**Supplement table 1**

*Characteristics of included and excluded adult patients with invasive pneumococcal disease at admission to Aker University Hospital between 1993-2008.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Included (416 patients)** | | **Excluded due to missing data (38 patients)** | | **p-value** |
| **Average age in years (95% CI)** | 65.0 | (63.3-66.7) | 68.3 | (61.4-75.3) | 0.860 |
| **Average days hospitalized (95% CI)\*** | 15.2 | (13.5-16.9) | 11.3 | (7.9-14.7) | 0.092 |
| **Male (%)** | 183 | (44.0) | 23 | (60.5) | 0.050 |
| **Inflammatory markers at admission:** |  |  |  |  |  |
| ***Mean CPR (95% CI)+*** | 278.6 | (262.6-294.6) | 293.0 | (246.5-339.5) | 0.597 |
| ***White blood cell count <4 or >12 (%)#*** | 281 | (69.9) | 31 | (81.6) | 0.130 |
| **Comorbidities (%):** |  |  |  |  |  |
| ***Cardiovascular disease*** | 152 | (36.5) | 19 | (50.0) | 0.101 |
| ***Pulmonary disease*** | 111 | (26.7) | 6 | (15.8) | 0.142 |
| ***Cancer*** | 74 | (17.8) | 9 | (23.7) | 0.368 |
| ***Diabetes*** | 35 | (8.4) | 3 | (7.9) | 1.000 |
| **Risk factors (%):** |  |  |  |  |  |
| ***Steroid use*** | 39 | (9.4) | 1 | (2.6) | 0.233 |
| ***Smoking*** | 165 | (39.7) | 5 | (50.0) | 0.510 |
| ***Alcohol*** | 46 | (11.1) | 3 | (7.9) | 0.206 |
| ***Immunosuppressed¤*** | 59 | (14.2) | 3 | (16.2) | 0.456 |
| *\*info missing for 2 patients in the included group*  *+info missing for 14 in the included group*  *#info missing for 22 in the included group*  *¤defined as hematological cancer, oral or intravenous steroid treatment, cytotoxic drug treatment and asplenia)* | | | | | |

**Supplement table 2**

*Serotype of invasive pneumococcal disease stratified by symptoms for 416 adult patients admitted to Aker University Hospital between 1993-2008.*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Serotype** | **No gastrointestinal symptoms** | **Proportion of typable** | **Gastrointestinal symptoms** | **Proportion of typable** | **Only gastrointestinal symptoms** | **Proportion of typable** |
| 1 | 33 | 15.1 % | 22 | 26.5 % | 10 | 33.3 % |
| 3 | 8 | 3.7 % | 3 | 3.6 % | 2 | 6.7 % |
| 4 | 32 | 14.7 % | 10 | 12.1 % | 0 | 0.0 % |
| 5 | 0 | 0.0 % | 0 | 0.0 % | 0 | 0.0 % |
| 6A | 7 | 3.2 % | 1 | 1.2 % | 1 | 3.3 % |
| 6B | 2 | 0.9 % | 3 | 3.6 % | 1 | 3.3 % |
| 7F | 16 | 7.3 % | 6 | 7.2 % | 3 | 10.0 % |
| 8 | 8 | 3.7 % | 4 | 4.8 % | 2 | 6.7 % |
| 9N | 6 | 2.8 % | 0 | 0.0 % | 0 | 0.0 % |
| 9V | 18 | 8.3 % | 3 | 3.6 % | 1 | 3.3 % |
| 10A | 6 | 2.8 % | 1 | 1.2 % | 0 | 0.0 % |
| 11A | 2 | 0.9 % | 0 | 0.0 % | 0 | 0.0 % |
| 11B | 0 | 0.0 % | 0 | 0.0 % | 0 | 0.0 % |
| 12F | 6 | 2.8 % | 3 | 3.6 % | 1 | 3.3 % |
| 14 | 24 | 11.0 % | 11 | 13.3 % | 2 | 6.7 % |
| 15B | 1 | 0.5 % | 0 | 0.0 % | 0 | 0.0 % |
| 15C | 0 | 0.0 % | 1 | 1.2 % | 1 | 3.3 % |
| 16F | 4 | 1.8 % | 1 | 1.2 % | 1 | 3.3 % |
| 17F | 2 | 0.9 % | 0 | 0.0 % | 0 | 0.0 % |
| 18C | 3 | 1.4 % | 1 | 1.2 % | 0 | 0.0 % |
| 19A | 4 | 1.8 % | 1 | 1.2 % | 0 | 0.0 % |
| 19F | 4 | 1.8 % | 2 | 2.4 % | 0 | 0.0 % |
| 20 | 1 | 0.5 % | 0 | 0.0 % | 0 | 0.0 % |
| 22F | 6 | 2.8 % | 3 | 3.6 % | 3 | 10.0 % |
| 23A | 1 | 0.5 % | 0 | 0.0 % | 0 | 0.0 % |
| 23F | 13 | 6.0 % | 2 | 2.4 % | 0 | 0.0 % |
| 24F | 2 | 0.9 % | 0 | 0.0 % | 0 | 0.0 % |
| 25A | 1 | 0.5 % | 0 | 0.0 % | 0 | 0.0 % |
| 31 | 1 | 0.5 % | 3 | 3.6 % | 2 | 6.7 % |
| 33 | 1 | 0.5 % | 0 | 0.0 % | 0 | 0.0 % |
| 33F | 2 | 0.9 % | 2 | 2.4 % | 0 | 0.0 % |
| 35F | 2 | 0.9 % | 0 | 0.0 % | 0 | 0.0 % |
| 40 | 2 | 0.9 % | 0 | 0.0 % | 0 | 0.0 % |
| **Typable** | 218 | 70.8 % | 83 | 76.9 % | 30 | 63.8 % |
| **Non-typable/missing info** | 90 | 29.2 % | 25 | 23.2 % | 17 | 36.2 % |
| *Sum* | 308 |  | 108 |  | 47 |  |

**Supplement table 3**

*Empirical antibiotic treatment initiated after blood culture in 416 adult patients with invasive pneumococcal disease admitted to Aker University Hospital between 1993-2008. n:number.*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Class of antibiotic:** | **No gastrointestinal symptoms** | | **Gastrointestinal symptoms** | | **p-value\*** | **Only gastrointestinal symptoms** | | **p-value\*** |
|  | *n* | *(%)* | *n* | *(%)* |  | *n* | *(%)* |  |
| **No antibiotic given** | 8 | 3 | 7 | 6 | 0.062 | 6 | 13 | **0.001** |
| **Penicillin ampicillin or dicloxacillin** | 142 | 46 | 35 | 32 | **0.013** | 12 | 26 | **0.008** |
| **Penicillin ampicillin or dicloxacillin combined with gentamicin** | 90 | 29 | 37 | 34 | 0.328 | 9 | 19 | 0.152 |
| **Other** | 68 | 22 | 29 | 27 | 0.220 | 20 | 43 | **<0.001** |
|  | 308 |  | 108 |  |  | 47 |  |  |
| *\*compared to no gastrointestinal symptoms* |  |  |  |  |  |  |  |  |

**Supplement table 4**

*Multivariate survival analysis by Cox regression for 416 adult patients with invasive pneumococcal disease at admission to Aker University Hospital between 1993-2008 by time period. GI: Gastrointestinal*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ***Gastrointestinal symptoms (416 patients in total)*** | | | | ***Gastrointestinal symptoms only (355 patients in total)*** | | | |
| ***1993-2008 (61 deaths)*** | | | | ***1993-2008 (53 deaths)*** | | | |
| ***Variables*** | ***Hazard ratio*** | ***p-value*** | ***95 % CI*** | ***Variables*** | ***Hazard ratio*** | ***p-value*** | ***95 % CI*** |
| ***GI symptoms*** | 2.11 | 0.007 | 1.23 - 3.63 | ***GI symptoms only*** | 4.00 | 0.000 | 2.04 - 7.84 |
| ***Age*** | 1.04 | 0.000 | 1.02 - 1.06 | ***Age*** | 1.05 | 0.000 | 1.03 - 1.07 |
| ***Being female*** | 0.48 | 0.005 | 0.29 - 0.80 | ***Being female*** | 0.46 | 0.007 | 0.26 - 0.81 |
|  | | | |  | | | |
| ***1993-2000 (30 deaths)*** | | | | ***1993-2000 (25 deaths)*** | | | |
| ***GI symptoms*** | 3.93 | 0.001 | 1.75 - 8.82 | ***GI symptoms only*** | 4.26 | 0.008 | 1.45 - 12.50 |
| ***Age*** | 1.07 | 0.000 | 1.04 - 1.10 | ***Age*** | 1.08 | 0.000 | 1.04 - 1.12 |
| ***Being female*** | 0.18 | 0.000 | 0.08 - 0.40 | ***Being female*** | 0.22 | 0.001 | 0.09 - 0.54 |
|  | | | |  | | | |
| ***2001-2008 (31 deaths)*** | | | | ***2001-2008 (28 deaths)*** | | | |
| ***GI symptoms*** | 1.66 | 0.197 | 0.77 - 3.57 | ***GI symptoms only*** | 3.93 | 0.003 | 1.61 - 9.59 |
| ***Age*** | 1.03 | 0.039 | 1.00 - 1.05 | ***Age*** | 1.03 | 0.038 | 1.00 - 1.05 |
| ***Being female*** | 0.84 | 0.627 | 0.41 - 1.71 | ***Being female*** | 0.80 | 0.561 | 0.37 - 1.72 |

**Supplement table 5**

*Proportion dead within 28 days for 416 adult patients with invasive pneumococcal disease at admission to Aker University Hospital between 1993-2008 by sex and time period.*

|  |  |  |  |
| --- | --- | --- | --- |
| Time period | Proportion (%) dead within 28 days | | p-value |
| male | female |
| 1993-2008 | 18.6 | 11.6 | **0.045** |
| 1993-1999 | 27.9 | 10.9 | **0.004** |
| 2000-2008 | 13.0 | 12.1 | 0.827 |