromosomal abnormality; complement deficiency; or current immunosuppressive therapy. Vaccine serotype: *Haemophilus influenzae* type b serotype. Resistant organism: organism was not susceptible to ampicillin. Appropriate empiric therapy initiated within 24hours: intravenous third generation cephalosporin. Directed antibiotic therapy initiated: antibiotics given which are appropriate to susceptibility profile of the organism.

Case-fatality and sequelae following bacterial meningitis

Table S_D: Risk factors for sequelae amongst survivors of pneumococcal meningitis in South Africa, 2016-2020, n=712

| | SEQUELAE at DISCHARGE | | | | Univariate analysis | | | Multivariable analysis | | |
|---|-----------------------|---------|-----|---------|---------------------|--------------------------|-----------|------------------------|--------------------------|---------|
| | NO | % | YES | % | Odds Ratio | 95% confidence intervals | p-value | Odds Ratio | 95% confidence intervals | p-value |
| Sex | | | | | | | | | | |
| female | 357/712 | 271/357 | 76 | 86/357 | 24 | Reference | | | | |
| male | 355/712 | 262/355 | 74 | 93/355 | 26 | 1.12 | 0.80-1.57 | 0.517 | | |
| Age category | | | | | | | | | | |
| less than 5 years | 182/712 | 131/182 | 72 | 51/182 | 28 | 1.22 | 0.84-1.79 | 0.299 | | |
| 5 years and older | 530/712 | 402/530 | 76 | 128/530 | 24 | Reference | | | | |
| HIV | | | | | | | | | | |
| negative | 224/712 | 155/224 | 69 | 69/224 | 31 | Reference | | | | |
| positive | 389/712 | 298/389 | 77 | 91/389 | 23 | 0.69 | 0.47-0.99 | 0.045 | | |
| not done | 99/712 | 80/99 | 81 | 19/99 | 19 | 0.53 | 0.30-0.95 | 0.032 | | |
| HIV category with CD4 count values | | | | | | | | | | |
| HIV negative | 224/561 | 155/224 | 69 | 69/224 | 31 | Reference | | | | |
| HIV positive CD4 ≥200cells/μL | 133/561 | 104/133 | 78 | 29/133 | 22 | 0.63 | 0.38-1.03 | 0.067 | | |
| HIV positive CD4 <200cells/μL* | 204/561 | 149/204 | 73 | 55/204 | 27 | 0.83 | 0.55-1.26 | 0.382 | | |
| GCS category | | | | | | | | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | | |
|--|---------|---------|-----|---------|----|-----------|-----------|--------|-----------|------------------|
| GCS of 15 (alert) | 292/604 | 246/292 | 84 | 46/292 | 16 | Reference | | | Reference | |
| GCS <15 | 312/604 | 203/312 | 65 | 109/312 | 35 | 2.87 | 1.94-4.25 | <0.001 | 2.55 | 1.52-4.26 <0.001 |
| Pitt Bacteraemia Score on admission | | | | | | | | | | |
| 0 (mild) | 156/525 | 130/156 | 83 | 26/156 | 17 | Reference | | | | |
| 1-3 (moderate) | 344/525 | 246/344 | 72 | 98/344 | 28 | 1.99 | 1.23-3.22 | 0.005 | | |
| 4-12 (severe) | 25/525 | 10/25 | 40 | 15/25 | 60 | 7.5 | 3.04-18.5 | <0.001 | | |
| Underlying illness | | | | | | | | | | |
| yes | 85/712 | 59/85 | 69 | 26/85 | 31 | 1.37 | 0.83-2.24 | 0.219 | | |
| no | 627/712 | 474/627 | 76 | 153/627 | 24 | Reference | | | | |
| Specimen type | | | | | | | | | | |
| CSF | 575/712 | 432/575 | 75 | 143/575 | 25 | Reference | | | | |
| Blood | 135/712 | 99/135 | 73 | 36/135 | 27 | 1.1 | 0.72-1.68 | 0.665 | | |
| Other | 2/712 | 2/2 | 100 | 0/2 | 0 | . | | | | |
| Serotype category | | | | | | | | | | |
| PCV7 | 69/710 | 48/69 | 70 | 21/69 | 30 | Reference | | | | |
| PCV13 add | 64/710 | 50/64 | 78 | 14/64 | 22 | 0.64 | 0.29-1.40 | 0.264 | | |
| non PCV | 423/710 | 320/423 | 76 | 103/423 | 24 | 0.74 | 0.42-1.29 | 0.282 | | |
| Not-typed | 154/710 | 114/154 | 74 | 40/154 | 26 | 0.8 | 0.43-1.50 | 0.49 | | |
| Vaccine serotype | | | | | | | | | | |
| yes | 134/558 | 99/134 | 74 | 35/134 | 26 | 1.09 | 0.70-1.70 | 0.711 | | |
| no | 424/558 | 320/424 | 75 | 104/424 | 25 | Reference | | | | |
| Resistant organism | | | | | | | | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | | | |
|---|---------|--------------|----|---------|----|-----------|-----------|-------|-----------|-----------|-------|
| yes | 93/425 | 56/93 | 60 | 37/93 | 40 | 2.39 | 1.46-3.90 | 0.001 | 2.06 | 1.18-3.62 | 0.011 |
| no | 332/425 | 260/332 | 78 | 72/332 | 22 | Reference | | | Reference | | |
| Appropriate empiric therapy initiated within 24hrs | | | | | | | | | | | |
| yes | 461/712 | 333/461 | 72 | 128/461 | 28 | 1.51 | 1.04-2.18 | 0.029 | | | |
| no | 251/712 | 200/251 | 80 | 51/251 | 20 | Reference | | | | | |
| Directed therapy initiated | | | | | | | | | | | |
| yes | 554/712 | 417/554 5 | 75 | 137/554 | 25 | 0.91 | 0.61-1.36 | 0.636 | | | |
| no | 158/712 | 116/158 | 73 | 42/158 | 27 | Reference | | | | | |

*HIV-infected children <5 years of age and with CD4 T lymphocyte percentage <15% were included in the group “HIV positive CD4 <200cells/μL”

irrespective of their CD4 T lymphocyte count. GCS: Glasgow Coma Scale. Underlying illness: chronic lung, renal, heart or liver disease; previous cerebrovascular accident; previous head injury; connective tissue disease; asplenia (functional/anatomical); previous malignancy; solid organ transplant; diabetes; chromosomal abnormality; complement deficiency; or current immunosuppressive therapy. Serotype category: PCV pneumococcal conjugate vaccine, PCV7 – 4, 6B, 9V, 14, 18C, 19F and 23F, PCV13 additional – 1, 3, 5, 6A, 7F and 19A, non PCV – serotypes not in the 13-valent PCV, Not-typed – episodes where the pneumococcus was not serotyped. Vaccine serotype: pneumococcal serotype present in 13-valent PCV. Resistant organism: organism was not susceptible to penicillin (minimum inhibitory concentration >0.6μg/ml). Appropriate empiric therapy initiated within 24hours: intravenous third generation cephalosporin. Directed antibiotic therapy initiated: antibiotics given which are appropriate to susceptibility profile of the organism.

Case-fatality and sequelae following bacterial meningitis

Table S_E: Risk factors for sequelae amongst survivors of meningococcal meningitis in South Africa, 2016-2020, n=118

| | SEQUELAE at DISCHARGE | | | | Univariate analysis | | | Multivariable analysis | | |
|---|-----------------------|-------|-----|-------|---------------------|--------------------------|-----------|------------------------|--------------------------|---------|
| | NO | % | YES | % | Odds Ratio | 95% confidence intervals | p-value | Odds Ratio | 95% confidence intervals | p-value |
| Sex | | | | | | | | | | |
| female | 56/118 | 45/56 | 80 | 11/56 | 20 | Reference | | | | |
| male | 62/118 | 49/62 | 79 | 13/62 | 21 | 1.09 | 0.44-2.67 | 0.858 | | |
| Age category | | | | | | | | | | |
| less than 5 years | 54/118 | 42/54 | 78 | 12/54 | 22 | 1.24 | 0.50-3.04 | 0.641 | | |
| 5 years and older | 64/118 | 52/64 | 81 | 12/64 | 19 | Reference | | | | |
| HIV | | | | | | | | | | |
| negative | 82/118 | 66/82 | 80 | 16/82 | 20 | Reference | | | | |
| positive | 19/118 | 13/19 | 68 | 6/19 | 32 | 1.9 | 0.63-5.78 | 0.256 | | |
| not done | 17/118 | 15/17 | 88 | 2/17 | 12 | 0.55 | 0.11-2.65 | 0.456 | | |
| HIV category with CD4 count values | | | | | | | | | | |
| HIV negative | 82/97 | 66/82 | 80 | 16/82 | 20 | | | | | |
| HIV positive CD4 ≥200cells/μL | 10/97 | 6/10 | 60 | 4/10 | 40 | | | | | |
| HIV positive CD4 <200cells/μL* | 5/97 | 4/5 | 80 | 1/5 | 20 | | | | | |
| GCS category | | | | | | | | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | | | |
|--|---------|--------|-----|--------|----|-----------|------------|-------|-----------|------------|-------|
| GCS of 15 (alert) | 65/98 | 53/65 | 82 | 12/65 | 18 | Reference | | | Reference | | |
| GCS <15 | 33/98 | 22/33 | 67 | 11/33 | 33 | 2.21 | 0.85-5.75 | 0.105 | 7.21 | 1.09-47.68 | 0.04 |
| Pitt Bacteraemia Score on admission | | | | | | | | | | | |
| 0 (mild) | 34/78 | 28/34 | 82 | 6/34 | 18 | Reference | | | | | |
| 1-3 (moderate) | 42/78 | 30/42 | 71 | 12/42 | 29 | 1.87 | 0.62-5.65 | 0.269 | | | |
| 4-12 (severe) | 2/78 | 2/2 | 100 | 0/2 | 0 | 1 | | | | | |
| Underlying illness | | | | | | | | | | | |
| yes | 5/118 | 5/5 | 100 | 0/5 | 0 | 1 | | | | | |
| no | 113/118 | 89/113 | 79 | 24/113 | 21 | Reference | | | | | |
| Specimen type | | | | | | | | | | | |
| Cerebrospinal fluid | 95/118 | 77/95 | 81 | 18/95 | 19 | Reference | | | | | |
| Blood | 23/118 | 17/23 | 74 | 6/23 | 26 | 1.51 | 0.52-4.37 | 0.447 | | | |
| Other | | | | | | 1 | | | | | |
| Serogroup category | | | | | | | | | | | |
| B | 48/97 | 38/48 | 79 | 10/48 | 21 | Reference | | | | | |
| ACWY | 48/97 | 41/48 | 85 | 7/48 | 15 | 0.65 | 0.22-1.88 | 0.425 | | | |
| other | 1/97 | 1/1 | 100 | 0/1 | 0 | 1 | | | | | |
| Vaccine serogroup | | | | | | | | | | | |
| yes | 48/98 | 41/48 | 85 | 7/48 | 15 | 0.61 | 0.21-1.72 | 0.346 | | | |
| no | 50/98 | 39/50 | 78 | 11/50 | 22 | Reference | | | | | |
| Resistant organism | | | | | | | | | | | |
| yes | 5/56 | 4/5 | 80 | 1/5 | 20 | 2.3 | 0.21-24.80 | 0.492 | 2.77 | 0.20-37.96 | 0.445 |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | |
|---|---------|--------|----|--------|----|-----------|-----------|-----------|
| no | 51/56 | 46/51 | 90 | 5/51 | 10 | Reference | | Reference |
| Appropriate empiric therapy initiated within 24hrs | | | | | | | | |
| yes | 84/118 | 66/84 | 79 | 18/84 | 21 | 1.27 | 0.46-3.54 | 0.644 |
| no | 34/118 | 28/34 | 82 | 6/34 | 18 | Reference | | |
| Directed therapy initiated | | | | | | | | |
| yes | 108/118 | 86/108 | 80 | 22/108 | 20 | 1.02 | 0.20-5.16 | 0.978 |
| no | 10/118 | 8/10 | 80 | 2/10 | 20 | Reference | | |

*HIV-infected children <5 years of age and with CD4 T lymphocyte percentage <15% were included in the group “HIV positive CD4 <200cells/ μ L” irrespective of their CD4 T lymphocyte count.

GCS: Glasgow Coma Scale. Underlying illness: chronic lung, renal, heart or liver disease; previous cerebrovascular accident; previous head injury; connective tissue disease; asplenia (functional/anatomical); previous malignancy; solid organ transplant; diabetes; chromosomal abnormality; complement deficiency; or current immunosuppressive therapy. Vaccine serogroup: meningococcal serogroup present in quadrivalent meningococcal conjugate vaccine (A, C, W or Y). Resistant organism: organism was not susceptible to penicillin. Appropriate empiric therapy initiated within 24hours: intravenous third generation cephalosporin. Directed antibiotic therapy initiated: antibiotics given which are appropriate to susceptibility profile of the organism.

Case-fatality and sequelae following bacterial meningitis

Table S_F: Risk factors for sequelae amongst survivors of *Haemophilus influenzae* meningitis in South Africa, 2016-2020, n=91

| | SEQUELAE at DISCHARGE | | | | Univariate analysis | | | Multivariable analysis | | | |
|---|-----------------------|-------|-----|-------|---------------------|--------------------------|------------|------------------------|--------------------------|------------|-------|
| | NO | % | YES | % | Odds Ratio | 95% confidence intervals | p-value | Odds Ratio | 95% confidence intervals | p-value | |
| Sex | | | | | | | | | | | |
| female | 44/91 | 37/44 | 84 | 7/44 | 16 | Reference | | | | | |
| male | 47/91 | 35/47 | 74 | 12/47 | 26 | 1.81 | 0.64-5.13 | 0.263 | | | |
| Age category | | | | | | | | | | | |
| less than 5 years | 54/91 | 37/54 | 69 | 17/54 | 31 | 8.04 | 1.73-37.36 | 0.008 | 5.59 | 1.01-30.84 | 0.048 |
| 5 years and older | 37/91 | 35/37 | 95 | 2/37 | 5 | Reference | | | Reference | | |
| HIV | | | | | | | | | | | |
| negative | 52/91 | 38/52 | 73 | 14/52 | 27 | Reference | | | | | |
| positive | 25/91 | 25/25 | 100 | 0/25 | 0 | 1 | | | | | |
| not done | 14/91 | 9/14 | 64 | 5/14 | 36 | 1.51 | 0.43-5.28 | 0.521 | | | |
| HIV category with CD4 count values | | | | | | | | | | | |
| HIV negative | 52/76 | 38/52 | 73 | 14/52 | 27 | Reference | | | | | |
| HIV positive CD4 | | | | | | | | | | | |
| ≥200cells/μL | 11/76 | 11/11 | 100 | 0/11 | 0 | 1 | | | | | |
| HIV positive CD4 | | | | | | | | | | | |
| <200cells/μL* | 13/76 | 13/13 | 100 | 0/13 | 0 | 1 | | | | | |
| GCS category | | | | | | | | | | | |

Case-fatality and sequelae following bacterial meningitis

| | | | | | | | | | |
|--|-------|-------|-----|-------|----|-----------|------------|-----------|----------------------|
| GCS of 15 (alert) | 65/76 | 54/65 | 83 | 11/65 | 17 | Reference | | | |
| GCS <15 | 11/76 | 7/11 | 64 | 4/11 | 36 | 2.81 | 0.70-11.25 | 0.146 | |
| Pitt Bacteraemia Score on admission | | | | | | | | | |
| 0 (mild) | 27/55 | 21/27 | 78 | 6/27 | 22 | Reference | | | |
| 1-3 (moderate) | 26/55 | 21/26 | 81 | 5/26 | 19 | 0.83 | 0.22-3.16 | 0.788 | |
| 4-12 (severe) | 2/55 | 1/2 | 50 | 1/2 | 50 | 3.5 | 0.19-64.67 | 0.4 | |
| Underlying illness | | | | | | | | | |
| yes | 11/91 | 7/11 | 64 | 4/11 | 36 | 2.48 | 0.64-9.56 | 0.188 | |
| no | 80/91 | 65/80 | 81 | 15/80 | 19 | Reference | | | |
| Specimen type | | | | | | | | | |
| Cerebrospinal fluid | 66/91 | 51/66 | 77 | 15/66 | 23 | Reference | | | |
| Blood | 24/91 | 20/24 | 83 | 4/24 | 17 | 0.68 | 0.20-2.30 | 0.535 | |
| Other | 1/91 | 1/1 | 100 | 0/1 | 0 | 1 | | | |
| Serotype category | | | | | | | | | |
| NT | 19/69 | 16/19 | 84 | 3/19 | 16 | Reference | | | |
| a,c,d,e,f | 18/69 | 13/18 | 72 | 5/18 | 28 | 2.05 | 0.41-10.24 | 0.381 | |
| b | 32/69 | 29/32 | 91 | 3/32 | 9 | 0.55 | 0.10-3.06 | 0.496 | |
| Vaccine serotype | | | | | | | | | |
| yes | 32/69 | 29/32 | 91 | 3/32 | 9 | 0.38 | 0.09-1.56 | 0.177 | 0.23 0.05-1.03 0.054 |
| no | 37/69 | 29/37 | 78 | 8/37 | 22 | Reference | | Reference | |
| Resistant organism | | | | | | | | | |
| yes | 12/42 | 12/12 | 100 | 0/12 | 0 | 1 | | | |

Case-fatality and sequelae following bacterial meningitis

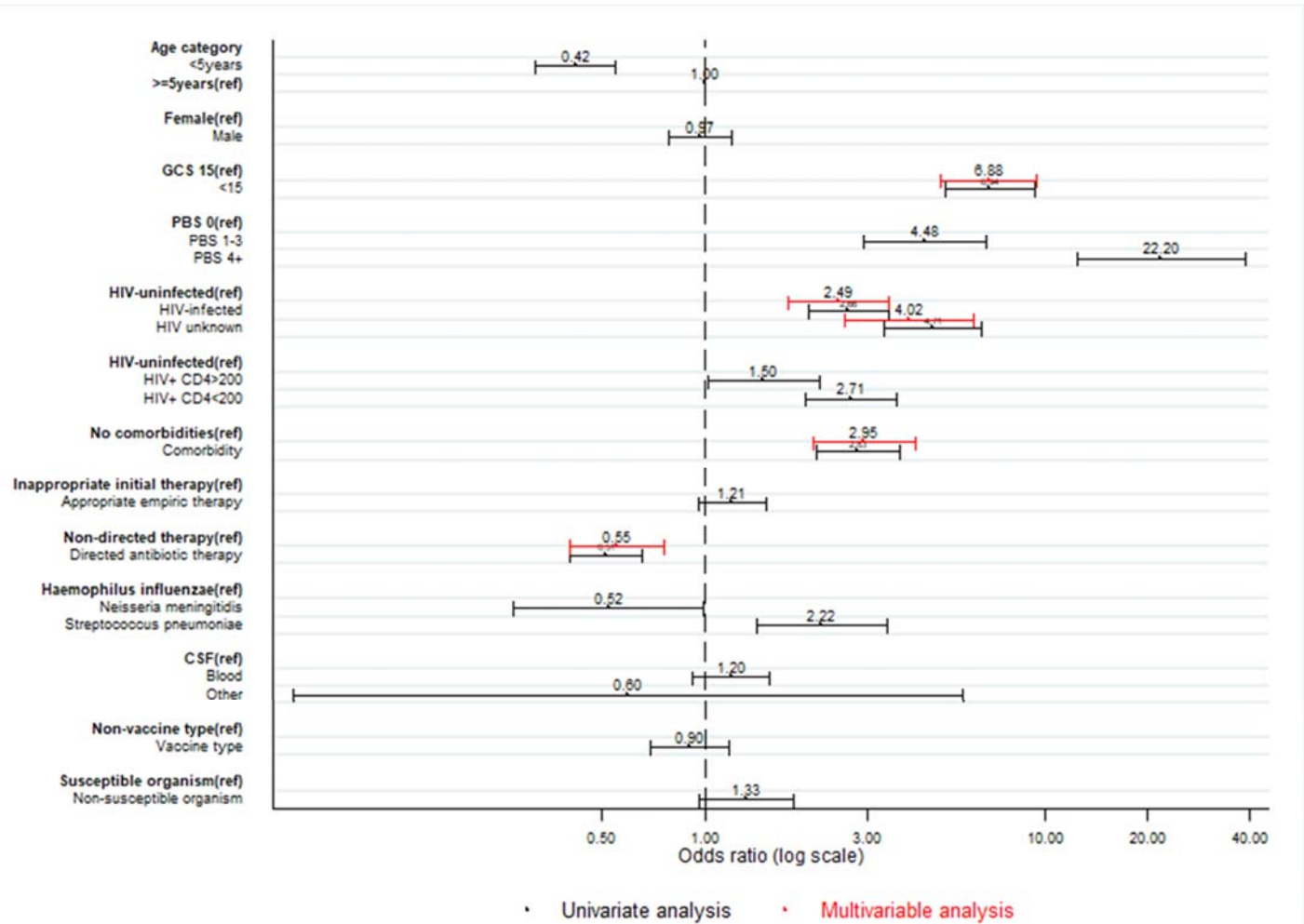
| | | | | | | | | |
|---|-------|-------|-----|-------|----|-----------|-----------|-------|
| no | 30/42 | 26/30 | 87 | 4/30 | 13 | Reference | | |
| Appropriate empiric therapy initiated within 24hrs | | | | | | | | |
| yes | 53/91 | 42/53 | 79 | 11/53 | 21 | 0.98 | 0.35-2.74 | 0.972 |
| no | 38/91 | 30/38 | 79 | 8/38 | 21 | Reference | | |
| Directed therapy initiated | | | | | | | | |
| yes | 78/91 | 59/78 | 76 | 19/78 | 24 | 1 | | |
| | | | | | | Reference | | |
| no | 13/91 | 13/13 | 100 | 0/13 | 0 | | | |

*HIV-infected children <5 years of age and with CD4 T lymphocyte percentage <15% were included in the group “HIV positive CD4 <200cells/ μ L” irrespective of their CD4 T lymphocyte count.

GCS: Glasgow Coma Scale. Underlying illness: chronic lung, renal, heart or liver disease; previous cerebrovascular accident; previous head injury; connective tissue disease; asplenia (functional/anatomical); previous malignancy; solid organ transplant; diabetes; chromosomal abnormality; complement deficiency; or current immunosuppressive therapy. Vaccine serotype: *Haemophilus influenzae* type b serotype. Resistant organism: organism was not susceptible to ampicillin. Appropriate empiric therapy initiated within 24hours: intravenous third generation cephalosporin. Directed antibiotic therapy initiated: antibiotics given which are appropriate to susceptibility profile of the organism.

Case-fatality and sequelae following bacterial meningitis

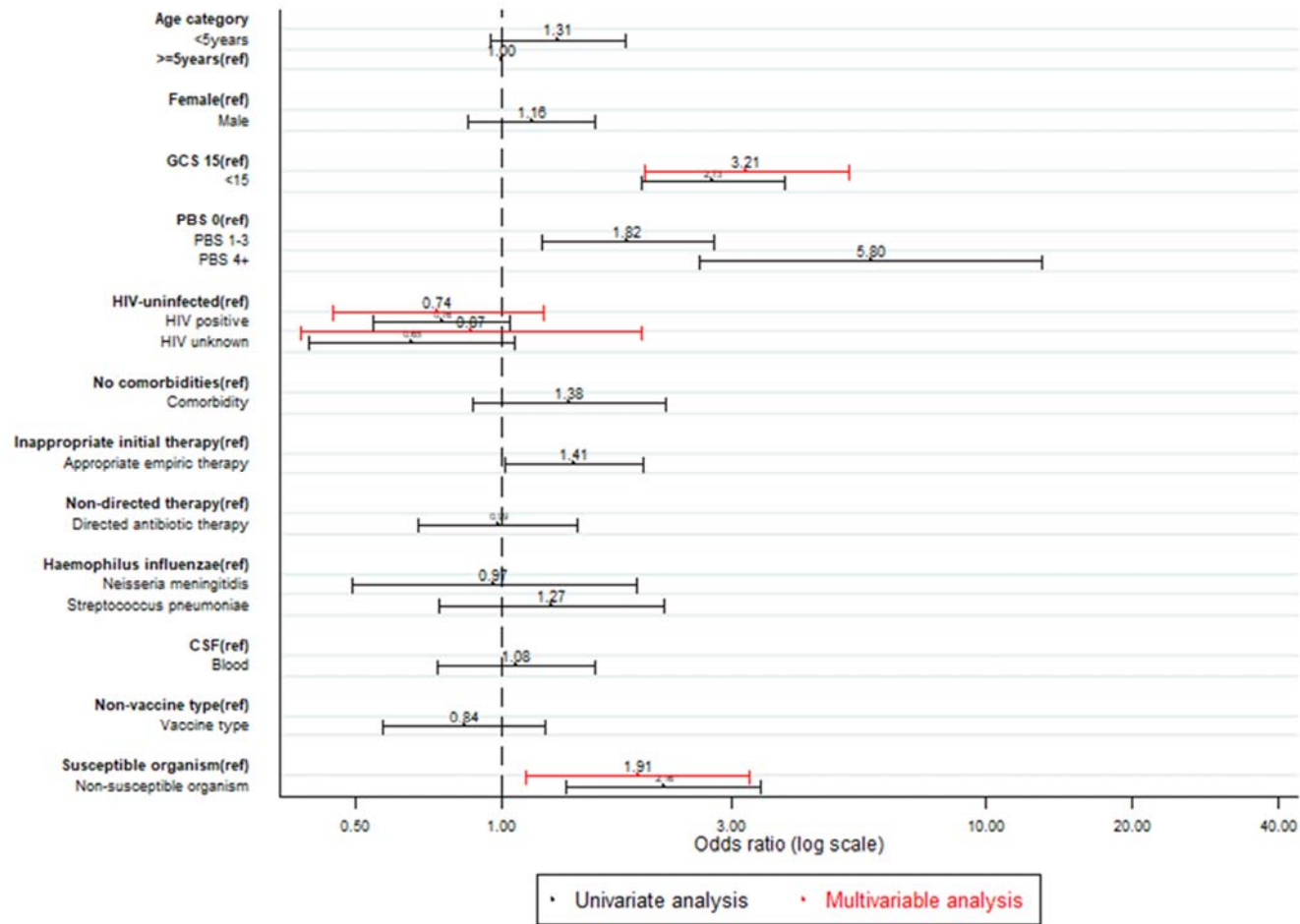
Supplementary figure 1: Forest plot: univariate and multivariable analysis of risk factors for mortality following bacterial meningitis, 2016-2020



Footnote: GCS: Glasgow coma score; PBS: Pitt Bacteraemia Score for severity of illness

Case-fatality and sequelae following bacterial meningitis

Supplementary figure 2: Forest plot: univariate and multivariable analysis of risk factors for developing sequelae following bacterial meningitis, 2016-2020



Case-fatality and sequelae following bacterial meningitis

Footnote: GCS: Glasgow coma score; PBS: Pitt Bacteraemia Score for severity of illness