Meningococcal meningitis, caused by the bacterium *Neisseria meningitidis*, is a public health priority in the sub-Saharan region of Africa known as the ‘meningitis belt’. In this area, meningococcal meningitis is endemo-epidemic, with tens of thousands of cases and thousands of deaths reported during epidemic years. The strategy currently recommended by the World Health Organization (WHO) to control meningococcal meningitis epidemics is based upon therapeutic case management and mass vaccination with polysaccharide vaccine at the beginning of an epidemic. As seasonal variations in the number of meningitis cases are observed in the meningitis belt with an annual increase at the end of the dry season (December–April), it is necessary to identify a threshold which is generally exceeded at the beginning of an epidemic but not during endemic cycles.

Based on meningitis case data from Burkina Faso (1979–1984), Moore *et al.* proposed the use of a weekly meningitis incidence rate of 15 cases per 100 000 inhabitants, averaged over 2 consecutive weeks, as a threshold to predict the subsequent occurrence of a meningitis epidemic and a lower ‘alert’ threshold of 5 cases per 100 000 inhabitants per week in districts contiguous to areas already declared epidemic. Experience has shown, however, that under field conditions, the time required to decide upon and organize mass vaccination campaigns may delay interventions, resulting in a limited overall impact.

The northern part of Togo, at the southern edge of the African meningitis belt, suffered a major group A meningococcal meningitis epidemic in 1996–1997 as a wave of epidemics swept through the region. This study, with data from northern Togo, explores the effectiveness of different weekly incidence thresholds for detection and control of meningococcal meningitis epidemics in northern Togo.
assesses the validity of the currently recommended threshold and studies other thresholds that might allow an earlier detection of meningococcal meningitis epidemics and thereby increase the impact of reactive mass vaccination campaigns.

**Methods**

**Meningitis incidence**
The study took place in the Région des Savanes, in northern Togo, which is divided into four préfectures (districts)—Tone, Oti, Kpendjal and Tandjoaré (Figure 1).

Clinic logbooks of health-care facilities of the study area were reviewed for cases of meningitis which occurred between 1 August 1990 and 31 July 1997. A case was defined as a person diagnosed with meningitis as written in the clinic logbook by the consulting physician or nurse. The date of presentation to the health centre was considered to be the date of onset. Age, sex and residence were recorded for each case. Population figures were determined for each year 1990–1997 from a 1996 census conducted in the Région des Savanes (source: Direction Régionale de la Santé des Savanes) and retrospectively adjusted for a 3% annual growth rate.10

Meningitis incidence rates were calculated for each district by dividing the number of new cases occurring in the area per unit of time (week or year) by the annually adjusted population of the area. For this study, the year span was defined as 1 August through 31 July of the following year in order to include a complete meningitis season (December–May).

![Figure 1](image)
Definition of an epidemic
An epidemic year was retrospectively defined in a district by a yearly meningitis incidence of \( \geq 100 \) cases per 100 000 inhabitants.\(^3\) The peak of the epidemic was defined as the week with the maximum weekly incidence. Threshold analyses were repeated for other hypothetical definitions of an epidemic (70, 80 and 90 cases/100 000 inhabitants/year).

Threshold study
Weekly meningitis incidences between 2 and 25 cases/100 000 inhabitants were investigated as potential thresholds for predicting the emergence of an epidemic during the corresponding year. The WHO recommended threshold of 15 cases/100 000 inhabitants averaged over 2 consecutive weeks was also tested.

Estimates of the sensitivity, specificity, positive predictive value and negative predictive value of these thresholds were calculated by determining which district crossed, at least once, the given threshold and experienced an epidemic during the same year. The sensitivity is the probability that the threshold was crossed during an epidemic year; the specificity is the probability that the threshold was not crossed during a non-epidemic year; the positive predictive value is the probability that there was an epidemic if the threshold had been crossed at least once; the negative predictive value is the probability that there was no epidemic if the threshold had never been crossed during a given year.

The time available for intervention was also studied for the various thresholds. It was calculated as the number of weeks elapsed between the first week the threshold was crossed and the week of the epidemic peak. Thresholds were analysed for their ability to predict the occurrence of an epidemic within the year during which they were crossed.

Impact study
The number of cases which may have been prevented by a mass vaccination campaign during the 1996–1997 epidemic in the Région des Savanes was estimated using a method described by Pinner et al.\(^1\) The number of meningitis cases which would have occurred in the absence of a vaccination campaign was estimated on the basis of the weekly meningitis incidence, the meningitis vaccination coverage obtained during this epidemic and the vaccine effectiveness. The number of cases potentially prevented was then estimated through different scenarios, depending on the threshold and vaccination strategy used. This method assumes that vaccination does not interfere with meningococcal carriage or transmission,\(^7,11\) an assumption that seems valid for group A meningococcal polysaccharide vaccines in African populations.\(^12\)

Vaccine coverage for the study area was assumed to be 0% prior to the 1996–1997 epidemic and was calculated after the epidemic by dividing the number of doses administered to individuals in each district during this epidemic by the 1997 population of the district. Vaccine coverage was stratified according to age (0–14 and \( \geq 15 \) years). Vaccine efficacy was assumed to be 85%,\(^15\) and time for seroconversion was set at one week after vaccination. After the threshold was crossed, a theoretical time-frame of a week was initially allocated for gathering and analysing data, ordering vaccines, organizing the campaigns and achieving vaccination objectives. The influence of delay in the initiation of vaccination on the number of cases which may have been prevented was studied with a sensitivity analysis allowing the time to achieve vaccination objectives to vary from 2 to 8 weeks. Vaccine coverage was either the actual coverage achieved by the mass campaign in Togo or a theoretical coverage of 85% of the entire population.

Results
Descriptive epidemiology
The 1997 population of the study area was estimated to be 550 524 people (82 708 in Tandjoaré, 104 511 in Kpendjal, 127 567 in Oti and 235 738 in Tone). Mean population density is 63 inhabitants/km\(^2\). From August 1990 through July 1997, 5562 meningitis cases were counted in the clinic logbooks of the health facilities, among which 4952 (89%) reported a residence in the Région des Savanes. The weekly meningitis incidence in the region is presented in Figure 2.

Annual meningitis incidence for each district is presented in Table 1. From 1990 to 1995, no epidemic was noted. In non-epidemic years, the incidence ranged from 4 to 86 cases/100 000 inhabitants/year with a mean of 35 and a median of 27. An epidemic occurred in early 1996 in Tone district with an annual incidence of 168 cases/100 000 inhabitants. During this epidemic, the maximum weekly incidence was 14.9 cases/100 000 inhabitants. In early 1997, another epidemic occurred in all four districts of the Région des Savanes, accounting for 3590 cases between 2 December 1996 and 1 June 1997. Overall annual incidence was 652 cases/100 000 inhabitants, varying from 154 in Oti district to 1135 in Tone. The epidemic threshold of 15 cases/100 000 inhabitants averaged over 2 weeks was exceeded in Tone during the first week of 1997 and the alert threshold of 5 cases/100 000 inhabitants/week was exceeded in Kpendjal during week 2, in Oti during week 5 and in Tandjoaré during week 6.

Performance of epidemic thresholds
Crossing a threshold of 15 cases/100 000 inhabitants/week averaged over 2 consecutive weeks yielded both specificity and positive predictive value of 100% for the prediction of an epidemic (\( \geq 100 \) cases per 100 000 inhabitants) in a district during a given year. Sensitivity was 80% and negative predictive value was 96% (Table 2). Results were exactly the same when testing a threshold of 15 cases/100 000 inhabitants/week calculated over one week only.

Thresholds between 7 and 10 cases/100 000 inhabitants/week calculated over one week in a district resulted in sensitivity, specificity, positive and negative predictive values of 100%.

Thresholds below 7 cases/100 000 inhabitants/week resulted in sensitivity and negative predictive value of 100%, but low to medium specificity and positive predictive value, whereas thresholds over 15 cases/100 000 inhabitants/week resulted in lower sensitivity and negative predictive value, but specificity and positive predictive value of 100%.

Results were identical for an epidemic defined as \( \geq 90 \) cases/100 000 inhabitants/year. Due to the high endemic rates of meningitis in Tone district in all years (Table 1), use of lower annual incidences to define an epidemic year resulted in lower sensitivity for all thresholds tested, as years are declared ‘epidemic’ in spite of low weekly incidences.
Time available for intervention

The mean time elapsed between the threshold and the peak of the epidemic ranged from 2.3 weeks, after surpassing 25 cases/100 000 inhabitants/week, to a maximum of 8.6 weeks with a threshold of 2 cases/100 000 inhabitants in one week. The threshold of 10 cases/100 000 inhabitants/week left 4.2 weeks for intervention before the epidemic peak whereas 7 cases/100 000 inhabitants/week left 5.4 weeks on average (Table 3).

Source: clinic logbooks from the Région des Savanes.

Figure 2  Meningitis weekly incidence in the Région des Savanes (a), and in each district (b, c, d, e), northern Togo, 1990–1997

In the four districts (b, c, d, e) the incidence is truncated at 20 cases/100 000 inhabitants/week.
The impact of the 1997 mass vaccination campaign

A serogroup A meningococcal meningitis epidemic occurred in the Région des Savanes from December 1996 through May 1997, accounting for 3590 cases. Mass vaccination campaigns were organized and a total of 346,469 doses of vaccine were administered in the four districts in February 1997. Vaccine coverage in the four districts ranged from 58% to 69%, yielding a weighted average administrative coverage for the region of 63%. The 1996–1997 epidemic curve and a projection of the curve, had there been no vaccination during this epidemic, are presented in Figure 3. According to the model, 49% (3419) of the projected cases were prevented by the vaccination campaign. If the WHO recommendations had been strictly followed (vaccination following a 2-week average of 15 cases/100,000 inhabitants/week for the first district and 5 cases/100,000 inhabitants/week for subsequent districts), 65% (4549) of the cases could have been prevented if 85% vaccine coverage had been achieved by the end of the second week of 1997 in Tone, the third week in Kpendjal, the sixth week in Oti and the seventh week in Tandjoaré district.

The effect of time needed to achieve vaccination on the proportion of cases prevented is presented in Figure 4. For each week of delay, 3% to 8% fewer cases could be prevented and for each drop in vaccine coverage of 10%, approximately 5% fewer cases are prevented. In order to prevent a minimum of 60% of cases with an 85% vaccine coverage in the Région des Savanes, vaccination should be achieved within 3.5 weeks after the threshold of 7 cases/100,000 inhabitants/week is crossed or within 2.5 weeks with WHO guidelines. To achieve the same impact, the lower threshold would have provided one extra week to plan a response.

### Table 1: Annual meningitis incidence, Région des Savanes, northern Togo, 1990–1997

<table>
<thead>
<tr>
<th>Year</th>
<th>Kpendjal</th>
<th>Oti</th>
<th>Tandjoaré</th>
<th>Tone</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990–1991</td>
<td>15</td>
<td>8</td>
<td>26</td>
<td>58</td>
</tr>
<tr>
<td>1991–1992</td>
<td>22</td>
<td>7</td>
<td>29</td>
<td>70</td>
</tr>
<tr>
<td>1992–1993</td>
<td>23</td>
<td>4</td>
<td>50</td>
<td>72</td>
</tr>
<tr>
<td>1993–1994</td>
<td>27</td>
<td>9</td>
<td>28</td>
<td>81</td>
</tr>
<tr>
<td>1994–1995</td>
<td>23</td>
<td>17</td>
<td>51</td>
<td>86</td>
</tr>
<tr>
<td>1995–1996</td>
<td>33</td>
<td>20</td>
<td>54</td>
<td>168</td>
</tr>
<tr>
<td>1996–1997</td>
<td>347</td>
<td>154</td>
<td>197</td>
<td>1135</td>
</tr>
</tbody>
</table>

Source: clinic logbooks from the Région des Savanes.

### Table 2: Test characteristics of weekly meningitis incidence as predictor of meningitis epidemics, northern Togo, 1990–1997

<table>
<thead>
<tr>
<th>Epidemic threshold (cases/100,000 inhabitants/week)</th>
<th>No. of times the threshold was crossed in a district</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Positive predictive value (95% CI)</th>
<th>Negative predictive value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>24</td>
<td>100 (46.3, 100.0)</td>
<td>17 (5.7, 39.5)</td>
<td>21 (7.9, 42.7)</td>
<td>100 (39.6, 100.0)</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>100 (46.3, 100.0)</td>
<td>87 (65.5, 96.6)</td>
<td>62 (25.9, 89.8)</td>
<td>100 (80.0, 100.0)</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>100 (46.3, 100.0)</td>
<td>100 (82.2, 100.0)</td>
<td>100 (46.3, 100.0)</td>
<td>100 (82.2, 100.0)</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>100 (46.3, 100.0)</td>
<td>100 (82.2, 100.0)</td>
<td>100 (46.3, 100.0)</td>
<td>100 (82.2, 100.0)</td>
</tr>
<tr>
<td>15b</td>
<td>4</td>
<td>80 (29.9, 98.9)</td>
<td>100 (82.2, 100.0)</td>
<td>100 (39.6, 100.0)</td>
<td>96 (76.9, 99.8)</td>
</tr>
<tr>
<td>20</td>
<td>4</td>
<td>80 (29.9, 98.9)</td>
<td>100 (82.2, 100.0)</td>
<td>100 (39.6, 100.0)</td>
<td>96 (76.9, 99.8)</td>
</tr>
<tr>
<td>25</td>
<td>3</td>
<td>60 (17.0, 92.7)</td>
<td>100 (82.2, 100.0)</td>
<td>100 (31.0, 100.0)</td>
<td>92 (72.5, 98.6)</td>
</tr>
</tbody>
</table>

* 28 units of observation: 4 districts × 7 years of observation per district.
* Results are the same for an incidence of 15 cases/100,000 inhabitants/week during one week or averaged over 2 consecutive weeks, and when the 2-week average is used for the first district in combination with the alert threshold of 5 cases/100,000 inhabitants/week for the remaining districts.

### Table 3: Time elapsed between threshold and peak during the 1996–1997 meningitis epidemic, Région des Savanes, northern Togo

<table>
<thead>
<tr>
<th>Epidemic threshold (cases/100,000 inhabitants/week)</th>
<th>Average time between threshold and epidemic peak (weeks)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>8.6</td>
<td>(5.0, 12.2)</td>
</tr>
<tr>
<td>5</td>
<td>5.4</td>
<td>(3.3, 7.5)</td>
</tr>
<tr>
<td>7</td>
<td>5.4</td>
<td>(3.3, 7.5)</td>
</tr>
<tr>
<td>10</td>
<td>4.2</td>
<td>(1.2, 7.2)</td>
</tr>
<tr>
<td>15</td>
<td>4.0</td>
<td>(0.1, 7.9)</td>
</tr>
<tr>
<td>15b</td>
<td>3.0</td>
<td>(–0.9, 6.9)</td>
</tr>
<tr>
<td>20</td>
<td>2.5</td>
<td>(–1.3, 6.3)</td>
</tr>
<tr>
<td>25</td>
<td>2.3</td>
<td>(–1.7, 6.2)</td>
</tr>
</tbody>
</table>

* Confidence interval calculated with the t distribution.
* Results are the same for an incidence of 15 cases/100,000 inhabitants/week during one week or averaged over 2 consecutive weeks.
Discussion

In the management of meningococcal meningitis epidemics, time is of the essence. It is imperative to detect an impending epidemic and institute control measures as early as possible if large numbers of cases and deaths are to be prevented. In Togo, the 1997 meningitis epidemic spread rapidly. This study shows that, following detection of an epidemic, the time available for intervention and the vaccination coverage achieved are critical to the success of the reactive vaccination strategy recommended for Africa by the WHO. Our findings confirm the validity of the threshold approach but questions are raised as to whether the currently recommended threshold is the most appropriate one.

Meningitis incidence thresholds of 7 and 10 cases/100 000 inhabitants/week both achieved 100% sensitivity and specificity, accurately predicting all epidemics in the four districts of northern Togo over the period 1990–1997. In contrast, the threshold of 15 cases/100 000 inhabitants/week, averaged over 2 consecutive weeks, predicted meningitis epidemics with excellent specificity and positive predictive value but failed to detect one epidemic in Tone district in 1995–1996 (population >225 000), resulting in a lower sensitivity and negative predictive value, as previously shown. This may serve to illustrate the lower sensitivity of this threshold in larger populations. In this study, we chose to work with the actual district population figures, rather than dividing them arbitrarily into smaller units, in order to test thresholds in the real-life situations faced by district health officers.

Lower thresholds also allowed earlier detection of epidemics. In this study, thresholds of 7 and 10 cases/100 000 inhabitants/week offer on average 2.4 and 1.2 weeks, respectively, more time to achieve vaccination coverage than current recommendations. The time elapsed between epidemic threshold and peak is critical in a strategy based on reactive mass vaccination. The reactive strategy must allow time to collect and analyse field data (usually through a surveillance system), decide on mass vaccination, order the vaccines, and organize and implement the vaccination campaign. Our baseline model allowed just one week for these activities but field experience shows that it takes at least 2–3 weeks to mount such a response. In our study, each week of delay in completing the vaccination campaign resulted in a 3–8% decrease in the number of cases prevented, similar to what was found using meningitis data from Ghana. Therefore any strategy that increases the time available for a response should be seriously considered. Woods et al. have demonstrated that knowledge of meningitis epidemics in neighbouring countries could provide an earlier alert. Although the Région des Savanes borders Bénin, Burkina Faso and Ghana, data from these countries were not available to us at the time of the study.

The potential impact of reactive mass vaccination is inherently limited by vaccination coverage achieved, as this study illustrates, and by the efficacy of the polysaccharide vaccine. In the model presented here, even with a highly sensitive threshold and ‘ideal’ conditions where 85% of the population can be vaccinated within one week of crossing the threshold, a maximum of 65% of the meningitis cases could have been prevented during the 1996–1997 epidemic in Togo. In reality, an estimated 49% or 3419 cases of meningitis were prevented, a figure which still fully justifies the vaccination campaign.
A large amount of data collected, the number of observations representative of the entire region. As characteristics of men-
at the southern edge of the meningitis belt and may not be the estimates of performance characteristics. The small data set available for the threshold study was 28 district-years (four
Preventive vaccination would be a suitable alternative with a
studies are needed in other sub-Saharan Africa countries. In addition, study of thresholds at a sub-district level may provide
further useful information. Recommendations regarding detection of meningitis outbreaks in small populations using absolute numbers of cases (e.g. doubling of number of cases over 3 weeks or comparison with previous years) could be tested and validated.

At the present time, the reactive vaccination strategy is the only one possible for most regions of the meningitis belt due to limited resources. Preventive mass vaccination with the polysaccharide vaccine has been discussed as an alternative but this approach would suffer from the same flaws as the reactive strategy, i.e. the absence of herd immunity and a moderate vaccine efficacy. In addition, the short duration of protection offered by the polysaccharide vaccine and the unpredictability of meningitis epidemics has so far limited its potential usefulness. Where resources permit, a preventive strategy could be considered for areas with very high endemic rates of disease. Preventive vaccination would be a suitable alternative with a vaccine inducing long-term immunity in children and herd immunity in the populations vaccinated. Meningococcal conjugate vaccines currently under development seem to have these characteristics and represent the best hope for the improvement of meningitis epidemic control in Africa, provided that they are affordable for countries with limited resources.

In the meantime, efforts must continue to improve the impact of mass vaccination in the face of devastating meningitis epidemics. Avenues to pursue include improving surveillance systems and encouraging international collaboration. Use of lower, more sensitive, epidemic thresholds should be preferred over specific ones to enable quicker action and the time required to mount an appropriate and comprehensive response should be accounted for. New recommendations concerning meningitis epidemic thresholds have been drafted, taking into consideration these and other important elements.

Acknowledgements

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References


