Response Strategies against Meningitis Epidemics after Elimination of Serogroup A Meningococci, Niger

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To inform epidemic response strategies for the African meningitis belt after a meningococcal serogroup A conjugate vaccine was introduced in 2010, we compared the effectiveness and efficiency of meningitis surveillance and vaccine response strategies at district and health area levels using various thresholds of weekly incidence rates. We analyzed reports of suspected cases from 3 regions in Niger during 2002–2012 (154,392 health area weeks), simulating elimination of serogroup A meningitis by excluding health area years with identification of such cases. Effectiveness was highest for health area surveillance and district vaccination (58–366 cases; thresholds 7–20 cases/100,000 doses), whereas efficiency was optimized with health area vaccination (5.6–7.7 cases/100,000 doses). District-level intervention prevented ≤6 cases (0.2 cases/100,000 doses). Reducing the delay between epidemic signal and vaccine protection by 2 weeks doubled efficiency. Subdistrict surveillance and response might be most appropriate for meningitis epidemic response after elimination of serogroup A meningitis.

For several decades, epidemic meningitis has been a major health problem in the African meningitis belt. Neisseria meningitidis serogroup A (NmA) has been responsible for most localized epidemics or epidemic waves, and other meningococcal serogroups occasionally caused epidemics (1,2). After the introduction of an NmA conjugate vaccine (PsA-TT, MenAfrivac; Serum Institute of India Ltd., Hadapsar, Pune, India), implemented since 2010 in mass campaigns focused on persons 1–29 years of age, no epidemics caused by NmA have occurred in countries where the vaccine is administered (i.e., vaccinated countries). Seasonal hyperendemicity continues to occur during the dry season because of meningococci and pneumococci in similar proportions (3), and NmA has been identified only exceptionally (4,5). So far, epidemic control measures have consisted of reactive vaccination campaigns in epidemic districts by using serogroup A/C or A/C/W polysaccharide vaccines combined with adapted treatment protocols. To detect epidemics, national routine surveillance of suspected cases of acute bacterial meningitis has been conducted in all meningitis belt countries according to World Health Organization (WHO) guidelines (1), although the recommendation of splitting large districts (>100,000 inhabitants) into subdistricts is not always followed. Districts notifying weekly incidences of 5 cases/100,000 persons were considered in alert, and those notifying weekly incidences of 15 cases/100,000 persons were considered in epidemic (6); however, specific conditions enabled declaration of an epidemic at a threshold of 10 cases/100,000 persons.

Since PsA-TT was introduced in 2010, NmA incidence has been substantially lower than historical levels, and no replacement by other serogroups has been observed (7). Consequently, the overall incidence of suspected meningitis cases has declined in all vaccinated countries, and established surveillance and vaccination strategies might no longer be appropriate. Epidemic detection and response remains important because serogroups W and X have epidemic potential (1,2,4,8,9). A polysaccharide vaccine is available against N. meningitidis serogroup W (NmW); vaccines for serogroup X (NmX) are under development. NmA epidemics might continue to occur, requiring mass vaccination campaigns with PsA-TT.

One approach to adapting epidemic response strategies to the changing epidemiology is to lower the weekly incidence thresholds to <10 cases/100,000 persons, which would increase the risk for an increased number of false alerts in small districts. Another approach is to analyze surveillance data at a finer spatial scale than district level. As in Burkina Faso (2,10) and Niger (11), epidemics of any serogroup usually are highly localized in few neighboring health centers, whereas most health centers in the district in question remain (hyper-)endemic. District-level incidences are therefore diluted and may hide epidemic activity. Consequently, surveillance at the health center...
level could detect epidemics earlier and enable targeting of reactive vaccination, making the overall strategy more effective and efficient. Early epidemic detection through surveillance at the health center level could increase the effectiveness and efficiency of response strategies, particularly in the anticipated situation of eliminated NmA meningitis and overall reduced meningitis incidence.

Therefore, during 2002–2012, we evaluated the effectiveness and efficiency of surveillance and vaccine response strategies in Niger using various epidemic thresholds and comparing health area and district intervention. Our analysis was based on surveillance data of suspected and confirmed cases and considered 2 scenarios: the historical situation before PsA-TT introduction (PsA-TT was introduced in Niger in 3 phases: the first in August 2010, the second in November 2010, and the third in October 2011) and a simulation of NmA elimination.

Methods

Databases

The surveillance data used for this analysis were collected during 2002–2012 in Niger. For national routine surveillance, all health centers in Niger report suspected meningitis case counts each week to health district administration, where data are aggregated to a district case count and forwarded to the national level for reporting (online Technical Appendix Figure 1, http://wwwnc.cdc.gov/EID/article/21/8/14-1316-Techapp1.pdf) (12,13). To analyze response strategies at the health area level, we retrieved the original health center counts of suspected meningitis cases from health district administrations and compiled them in a new database. A health area is a geographic area that encompasses all villages served by the same health center, which is an exclusive association. We assessed the completeness of this health area database of suspected cases by comparing the resulting weekly district case counts with those in the national surveillance reports. On the basis of the completeness of this health area–level database (online Technical Appendix), we selected 3 regions—Tahoua, Tillabery, and Dosso—for further analysis (Figure 1). Together, these regions had 7,648,150 inhabitants during 2012 (48% of Niger’s population), 19 health districts (47%), and 373 health areas (51%). Niger used Haemophilus influenzae type b vaccine since 2006 but uses no pneumococcal vaccine in the widened vaccine program.

Data on confirmed cases came from countrywide surveillance based on PCR (11). For this surveillance, we requested that all cerebrospinal fluid samples from persons with suspected meningitis in the health centers be sent to the Centre de Recherche Médicale et Sanitaire (Niamey, Niger) for testing by multiplex PCR (14). After merging with the study database of suspected cases, we obtained the combined information about suspected and confirmed meningococcal case counts for every health area and week.

Using these data, we prepared a database simulating the situation after NmA elimination by excluding all health area years with at least 1 NmA case or without any laboratory information. A health area year corresponded to a health area that appears in the annual reporting file, so that in our analysis health area years represented all the health areas that appear in annual reporting files during the study period.

![Figure 1. Location of the study area, Niger. This area comprises the 379 health areas in 3 regions (Tahoua, Tillabery, and Dosso).](image-url)
period. Only 1 NmA case was identified in the study region after PsA-TT introduction. To validate the representativeness of this database for meningitis epidemiology after NmA elimination, we compared the distribution of annual incidences between health areas before and after PsA-TT introduction (Figure 2). To prepare the database simulating the situation after NmA elimination, we took into account the exact week of district vaccination, which was conducted in 3 phases: September 2010, December 2010, and November 2011. The Niger national ethics committee approved this research (no. 014/2012/CCNE).

Statistical Analysis
The Institut National de la Statistique provided the number of inhabitants in each village according to the 2001 national census. We aggregated the villages’ populations at the health area level and applied a mean annual growth rate of 3.3% (15). We calculated weekly incidence rates (WIR) as the weekly number of cases per 100,000 inhabitants and annual incidence (AI) as the number of cases per 100,000 inhabitants during an epidemiologic year. To compile cases belonging to the same meningitis season (approximately December–May), we defined an epidemiologic year as July 1 of calendar year n–1 through June 30 of calendar year n.

We evaluated the effectiveness and efficiency of surveillance and vaccine response strategies by calculating the number of potentially vaccine-preventable cases and the number of vaccine doses needed per epidemic. These calculations were repeated with the database including NmA to determine whether the situation differed from that simulating NmA elimination.

Using receiver-operator curves as previously described (10), we chose candidate epidemic thresholds to optimize the detection of annual incidences that are above the 95th or 97.5th percentiles of health area annual incidences in the databases (online Technical Appendix Figure 3). An epidemic was defined as weekly incidence rate in a health area that exceeded the corresponding threshold for at least 1 week.

We evaluated 3 strategies: 1) surveillance (including data analysis) and vaccination at health area level; 2) surveillance at health area level and vaccination of the entire district; and 3) surveillance and vaccination at district level. We approximated the number of potentially vaccine-preventable cases (Nvp) as Nvp = N3w × PNm × VC × VE, where N3w is the number of suspected cases in the surveyed health area or district from 3 weeks after the threshold is exceeded (assuming that campaign implementation and effective protection from vaccine antibody would take at least 3 weeks after signal detection); PNm is the percentage of suspected cases confirmed as Nm, estimated as 50% in both epidemic and endemic periods, on the basis of previous surveillance reports (16); VC is the expected vaccine coverage during a mass campaign in response to an outbreak, estimated at 80% (5); and VE is the expected vaccine effectiveness, estimated at 80%. Because no data for NmW and future NmX vaccines (polysaccharide or conjugate) were available to inform this assumption, we used the available vaccine effectiveness data of NmA polysaccharide vaccine (17) and NmW and NmA polysaccharide vaccine combined (18). This assumption might be conservative, in particular because conjugate vaccines will be used for epidemic response against non-A serogroups (19). We calculated the number of vaccine doses needed per epidemic as the age group 1–29 years of the total population, which was 74% for the study regions according to census data (20); and the total number of preventable cases

![Figure 2. Annual incidences of suspected meningitis per 100,000 inhabitants in health areas before and after introduction of PsA-TT (in 2010) in a database simulating elimination of serogroup A meningococci. Tahoua, Tillabery, and Dosso regions, Niger, 2002–2012. The period before PsA-TT (2002–October 2011, last phase of vaccination during November 2011) (white bars) comprises 433 health area years. The period after PsA-TT (October 2010–December 2012, first phase of vaccination during September 2010) (gray bars) comprises 98 health area years. Excluded were health area years during which at least 1 serogroup A case was detected or for which no serogroup information was available. The number of health areas in this database varied by year from 2 (2002) and 10 (2003) to 126 (2011). Each circle corresponds to annual incidence in a health area. Dark lines are parts of the boxplot, as follows: for 2003 (complete boxplot), the first line corresponds to the minimal annual incidence of health area, the second line corresponds to the limit of the first quartile, and the third (darkest) corresponds to the median. The space between the second and third lines corresponds to the second quartile. The fourth line is the limit of the third quartile and the last line is the limit of the fourth quartile of annual health area incidence. PsA-TT, serogroup A meningococcal conjugate vaccine (MenAfrivac [Serum Institute of India Ltd., Hadapsar, Pune, India]).]
in the population of interest for 100,000 vaccine doses. To evaluate the sensitivity of our estimates to a longer delay from signal detection to effective vaccine protection, we varied this delay from 3 weeks to 6 weeks. We used the rate ratio test to compare annual incidences assuming that they follow a Poisson distribution.

All analyses were performed in R software version 2.15.2 (http://www.R-project.org). Maps were created with QGIS software version 1.8.0 (http://qgis.osgeo.org).

Results

Descriptive Epidemiology

Our study comprised 154,392 weekly health area reports. Among the reports were 14,921 suspected cases, of which 13,620 (91.3%) occurred during calendar weeks 1–20, corresponding to the meningitis season (online Technical Appendix Figure 2). At district level, median AI was 10.5 cases per 100,000 inhabitants; WIR peak was a median of 2 (maximum 50) cases per 100,000 inhabitants, with a maximum of 1,384 cases per 100,000 inhabitants during most years, and maximum incidences were beyond the 95th and 97.5th percentiles were, at health area level, WIR of 20 and 15 cases per 100,000 inhabitants, respectively, and at district level, WIR of 4 per 100,000, for both percentiles (online Technical Appendix Figures 3, 4).

The total number of epidemics requiring a response during the 11-year period in the study area varied from 3 to 15 for district surveillance and from 49 to 233 for health area surveillance. The number of total vaccine-preventable cases varied from 0 to 6 (thresholds 2–7/100,000) with district surveillance and vaccination, from 27 to 213 cases (thresholds 7–20/100,000) with health area surveillance combined with district-level vaccination (thresholds 7–20/100,000) (Table 1). Although the latter strategy was most effective, it required the largest number of vaccine doses (8.7–25.7 million, depending on the threshold), whereas the 2 other strategies consumed a similar number of doses (≈0.5–3 million). Efficiency was lowest for district surveillance (≤0.24 vaccine-preventable cases/100,000 doses) and highest for health area surveillance combined with district-level vaccination (7.7 cases/100,000 doses). Overall, the difference in effectiveness or efficiency for different geographic levels of intervention was greater than for any

| Table 1. Comparison of estimated vaccine-preventable meningitis cases using different strategies of surveillance and meningococcal vaccine response in a situation simulating elimination of meningococcal serogroup A, Tahoua, Tillabery and Dosso regions, Niger, 2002–2012* |
|-----------------|--------------|-----------------|-----------------|-----------------|-----------------|
| **Strategies**  | **Total no.** | **Population**  | **Vaccine doses** | **Vaccine-preventable cases‡** |
| **surveillance-**| **epidemic**  | **affected by**  | **in persons 1–29 y†** | **No.** | **Per 100,000 cases** |
| **vaccination** | **signals**   | **signal**       | **Total Median** | **Total Median Range** |
| Health area-     |              |                 |                 |                  |
| health area      | 7            | 233             | 3,741,116       | 2,768,426 9,721 | 213 0.32 7.70 2.31 0–178.35 |
| 10              | 165          | 2,453,831       | 1,815,835 9,346 | 119 0.32 6.54 2.38 0–178.35 |
| 15              | 80           | 1,142,888       | 845,757 8,817  | 53 0.00 6.32 0.00 0–178.35 |
| 20              | 49           | 641,378         | 474,620 8,272  | 27 0.00 5.60 0.00 0–41.02 |
| Health area-     |              |                 |                 |                  |
| district        | 7            | 233             | 35,297,443      | 25,866,453 258,625 | 366 0.96 1.42 0.44 0–14.38 |
| 10              | 165          | 31,304,108      | 23,165,040 259,647 | 246 2.80 1.06 0.27 0–13.23 |
| 15              | 80           | 17,062,861      | 12,628,517 284,407 | 126 0.96 1.00 0.30 0–7.87 |
| 20              | 49           | 11,757,953      | 8,700,885 287,661 | 58 0.80 0.66 0.23 0–3.36 |
| District-        |              |                 |                 |                  |
| district        | 2            | 15              | 4,053,961       | 2,999,931 216,403 | 6 0.00 0.20 0.00 0–1.56 |
| 4               | 8            | 2,710,118       | 2,005,487 269,749 | 5 0.00 0.24 0.00 0–1.56 |
| 7               | 3            | 934,406         | 692,940 250,957 | 0 0.00 0.00 0.00 0 |

*Weekly incidence rate thresholds (cases/100,000 inhabitants) were selected on the basis of best performance (sensitivity and specificity) to identify years of high annual incidence (531 health area years). The 3 regions had 7.5 million inhabitants.

†Case-patients <2 y of age were not excluded.

‡Median, across all health areas or districts with epidemic signal; total for entire study area of 3 regions (population 7,648,128); mean: mean per signal (health area or district level).
PsA-TT, a protein-conjugate vaccine, appears to have epidemiology beyond outbreak control. By contrast, evidence has been found of a major effect on meningococcal pneumococcus including occasionally for prevention strategies, no evidence has been used in the meningitis belt for several decades, and a minimum of individual events requiring a response. In light of these data, we recommend that more countries explore the introduction, the district-level strategy yielded good efficiency than with threshold; health area surveillance and vaccination prevented 21–26 cases per 100,000 doses, whereas the latter appeared more efficient relative to the number of vaccine doses required. An intermediate strategy might involve ring vaccination of health areas neighboring the epidemic area. In any case, because vaccine campaigns would be launched in small health areas after as few as 2 or 3 cases, the choice of exact strategy will need to account for country-specific factors, such as logistic and economic constraints and preferences. The availability of laboratory confirmation will provide further arguments.

Given the short duration of individual meningococcal meningitis epidemics, rapid decision making and implementation of mass campaigns is essential to maximizing the impact of the epidemic response. In our analysis, decreasing the delay from signal detection to effective vaccine protection by 2 weeks doubled efficiency (and number of cases prevented). The updated version of the WHO guidelines further emphasizes this aspect. However, several relatively fixed factors make it challenging to reduce the currently observed delay, such as weekly rhythm of data analysis, storage of vaccines at a central location in a country or even at international level, with corresponding administrative and transport delay, and time required to mobilize vaccination teams. More reactive signal detection in health areas, possibly combined with decentralized vaccine management at the regional level, is therefore an interesting option for improving the impact of reactive vaccination.

Our analysis indicated that several hundred cases were preventable during the 11-year period; however, among individual epidemics, a median of near 0 cases were prevented per 100,000 doses, and a maximum of 180 cases were prevented. This finding indicates that in many epidemic health areas, no cases would be prevented by reactive vaccination,
but a large benefit would appear in a few situations, probably where the outbreak is longer. Our analysis overestimates current potential vaccine impact because a portion of the outbreaks resulted from NmA, for which no vaccine exists. Other assumptions may lead to overestimation or underestimation of vaccine-preventable cases, but regardless, the overall expected impact from reactive vaccination after NmA elimination may be limited. An exception might be a strong increase in the percentage of Nm among suspected cases that result from emergence of non-A serogroups which might increase the effectiveness of any strategy.

Bringing data resolution for meningitis surveillance to the health area level would require relatively few additional means: throughout the meningitis belt, suspected case data are collected in health centers and transmitted in aggregate form by districts to the national level so that a lower degree of aggregation would accelerate data availability. Routine procedures for data management and analysis would need to be slightly modified, but analyses would consist mostly of aggregation would accelerate data availability. Routine data collection by districts to the national level so that a lower degree of aggregation would accelerate data availability.

Table 2: Comparison of estimated vaccine-preventable meningitis cases using different strategies of surveillance and meningococcal vaccine response before introduction of PsA-TT, Tahoua, Tillaberry, and Dosso regions, Niger, 2002–September 2011

<table>
<thead>
<tr>
<th>Strategy, surveillance–vaccination</th>
<th>Total no. of signals</th>
<th>Population affected by signal</th>
<th>Vaccine doses in persons 1–29 y</th>
<th>Vaccine preventable cases</th>
</tr>
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<tbody>
<tr>
<td>Health area—district</td>
<td>7</td>
<td>844</td>
<td>14,742,136</td>
<td>10,909,180</td>
</tr>
<tr>
<td>health area</td>
<td>10</td>
<td>679</td>
<td>11,567,626</td>
<td>8,560,043</td>
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<tr>
<td>15</td>
<td>469</td>
<td>7,849,057</td>
<td>5,808,302</td>
<td>9,587</td>
</tr>
<tr>
<td>20</td>
<td>358</td>
<td>5,791,671</td>
<td>4,555,045</td>
<td>9,307</td>
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<tr>
<td>30</td>
<td>235</td>
<td>3,719,950</td>
<td>2,689</td>
<td>8,919</td>
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<td>Health area—district</td>
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<td>47,090,036</td>
<td>34,846,626</td>
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<tr>
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<td>250,956</td>
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<tr>
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<td>235</td>
<td>23,115,711</td>
<td>17,105,626</td>
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<td>21,069,851</td>
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</tr>
<tr>
<td>7</td>
<td>44</td>
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<td>10</td>
<td>18</td>
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<td>18</td>
<td>6,021,142</td>
<td>4,455,645</td>
<td>252,049</td>
</tr>
</tbody>
</table>

*Weekly incidence rate thresholds were selected on the basis of best performance (sensitivity and specificity) to identify years of high annual incidence (2,534 health area years). The 3 regions had 7.5 million inhabitants.
should analyze suspected case incidence after PsA-TT introduction at health center level over the next few years to validate our findings and to inform optimal epidemic surveillance and response strategies.

Our evaluation highlights the value of continuous meningitis surveillance over longer periods and at subdistrict resolution and has the potential to guide future recommendations for reactive vaccination. Also, given a possibly limited absolute impact of reactive vaccination, the results recall that improved prevention strategies should be developed to reduce the effects of acute bacterial meningitis in the African meningitis belt, for example using multivalent meningococcal and pneumococcal vaccines in extended target age groups.

Acknowledgments

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H.B.M. and J.E.M. contributed substantially to the conception of the work; H.B.M., I.I., J-P.M.P., O.O.M.O.-B., and A.F. acquired the data; H.B.M., J.P., and J.E.M. analyzed and interpreted the data; H.B.M. drafted the manuscript; J.P., I.I., J.M., O.O., A.F., and J.E.M. conducted the critical revision of the work for important intellectual content; H.B.M., J.P., I.I., J-P.M.P., O.O.M.O.-B, A.F., and J.E.M. gave final approval of the version submitted and agree to be accountable for all aspects of the work.

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Dr. Maïnassara is a medical doctor with a master’s degree in epidemiology working at the Centre de Recherche Médicale et Sanitaire de Niamey. Her primary research interest is bacterial meningitis.

References


Figure 3. Comparison of preventable meningitis cases per 100,000 vaccine doses, given different surveillance and meningococcal vaccine response strategies, in a situation simulating elimination of Neisseria meningitides serogroup A, Tahoua, Tillabery, and Dosso regions, Niger, 2002–2012. Three, 4, 5, and 6 weeks delay were considered between epidemic detection and effective vaccine protection. The strategies were surveillance and vaccination at health area level (health area–health area, top 3 lines), surveillance at health area level combined with vaccination of the district (health area–district, middle 3 lines), and surveillance and vaccination at district level (district–district, bottom 3 lines). For the health area–health area and health area–district strategies, the black line indicates preventable cases/100,000 vaccine doses at an incidence threshold of 7 cases/100,000 inhabitants; red line, threshold of 10 cases/100,000 inhabitants; and blue line, threshold of 15 cases/100,000 inhabitants. For the district–district strategy, the green line indicates preventable cases/100,000 vaccine doses at an incidence threshold of 4 cases/100,000 inhabitants; orange line, threshold of 2 cases/100,000 inhabitants; and black line, threshold of 7 cases/100,000 inhabitants.

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Dr. Sarah Hamer, Assistant Professor and Veterinary Ecologist with the College of Veterinary Medicine at Texas A&M University, discusses her investigation of ticks on wild birds in urban Chicago.

http://www2c.cdc.gov/podcasts/player.asp?f=8626456
Response Strategies against Meningitis Epidemics after Elimination of Serogroup A Meningococci, Niger

Technical Appendix

Technical Appendix Figure 1. Data transmission and collection for reporting of suspected meningitis cases, Niger. For national routine surveillance, all health facilities in Niger transmit weekly case counts to district hospitals, where data are aggregated to a district case count and transmitted to the Regional Directions of Public Health, then to the Direction of Surveillance and Response to Epidemics/Ministry of Health for reporting. To analyze epidemic dynamics at the health area level, we retrieved the original health facilities meningitis case counts at the district hospitals.
Evaluation of Completeness of the Health Center Database

The country has 8 regions (Tahoua, Tillabery, Agadez, Diffa, Maradi, Niamey, Zinder, and Dosso), 42 districts, and 732 health areas containing >1,500 health centers. To assess the completeness of this database, we compared the resulting district-level weekly case counts with those included in the national routine surveillance reports.

A ratio was calculated as the number of suspected meningitis cases in our database divided by the number of suspected meningitis cases in the national surveillance database. This ratio was calculated for every year (aggregated cases in our database by year/aggregated cases in the national surveillance database by year), then for every region (region-level aggregated cases in our database/region-level aggregated cases in the national surveillance database) and every district (district-level aggregated cases in our database/district-level aggregated cases in the national surveillance database). A ratio of 1 suggested no differences between the cases counts of the 2 databases. This ratio was \( \approx 1 \) during 2008–2012, suggesting that our data from the whole country were almost complete for this period. At the region level, a ratio \( \approx 1 \) was found for regions of Tahoua, Tillabery, Agadez, and Diffa. It was \( \approx 0.78, 0.77, \) and 0.71, respectively, for Dosso, Maradi, and Zinder regions. Data for Niamey were not complete because the ratio was 0.10, so we excluded it. At the district level, we calculated the number of districts that have ratios less than the first quartile, between the first and the third quartiles, and more than the third quartile of all the ratios.

The first quartile of these ratios was 0.8, the median 1, and the third quartile \( \approx 1.3 \). Over 70 district years, ratios were \(<0.8\), 69% were from the regions of Maradi and Zinder, so we excluded them. Tahoua, Tillabery, and Dosso presented the highest number of district years (ratios 0.8–1.3).

We then calculated for each region the rate of missing health center years using data collected by the Centre de Recherche Médicale et Sanitaire. This operation showed that the Tahoua, Tillabery, Dosso, and Diffa regions had the lowest rate of missing data during the study period (<40%). Maradi and Zinder presented >40% of health centers as missing for 2002–2006. Agadez had >40% of missing health centers for 2002–2005 and 2012. Niamey also had >40% of missing data from 2002 to 2010. Thus, Niamey data were not usable, Maradi and Zinder could
be used only from 2007 to 2012 and Agadez from 2006 to 2011. Diffa did not bring important notified cases. Tahoua, Tillabery, and Dosso data were the most usable for the study period. With these analyses, we selected the regions of Tahoua, Tillabery and Dosso on the basis of 3 criteria: less difference in notified cases in the 2 databases, fewer missing data (<40%), and the number of notified cases.

A

**Technical Appendix Figure 2.** Weekly incidence rates (WIR) of suspected meningitis cases by health district. Tahoua, Tillabery, and Dosso regions, Niger, 2002–2012. A) Tahoua region: The predominant etiology in the districts with peak WIR >10 cases per 100,000 inhabitants, where laboratory data were
available, was meningococcal serogroup A. B) Tillabery region: The predominant etiology in the districts with peak WIR >10 cases per 100,000 inhabitants, where laboratory data were available, was meningococcal serogroup X (Say). C) Dosso region: The predominant etiology in districts with peak WIR >10 cases per 100,000 inhabitants, where laboratory data were available, was meningococcal serogroup A (Gaya and Loga).

**Technical Appendix Figure 3.** Performance of epidemic threshold (ET) definitions in detecting elevated annual meningitis incidences at the health area level in a situation simulating elimination of meningococcal serogroup A meningitis (NmA). Tahoua, Tillabery, and Dosso regions, Niger, 2002–2012 (531 health area years). All health area years with ≥1 NmA cases or without serogroup information were excluded. Empty marks represent the performance of ETs in detecting annual incidences ≥0.08% which corresponds to the 95th percentile of all annual incidences in the database. Full and red marks represent the performance in detecting annual incidences ≥0.12%, which corresponds to the 97.5th percentile of all annual incidences of the database. ETs were defined as weekly incidence rates of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, and 100 cases per 100,000 inhabitants.
Technical Appendix Figure 4. Performance of epidemic threshold (ET) definitions in detecting elevated annual meningitis incidences at the district level, in a situation simulating elimination of serogroup A meningococcal meningitis, in Tahoua, Tillaberry, and Dosso regions, Niger, 2002–2012 (65 district years). All district years with ≥1 more NmA cases or without serogroup information were excluded. Empty marks represent the performance of ETs in detecting annual incidences ≥0.027% which corresponds to the 95th percentile of all annual incidences in the database. Full and red marks represent the performance in detecting annual incidences ≥0.029%, which corresponds to the 97.5th percentile of all annual incidences of the database. ETs were defined as weekly incidence rates of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, and 50 cases per 100,000 inhabitants.