Background. Acute bacterial meningitis (ABM) remains an important cause of mortality among African children. Epidemiologic data with regard to ABM infection are necessary for prioritizing public health interventions.

Methods. We strengthened hospital-based surveillance of ABM among children admitted to Manhiça District Hospital (Maputo, Mozambique). Cerebrospinal fluid (CSF) samples were collected from children admitted to the hospital who met clinical criteria of ABM. Laboratory determinations were performed. Clinical information and outcome of cases were recorded.

Results. During the first 12 months of surveillance, which began in January 2006, CSF samples were collected from 642 children <15 years of age with suspected meningitis (18% of all pediatric patients admitted to the hospital during that time). ABM was confirmed in 43 (7%) of the 642 cases. Haemophilus influenzae type b (Hib) (14 cases), pneumococcus (9 cases), and meningococcus (7 cases) represented ∼70% of confirmed cases. Four of the 9 pneumococci were serotypes covered by the 7-valent pneumococcal conjugate vaccine. The case fatality rate among patients with ABM was 24% (8 of 33 with known outcome); an additional 8 patients left the hospital before discharge. The incidence of ABM was 85 per 100,000 population, which peaked at 2–12 months of age at 1078 cases per 100,000 population. All 9 pneumococci isolates were susceptible to chloramphenicol, and 8 were susceptible to penicillin (the additional 1 had intermediate resistance). For the 10 Hib isolates tested, only 1 was susceptible to chloramphenicol, and 5 were susceptible to ampicillin.

Conclusion. These data reinforce the importance of ABM as a cause of hospital admission and death in rural sub-Saharan Africa. Most observed ABM cases could have been prevented by current pneumococcal and Hib conjugate vaccines.
limitations, nonculture approaches, such as latex agglutination, may be used to verify the etiologic agent [2]. Certain characteristics of the CSF samples (such as appearance, leukocyte count, presence of proteins, CSF glucose level, or glucose CSF: blood ratio) might also be considered to be indicators of probable bacterial meningitis [2, 12], but these characteristics do not provide etiological information.

Beginning in 1998, ABM surveillance among children admitted to the Manhiça District Hospital (MDH; Maputo, Mozambique) was gradually introduced. CSF specimens were collected through LPs, and samples were initially processed for bacterial culture and Gram staining. Apart from the intrinsic limitations of this method, there were challenges in introducing CSF collection as part of routine hospital activities. During the initial years, LPs were performed for <3% of admitted children, and pneumococcus and H. influenzae were the most common bacteria isolated. More-accurate data on the disease burden associated with ABM were needed to appropriately allocate both treatment and prevention resources. We present data on hospital-based minimum incidence rates of ABM during a 1-year period, beginning in January 2006, after the project strengthened surveillance by establishing clear clinical criteria for CSF collection. New laboratory tests were included to improve diagnosis for both epidemiologic and clinical purposes. In addition, we evaluated suitable methods for meningitis diagnosis in resource-poor settings. Meningitis surveillance will continue for the next few years.

**PATIENTS AND METHODS**

**Study area and population.** The study was conducted by the Manhiça Health Research Center (Centro de Investigacão em Saúde da Manhiça [CISM], Maputo, Mozambique) at the MDH, a 110-bed facility with 36 pediatric beds that serves as the referral health facility for the Manhiça district, a rural area of Maputo Province in southern Mozambique [13, 14]. The Manhiça district has an estimated population of 140,000 inhabitants [15]. The climate of the area is subtropical with 2 distinct seasons: a warm and rainy season in November–April and a cool and dry season during the rest of the year. Malaria is endemic all year and peaks in November–April [15].

During the study period, the CISM maintained a continuous demographic surveillance system (DSS), which included >70,000 people and covered an area of 400 km² surrounding the hospital; ~17% of these people were children <5 years of age, and ~26% of children were 5–14 years of age [15]. Each child living within the DSS study area is issued a unique permanent identification number that describes the geographic localization of his or her household. Dates of birth, death, immigrations, and emigrations are recorded. The CISM maintains morbidity surveillance in the MDH; the unique permanent identification number of residents from the DSS allows tracking of every hospital visit and hospital stay for each of these children.

From 2001 through 2003, the prevalence of severe malnutrition (defined as weight-to-height Z score <3 SDs) for children <5 years of age who were admitted to the hospital was 10% [16]. In 2004, the HIV prevalence among pregnant women attending the hospital antenatal clinic was 21% [17]. Antiretroviral therapy at the time of delivery (single-dose nevirapine) has been available since 2003, and mother-to-child transmission of HIV was estimated to occur at a rate of 12% during that period, which resulted in a 2% HIV prevalence in the birth cohort. More than 25% of HIV-infected children died before reaching age 1 year (D. Naniche, A. Bardají, M. Lahuerta, A. Berenguer, I. Mandomando, S. Sanz, J. J. Aponte, B. Sigauque, P. Alonso, and C. Menéndez, unpublished data). Hib, pneumococcal, and meningococcal vaccines were not part of the routine infant immunization schedule in Mozambique during the study period. The extended program of immunization included bacillus Calmette-Guérin vaccination for all children during their first days of life.

**Hospital surveillance.** Since January 1997, the CISM has collected data on all pediatric outpatient visits to and hospitalizations in the MDH. On admission, a physician or a trained medical officer completes a detailed clinical questionnaire. Outcome data are recorded at hospital discharge [13, 14, 16]. For determination of malaria parasites in thin and thick blood smears, a blood sample is obtained by finger prick from children with fever (axillary temperature ≥37.5°C) or a history of fever in the previous 24 h, and packed-cell volume is also measured. As part of routine clinical practice, cultures of blood samples are performed at hospital admission for all children <2 years of age, regardless of temperature, and for older children with an axillary temperature >39°C who present with clinical suspicion of sepsis or neurologic impairment. In January 2006, the meningitis surveillance among inpatients was strengthened. Since then, LPs were performed on children admitted to the hospital who met any of the following clinical criteria: neck stiffness or meningeal signs, bulging fontanel, impaired consciousness (Blantyre Coma Scale score ≤5), history of convulsions without known epilepsy, focal neurologic signs, irritability or drowsiness, or suspected clinical sepsis. In addition, CSF samples were collected for all newborns (children <28 days of age) who were admitted to the hospital with fever or suspected neonatal sepsis. Two different sterile plastic tubes were filled with ~0.5 and 1 mL of CSF samples. Assessment of CSF glucose, Gram staining, and bacterial culture were performed using contents of the first tube. Glucose was concurrently measured in CSF and blood samples with use of Accu-Chek (Roche) at the bed side. The second tube was used to perform cell count, protein measurement (with use of Pandy, a semiquantitative method), and latex agglutination for detection of pneumococ-
either a glucose level ≥10 × 10^3/L, or (3) a leukocyte count of 10–99 × 10^3/L and either a glucose level <40 mg/dL or the presence of protein as determined using a semiquantitative method (Pandy). Abnormal CSF was defined as a leukocyte count of 10–99 × 10^3/L and either normal or nontested glucose in the CSF sample and a CSF sample that had no protein or was not tested. A case of ABM was considered definite, according to the Pneumococcal Vaccines Accelerated Development and Introduction Plan (PneumoADIP) definition, when either (1) the culture of the CSF sample had positive results (coagulase-negative staphylococci, Corynebacterium species, and Bacillus species were considered to be contaminants), (2) the CSF was purulent and either the results of culture of blood samples were positive (the same contaminants as for CSF) or results of the CSF Gram stain were positive, or (3) when the CSF sample was either abnormal or purulent and the latex agglutination result was positive for any of the antigens included. A case of probable ABM was considered, also following PneumoADIP definitions, when results of culture of a CSF sample were negative and at least 1 of the following criteria was met: (1) purulent CSF, (2) abnormal CSF findings and positive results of either culture of a blood sample or Gram stain, or (3) normal CSF findings and positive results of latex agglutination.

Bacterial isolates were interpreted as susceptible, intermediate, or resistant to antibiotics according to the guidelines of the Clinical Laboratory Standard Institute [21]. In this article, nonsusceptible isolates refer to both intermediate and resistant levels.

For study purposes, we defined the case fatality rate (CFR) as the number of deaths that met specific criteria divided by the number of children who met the condition and with known hospital outcome (discharge or death). Those children who were transferred to other hospitals at hospital admission or who left the hospital against medical advice were not considered in the CFR measurements.

Data management and statistical analysis. Data were entered using Fox Pro software, version 2.6 (Microsoft), and were analyzed using STATA statistical software, version 8.0 (StataCorp). Clinical data were entered by key punch by 2 people; discrepancies were resolved by referring to original forms. Proportions were compared using χ^2 tests. Continuous variables were compared using Student’s t test or the Wilcoxon rank-sum test. Minimum incidence rates and 95% CIs were calculated using the quadratic approximation to the Poisson log-likelihood for the log rate parameter. Person-time of follow-up for children <15 years of age in the demographic surveillance area was calculated using dates of birth and death, excluding periods of emigration. Follow-up time was excluded for 15 days (lag period) after each meningitis episode; a recurrence during the lag period was considered to be the same episode. Incidence estimates were calculated for episodes of ABM among children <15 years of age who were admitted to the MDH and were residing within the surveillance area.

RESULTS

Study profile. During the first year after strengthening meningitis surveillance (9 January 2006 through 8 January 2007), 3507 children <15 years of age were admitted to the MDH (median age, 16 months; 54% were boys). CSF samples were collected from 642 children with suspected meningitis (642 [80%] of 800 children who met the clinical criteria for CSF collection at hospital admission), which represents 18% of pe-
Bacterial Meningitis in Mozambican Children

Figure 1. Study profile of children <15 years of age who were admitted to the hospital during the study period. ABM, acute bacterial meningitis; Hib, Haemophilus influenzae pneumonia.
<table>
<thead>
<tr>
<th>Variable</th>
<th>ABM, ((n = 43))^a</th>
<th>Probable ABM, ((n = 40))^a</th>
<th>Other CSF, ((n = 559))^a</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&lt;2 months</td>
<td>11 (26)</td>
<td>17 (43)</td>
<td>139 (25)</td>
<td></td>
</tr>
<tr>
<td>2–11 months</td>
<td>18 (42)</td>
<td>4 (10)</td>
<td>97 (17)</td>
<td></td>
</tr>
<tr>
<td>1–4 years</td>
<td>8 (19)</td>
<td>15 (38)</td>
<td>265 (47)</td>
<td></td>
</tr>
<tr>
<td>5–14 years</td>
<td>6 (14)</td>
<td>4 (10)</td>
<td>58 (10)</td>
<td></td>
</tr>
<tr>
<td>Previous antibiotic treatment reported</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Yes</td>
<td>10 (25)</td>
<td>10 (25)</td>
<td>46 (9)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>30 (75)</td>
<td>30 (75)</td>
<td>466 (91)</td>
<td></td>
</tr>
<tr>
<td>CSF appearance</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Clear</td>
<td>8 (20)</td>
<td>17 (43)</td>
<td>477 (94)</td>
<td></td>
</tr>
<tr>
<td>Turbid/cloudy</td>
<td>31 (78)</td>
<td>22 (55)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Bloody</td>
<td>1 (2)</td>
<td>1 (3)</td>
<td>29 (6)</td>
<td></td>
</tr>
<tr>
<td>Leukocyte count, cells/(\mu)L</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&lt;10</td>
<td>9 (26)</td>
<td>11 (30)</td>
<td>436 (96)</td>
<td></td>
</tr>
<tr>
<td>10–99</td>
<td>7 (21)</td>
<td>14 (38)</td>
<td>20 (4)</td>
<td></td>
</tr>
<tr>
<td>100–999</td>
<td>8 (24)</td>
<td>11 (30)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>&gt;1000</td>
<td>10 (29)</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>CSF glucose level, mg/dL</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&gt;40</td>
<td>15 (43)</td>
<td>20 (51)</td>
<td>402 (80)</td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>20 (57)</td>
<td>19 (49)</td>
<td>99 (20)</td>
<td></td>
</tr>
<tr>
<td>Proteins</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Absent</td>
<td>19 (53)</td>
<td>32 (94)</td>
<td>410 (99)</td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>17 (47)</td>
<td>2 (6)</td>
<td>3 (&lt;1)</td>
<td></td>
</tr>
<tr>
<td>Agglutination</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No</td>
<td>16 (46)</td>
<td>31 (100)</td>
<td>374 (100)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19 (54)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>CSF culture results</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Negative</td>
<td>13 (30)</td>
<td>41 (100)</td>
<td>569 (100)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>30 (70)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Gram stain results</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Negative</td>
<td>15 (37)</td>
<td>40 (100)</td>
<td>558 (100)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>26 (63)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Bacteremia</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Negative</td>
<td>8 (20)</td>
<td>36 (95)</td>
<td>486 (91)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>33 (80)</td>
<td>2 (5)</td>
<td>49 (9)</td>
<td></td>
</tr>
<tr>
<td>Parasitemia</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Negative</td>
<td>33 (77)</td>
<td>25 (63)</td>
<td>254 (46)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>10 (23)</td>
<td>15 (37)</td>
<td>303 (54)</td>
<td></td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospital discharge</td>
<td>26 (60)</td>
<td>34 (85)</td>
<td>496 (89)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>8 (19)</td>
<td>4 (10)</td>
<td>34 (6)</td>
<td></td>
</tr>
<tr>
<td>Left hospital</td>
<td>8 (19)</td>
<td>0 (0)</td>
<td>13 (2)</td>
<td></td>
</tr>
<tr>
<td>Transferred to another hospital</td>
<td>1 (2)</td>
<td>2 (5)</td>
<td>12 (2)</td>
<td></td>
</tr>
<tr>
<td>Duration of hospitalization, median days (25th percentile, 75th percentile)^b</td>
<td>8 (6, 9)</td>
<td>4 (3, 6)</td>
<td>4 (3, 5)</td>
<td>.098</td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. (%) of patients, unless otherwise indicated. Results are classified according to the final clinical group: acute bacterial meningitis (ABM), probable ABM, or other children with CSF collected (Other CSF).

^a Not all data are available for all specimens.

^b Including only children discharged from the hospital.
meningitis. Infection with *Pseudomonas* species was responsible for 2 other deaths, and *E. coli* was responsible for 1 death; all 3 of these deaths occurred among neonates. Most fatalities (6 [75%] of 8 fatalities) occurred among children <1 year of age, which is similar to the age distribution of the patients with ABM (67%). Almost 20% (8 patients) of hospitalized patients with ABM left the hospital against medical advice when their clinical condition worsened (4 patients with *Pneumococcus*, 2 patients with *Hib*, 1 patient with *S. aureus* infection, and 1 patient infected with *Proteus* species). Five of these children who left the hospital were residents of the DSS area (4 children with *Pneumococcus* and 1 child infected with *Proteus* species). Death was confirmed for 3 of them within 1 month after they had left the hospital (2 with *Pneumococcus* and 1 infected with *Proteus* species).

For the 25 patients discharged from the hospital, the median length of hospitalization was 8 days (3 days for the overall hospital stay among children <15 years of age; *P* < .001). Table 1 provides details on length of hospitalization only for children who had CSF samples collected.

**Incidence rates.** Minimum community-based incidence rates of ABM were calculated among children from the DSS study area through use of (1) the number of episodes occurring among these children (32 episodes) and (2) their individual time at risk. It yielded an overall incidence of confirmed ABM of 85 per 100,000 child-years at risk for children <15 years of age (1078 for children <2 months of age, 507 for children 2–11 months of age, 53 for children 1–4 years of age, and 26 for children 5–15 years of age). Table 2 gives the incidence rates for the most common bacterial pathogens, stratified by age group. The incidence for both *Hib* and *Pneumococcus* was highest for children 2–12 months of age, whereas the incidence of *Meningococcus* was similar for all age groups (table 2).

**Antibiotic susceptibility pattern.** We measured antibiotic susceptibility patterns for those patients with ABM for whom bacteria were isolated. All 9 *Pneumococcal* isolates were tested for chloramphenicol and penicillin; all isolates were susceptible to chloramphenicol, and 8 isolates were susceptible to penicillin. The penicillin isolate that was not susceptible had an MIC of 0.19 μg/mL, which meant it was of intermediate susceptibility. For the 10 *Hib* isolates tested, 1 was susceptible to chloramphenicol and 5 were susceptible to ampicillin. All meningococcal isolates tested (4 isolates) were susceptible to both chloramphenicol and ampicillin.

Overall, 23 *Hib*, *Pneumococcal*, and *Meningococcal* isolates were tested for chloramphenicol susceptibility, the first line of antibiotic used for ABM; 14 (61%) were susceptible. Rates of susceptibility varied according to age group and were higher among the oldest children (50% for children <2 years of age, compared with 100% for children ≥2 years of age; *P* = .043). Similar results were obtained for ampicillin and penicillin; of 23 isolates tested, 12 (52%) were nonsusceptible, all of which were isolated from the youngest age group (<2 years of age; *P* = .133).

**Value of different and alternative diagnostic methods.** When sufficient CSF volume was available, we tested CSF using latex agglutination for *Pneumococcus*, *Hib*, *Meningococcus* (A, B, C, and W135), and group B streptococcus. Overall, 20 of 32 patients with ABM whose disease was attributable to these causes were tested by latex agglutination, with a positive rate result of 90% (18 of 20 patients). However, only 2 of these 18 patients with positive latex agglutination results tested negative by both bacterial culture of CSF and Gram stain (1 *Hib* and 1 meningococcal A). Neither of these 2 children or their caregivers reported previous antibiotic use. Gram-stain results indicated positivity in 26 (63%) of all 41 patients with ABM who were tested. As indicated in table 1, sensitivity of CSF appearance was 78% (31 turbid/cloudy among 40 observed), compared with 53% (18 of 34) with a leukocyte count ≥100 cells/μL. Sensitivity could be improved using both CSF transparency and leukocyte count at the same time, for detection of 34 (87%) of 39 confirmed meningitis cases.

**CONCLUSIONS**

Our results confirm the high burden of disease associated with ABM in rural Mozambique. Most important, measured mortality rates were high and were probably underestimated, because 19% of patients left the hospital when their clinical condition worsened. More than 40% of the meningitis cases were potentially preventable by currently available Hib or pneumococcal conjugate vaccines. The burden of meningococcal meningitis was surprisingly high in an African region distant from the meningitis belt. However, only 1 isolate was serotype A.

In our previous report [22], CSF sample collection was performed for only 3% of all pediatric patients, far below the 18% in this study. Improvement in CSF sample collection during the present surveillance period was made possible by clearly...
establishing clinical criteria for identifying those children with possible meningitis and by providing the training and support needed for obtaining CSF specimens from such patients. Criteria were adhered to through specific training of the clinical personnel in signs recognition and sample collection. Procedures were closely supervised by the study pediatrician to guarantee adequate performance of LP procedures. Moreover, newborns with fever or suspected clinical sepsis were all screened for meningitis, something that had not previously been performed on a regular basis at the MDH (25% of confirmed meningitis cases and 40% of probable meningitis cases occurred among children <2 months of age). Improving coordination between the hospital and laboratory increased the validity of the laboratory CSF results obtained, because these were made readily available for the daily management of the patients, which highlighted the importance of sample collection to achieve early microbiological diagnosis. Likewise, meningitis diagnosis was also improved by increasing the number of laboratory tests conducted on the specimens to improve the diagnostic sensitivity.

Strengthening meningitis surveillance was necessary to document accurate data on the ABM burden in rural Mozambique. Measured overall incidences were >4 times higher than previously described in this location, although the definition of cases was more specific in our previous report (85 vs. 20 per 100,000 person-years at risk for children <15 years of age) [22]. When only cases with positive results of a bacterial CSF culture were considered (70% of overall cases, as we defined in our previous report), currently measured rates were still much higher than previously reported. As expected, the most common pathogens were Hib and pneumococcus, the former clearly the most common for children 2–12 months of age. Specific incidence rates for Hib were similar or higher than described in other African regions before the introduction of the Hib conjugate vaccine [5, 23, 24]. Documented pneumococcal meningitis incidence rates were also high, compared with data available from other countries [25, 26]. The high prevalence of potential risk factors for ABM in the study conditions, such as severe malnutrition or HIV infection, might partly explain the high incidence rates detected. HIV prevalence among patients with meningitis was probably as high as what we documented in another report involving children <2 years of age who were hospitalized with clinically severe pneumonia in the same hospital during 2005–2006 (A. Roca, B. Sigauque, Ll. Quintó, L. Morais, A. Berenguera, M. Corachan, J. L. Ribó, D. Naniche, I. Mandomando, E. Bassat, Ch. Sacoor, D. Nhalungo, A. Schuchat, M. Soriano-Gabarro, B. Flannery, and P. Alonso, unpublished data). The importance of HIV among patients might decrease over the years, because the mortality rate among these children is high (D. Naniche, A. Bardaji, M. Lahuer, A. Berenguera, I. Mandomando, S. Sanz, J. Aponte, B. Sigáquique, P. Alonso, and C. Menéndez, unpublished data). Unfortunately, individual data of HIV status among patients in the present study were not available.

The incidence of meningococcal meningitis (mostly W135) was unexpectedly high in this area and contrasted with our previous report [22] in which the prevalence of meningococcus was much lower than that of Hib or pneumococcus as a cause of ABM. In the present report, the incidence rate for meningococcal meningitis is similar to pneumococcal and Hib meningitis rates after the first year of life. Further molecular and epidemiologic analysis is needed to describe whether these meningococcal W135 cases represent a small outbreak in the study, a hypothesis supported by the small time frame during which most meningococci were isolated. Four meningococcal meningitis cases were diagnosed within 3 weeks.

Mortality associated with ABM was high. For every 4 patients with meningitis with known outcome, 1 died during hospitalization (most died during the first hours after admission). In addition, 1 in 5 children admitted to the hospital left the hospital against medical advice, with a high likelihood of death at home, as described for 3 of 5 patients from the DSS area. Despite these high rates, hospital mortality seems to have decreased, compared with rates described in our previous report [22]. Differences in mortality could be partially attributable to several issues. When systematic criteria are not applied for determining who should have CSF collected (as previously occurred), only the most severely ill or clinically symptomatic

### Table 2. Hospital-based minimum incidence rates of acute bacterial meningitis (ABM), crude and stratified by pathogen (only for the 3 most prevalent pathogens) and age groups.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Overall rate</th>
<th>Aged 2–11 months</th>
<th>Aged 1–4 years</th>
<th>Aged 5–14 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>Rate (95% CI)</td>
<td>No. of patients</td>
<td>Rate (95% CI)</td>
<td>No. of patients</td>
</tr>
<tr>
<td>ABM</td>
<td>32</td>
<td>14</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Pneumococcus</td>
<td>7</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Haemophilus influenza type b</td>
<td>10</td>
<td>8</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Meningococcus</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**NOTE.** Only children residents from the Centro de Investigación en Saúde da Manhiça study area were included in rate calculations (32 children). Incidence rates are per 100,000 person-years at risk.
children are likely to have an LP performed. Another expla-
nation for the reduction in the CFR is the increased access to
a third-generation cephalosporin (ceftriaxone) in the hospital
setting. If that has a role, the CFR might be higher in the rest
of the country, compared with Manhiça, because ceftriaxone
is not available in public Mozambican rural hospitals. In any
case, measured mortality might be an underestimation of the
real picture in this setting and in Mozambique, because we
would expect that patients with fulminating meningitis die before
reaching the hospital.

Meningitis diagnosis in children in sub-Saharan Africa relies
on clinical suspicion and the correct interpretation of data from
available laboratory tests [12]. For study purposes and to max-
imize meningitis detection, we used several diagnostic methods.
Bacterial culture remains the benchmark for specificity and for
isolating bacteria that can subsequently be serotyped and tested
for antimicrobial resistance [2, 12], but it is poorly sensitive,
is expensive, and is difficult to standardize in rural settings in
Africa. Latex agglutination tests are more sensitive and require
less expertise and laboratory equipment for their interpretation,
but the tests are expensive [2, 11]. Latex agglutination tests
detected up to 90% of Hib, pneumococcal, and meningococcal
cases. These 3 pathogens represented >90% of cases for children
after the first 2 months of life, although their importance was
small for the youngest infants (<2 months of age). On the other
hand, the gain by introducing latex agglutination for the overall
meningitis diagnosis was low when both culture and Gram
stain were in use and optimized; only 2 cases were positive by
latex agglutination and were negative by both culture and Gram
staining. On the other hand, Gram staining that requires a
medium level of expertise and laboratory facilities would have
identified 63% of the ABM cases. Other nonetiologic methods
easily applicable in poorly equipped laboratories may be useful
to identify probable ABM. For instance, combining the assess-
ment of CSF appearance and leukocyte count achieved a rea-
sonable level of sensitivity (87%). However, these methods pro-
vide no information on the likely etiologic agent, which is
important for assessing appropriate public health interventions.
Therefore, there remains an urgent need to strengthen etiologic
specific diagnostic capability for ABM [12].

Prevalence of malaria parasitemia was common among chil-
dren who had CSF collected. Although malaria parasites were
less prevalent among children with ABM, compared with other
children who had a CSF sample collected, it is important to
underline that 25% of patients with confirmed meningitis
had concurrent parasitemia. Therefore, detecting parasitemia
should not delay performing an LP and bacterial diagnostic
assays among children with clinical suspicion of meningitis.
Children admitted to hospitals in Africa have a high risk of
bacterial infection, justifying immediate treatment with anti-
biotics. The use of antibiotics is empirical and many times relies
on surveillance data from other settings. Our data show that
the susceptibility of bacterial pathogens that cause meningitis
to antibiotics that are commonly used and available in Mo-
zambique is low. As we showed in other reports and similar
to other neighbor countries, the pathogen most affected by
resistance was Hib [22, 27]. Both chloramphenicol and am-
picillin would still be useful for children >2 years of age because
Hib meningitis is concentrated in children <2 years of age.
Other African countries with similar concerns about nonsus-
sceptibility of bacterial isolates for common antibiotics [28, 29]
have adapted their guidelines to try to improve antibiotic cov-
ergie. So far, we have not detected resistances to ceftriaxone
among our isolates (data not shown). Adjustment of such
guidelines must take into account national budget limitations.

In addition to the lack of individual data on HIV status
among patients and the intrinsic sensitivity issues of bacteri-
ologic surveillance, other study limitations should be consid-
ered. On one hand, burden data might be significantly under-
estimated because access to health care facilities in rural Africa
is poor, which leads to many patients dying before reaching
the hospital. Sequelae data were not included as an outcome.
More important, data presented herein represent only 1 year
of hospital surveillance and, therefore, could be affected by
intrinsic annual variations of disease occurrence for specific
pathogens. Our surveillance is being extended for the next few
years.

Still, our results give a comprehensive picture of the con-
sequences of ABM in rural settings in Africa: a high disease
burden and a high mortality rate, children arriving at the hos-
pital in a critical condition, mortality concentrated in the first
hours after hospital admission, and a high level of antibiotic
resistance with no clear practical alternatives. Under these cir-
cumstances, the introduction of suitable conjugate vaccines,
such as Hib and pneumococcus, is critical to achieve the Mil-
leennium Development Goal of improving child survival. Studies
measuring population-based minimum incidence rates are es-
ternal to advocate for the introduction of these existing vac-
cines in sub-Saharan Africa. Mozambique has recently received
GAVI Alliance approval for the introduction in 2009 of the Hib
vaccine into the national Expanded Program on Immunization
scheme, along with diphtheria and tetanus toxoids and pertussis
and hepatitis B vaccines. Incorporating conjugate vaccines for
pneumococcus and the next generation of meningococcal vac-
cines, which should include serotype W135, should be consid-
ered in the future.

Acknowledgments

We thank Mariano Sitaúbe of the bacteriology laboratory of the Centro
de Investigação em Saúde da Manhiça (CISM), for culturing and identifying
bacterial isolates, and Madalena Ripinga, for collecting samples and com-
pleting questionnaires. We also thank other colleagues of the Manhiça
District Hospital and the CISM who collected or processed samples and completed questionnaires.

**Financial support.** CISM core funding is provided by the Spanish Agency for International Cooperation (AECl-Ministry of Foreign Affairs, Spain). The meningitis project was sponsored by the PneumoADIP at Johns Hopkins University. The PneumoADIP is funded in full by the GAVI Alliance and The Vaccine Fund.

**Supplement sponsorship.** This article was published as part of a supplement entitled “Coordinated Surveillance and Detection of Pneumococcal and Hib Disease in Developing Countries,” sponsored by the GAVI Alliance’s PneumoADIP of Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland.

**Potential conflicts of interest.** All authors: no conflicts.

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