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# MenAfriNet: A Network Supporting Case-Based Meningitis Surveillance and Vaccine Evaluation in the Meningitis Belt of Africa

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## Abstract

Meningococcal meningitis remains a significant public health threat, especially in the African meningitis belt where *Neisseria meningitidis* serogroup A historically caused large-scale epidemics. With the rollout of a novel meningococcal serogroup A conjugate vaccine (MACV) in the belt, the World Health Organization recommended case-based meningitis surveillance to monitor MACV impact and meningitis epidemiology. In 2014, the MenAfriNet consortium was established to support strategic implementation of case-based meningitis surveillance in 5 key countries: Burkina Faso, Chad, Mali, Niger, and Togo. MenAfriNet aimed to develop a high-quality surveillance network using standardized laboratory and data collection protocols, develop sustainable systems for data management and analysis to monitor MACV impact, and leverage the



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SUPPLEMENTARY DATA

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

surveillance platform to perform special studies. We describe the MenAfriNet consortium, its history, strategy, implementation, accomplishments, and challenges.

**Keywords**

meningitis; surveillance; sub-Saharan Africa; meningitis belt

Meningococcal meningitis, caused by the bacterium *Neisseria meningitidis*, remains a significant public health threat globally. The meningitis belt of sub-Saharan Africa—stretching from Senegal to Ethiopia—experiences the highest disease burden, with more than 400 million people at risk in 26 countries [1]. Countries in the African meningitis belt have historically experienced annual seasonal outbreaks with explosive epidemics every 5 to 10 years, with *N meningitidis* serogroup A (NmA) accounting for approximately 90% of cases during epidemics [1, 2]. After a large NmA epidemic in 1996-1997, which affected more 250 000 people and killed more than 25 000 people, African public health leaders signed the Yaounde Declaration, calling for the elimination of NmA epidemics in Africa [3]. In response, a low-cost meningococcal serogroup A conjugate vaccine ([MACV] MenAfriVac®) was developed solely for Africa [4]. The phased and rapid rollout of MACV starting in 2010 through mass vaccination campaigns drastically reduced NmA cases, eliminated NmA epidemics, and proved to be a highly effective intervention [2, 5, 6]. However, because MACV was licensed based solely on excellent safety and immunogenicity data without field effectiveness trials, there was a need to determine the direct and indirect effectiveness of this vaccine [7]. Several key questions remained including long-term effectiveness and impact of MACV on herd immunity and epidemiology of meningitis in Africa, potential meningococcal serogroup replacement, and the need for developing multivalent meningococcal conjugate vaccines for the region. To answer these questions, high-quality meningitis surveillance data in the meningitis belt were critical.

After MACV introduction, the World Health Organization (WHO) recommended implementing case-based meningitis surveillance in countries that introduced the vaccine [8]. Case-based surveillance includes systematic collection of epidemiologic, clinical, and laboratory data on each suspected case of meningitis year-round. Because bacterial meningitis can be caused by multiple pathogens with indistinguishable clinical presentations, including *N meningitidis, Haemophilus influenzae*, and *Streptococcus pneumoniae*, a key component of case-based meningitis surveillance is to collect cerebrospinal fluid (CSF) specimens and identify the causative pathogen via laboratory confirmation at a reference laboratory.

As a result of the WHO recommendation, the MenAfriNet consortium was established in 2014 to support strategic implementation of case-based meningitis surveillance in 5 key countries in the African meningitis belt: Burkina Faso, Chad, Mali, Niger, and Togo (Figure 1). MenAfriNet is an international consortium led and implemented by African Ministries of Health, Agence de Médicine Préventive (AMP), the US Centers for Disease Control and Prevention (CDC), and the WHO, with support and collaboration from other international and nongovernmental organizations. The primary goals of MenAfriNet were to (1) develop a

high-quality, sustainable, case-based meningitis surveillance network using standardized tools, (2) assess changes in meningitis epidemiology and vaccine impact, and (3) inform vaccine policy decisions and new vaccine development. In this study, we describe the MenAfriNet consortium, its history, strategy, implementation, accomplishments, and challenges.

## HISTORY

MenAfriNet was built upon a long history of strong national meningitis surveillance in the African meningitis belt, supported by many international partners. Established by WHO in the 1990s, national meningitis surveillance systems in the region were built upon the Integrated Disease Surveillance and Response (IDSR) framework for aggregate case reporting. The goal of IDSR was to strengthen overall disease surveillance and response systems [9]. After the large meningitis epidemics of 1996-1997, WHO built upon the IDSR framework to develop Enhanced Meningitis Surveillance protocols, to detect and respond to meningitis epidemics early and appropriately [8]. These protocols were designed to improve data collection and reporting, along with laboratory confirmation in a subset of cases in each district that crossed a predefined threshold suggesting risk of a meningitis epidemic [10]. Enhanced Meningitis Surveillance also helped inform critical decisions regarding the use of meningococcal vaccine supply during an outbreak, particularly considering limited global vaccine stocks.

Multiple countries in the meningitis belt had existing IDSR and Enhanced Meningitis Surveillance systems; however, baseline evaluations found that although surveillance infrastructures were strong, opportunities existed for improving data management, specimen transport to reference laboratories, and laboratory capacity for confirming cases [11]. More importantly, neither of the existing surveillance systems provided representative case-level demographic data nor laboratory confirmation for a large proportion of cases, which are critical for evaluating the impact of new vaccines on disease burden. In 2010, WHO provided case-based surveillance guidelines for meningitis belt countries that built on IDSR and Enhanced Meningitis Surveillance with the goal of evaluating MACV impact and estimating the incidence of non-NmA meningococcal serogroups to better inform emergency stockpile and new vaccine development strategies [8]. MenAfriNet was created to assist countries in the technical implementation and improvement of case-based meningitis surveillance and use of these data to evaluate and inform meningitis vaccine programs.

## STRATEGY

The MenAfriNet strategy included an approach that emphasized country-driven capacity building (bottom-up) rather than a partner-driven (top-down) effort. Although this approach was more challenging, MenAfriNet's 5-year commitment established sustainable capacity in the partner countries in the form of a country-owned case-based meningitis surveillance system and research platform, where data were available for national authorities to inform key policy decisions. The MenAfriNet consortium drew on decades of experience in the region and identified 3 key domains of focus: epidemiology, laboratory confirmation, and data management (Figure 2).

At the start of the project in 2014, the MenAfriNet consortium collaborated with partner countries to strengthen these domains through a cycle of support activities (Figure 2). The cycle started with an assessment of existing surveillance systems, followed by context-appropriate technology transfer to fill gaps identified through the assessment, training of country partners, and providing consistent mentorship to ensure enhanced capacity was maintained. This cycle of support continued throughout the course of the project, which enabled countries to routinely assess and improve the quality of activities implemented. It allowed country officials to work with international partners, and later with colleagues in other participating countries, to fill technical gaps.

## IMPLEMENTATION

### Country Selection and Engagement

To help in selection of partner countries to be included in MenAfriNet, an initial gap analysis was conducted. In addition to country interest and commitment, the main drivers of the country selection process included the following: whether inclusion of the country would contribute to the epidemiologic understanding of MACV impact in the African meningitis belt, existing in-country surveillance capacity, and resources needed to incorporate the existing system into the MenAfriNet network to collect high-quality, case-based data.

In 2014, MenAfriNet initially included 4 countries: Burkina Faso, Mali, Niger, and Togo. In 2016, Chad was added as a fifth country. By the end of 2014, all 5 countries had conducted MACV mass vaccination campaigns (Table 1). Although all districts in Burkina Faso were included in MenAfriNet, Chad, Mali, Niger, and Togo concentrated their surveillance-strengthening efforts in selected districts in the meningitis belt where meningitis disease burden was the greatest. By end of 2017, 115 (33%) of 347 districts in Burkina Faso, Chad, Mali, Niger, and Togo were included in MenAfriNet and approximately 33 million people were under MenAfriNet surveillance (Table 1).

Based upon past experience with project implementation in the African meningitis belt, it was clear that MenAfriNet's successful completion, impact, and sustainability depended on early engagement and strong support from in-country partners, WHO offices, and, most importantly, the Ministries of Health [12]. Hence, countries and partners were engaged early on through joint missions to meet with Ministry of Health officials to extend formal invitations to join the consortium with emphasis on local capacity building and country ownership of surveillance data and activities. Countries developed annual work plans, outlining detailed activities to implement case-based meningitis surveillance with a clear focus on improving epidemiology, laboratory, and data management systems (DMSs).

To implement MenAfriNet activities, 5 work groups were formed and charged with key functions: (1) surveillance and outbreak, (2) laboratory, (3) data management, (4) research and evaluation, and (5) communications. Representatives from partner organizations chaired the work groups and were supported and organized by a CDC co-lead. Each work group held monthly or quarterly teleconferences and had a specific mission that defined the scope of work, frequency of communication, and guided activity implementation (Appendix 1). The work groups were tasked with developing standardized operating procedures, tools,

training materials, and carrying out mission-related activities relevant to the goal of the work group. In general, during the development and implementation stages of MenAfriNet activities, these work groups communicated via teleconference more frequently (ie, monthly); as activities moved into the maintenance phase, work groups transitioned to meeting less frequently (ie, quarterly).

### Strengthening Case-Based Surveillance

To establish a high-quality, case-based meningitis surveillance network, MenAfriNet used several mechanisms to strengthen epidemiologic, laboratory, and data management capacity. Epidemiologic capacity was strengthened by developing standardized protocols and case investigation forms, identifying minimal data elements to be reported by each country, and developing surveillance performance indicators with target thresholds [13]. These tools facilitated data entry and transfer from the district to national level on a timely basis in each country and provided a common framework for surveillance activities in the region. Training workshops were held in each country to adapt these tools and implement new surveillance protocols.

To improve laboratory capacity, reference laboratories were identified at the national or regional level in each country. Lumbar puncture kits and Trans-isolate (TI) media were provided for CSF collection and transportation from diagnosing health facilities to reference laboratories. Direct real-time polymerase chain reaction (rt-PCR) testing was implemented in each country as a confirmatory test, to help increase diagnostic capacity in settings where culture-based methods were challenging. MenAfriNet trained public health laboratory scientists on specimen handling, diagnostic methods (ie, direct rt-PCR and bacterial culture), and laboratory data management and reporting [14]. MenAfriNet also implemented external quality-control and quality-assurance programs at the reference laboratories and assisted countries in procuring laboratory supplies needed for meningitis diagnostics.

To improve data management capacity, national level data managers and epidemiologists were trained in integrating laboratory data with clinical and demographic data into 1 master database with a unique identification number for each case. The MenAfriNet consortium developed an EpiInfo 7-based DMS that standardized data collection, transmission, and data harmonization among all MenAfriNet countries. MenAfriNet provided direct technical assistance in rollout of the DMS and held multiple training workshops for country data managers. In subsequent years, targeted workshops focusing on specific topics were held in each country to address ongoing data management gaps. Case-based data collected by MenAfriNet countries were sent to members of the WHO-AFRO, CDC, and AMP data management team to be merged into a central MenAfriNet database. Data were cleaned and analyzed to guide public health responses, monitor performance of the system using surveillance indicators, and provide critical feedback to countries. Data were also published in quarterly bulletins and presented at the annual WHO meeting on epidemic meningitis and at the annual MenAfriNet partners' meeting.

## ACCOMPLISHMENTS

MenAfriNet has been successful over its 5-year tenure in directly improving standardized meningitis case-based surveillance in 5 countries while also benefiting meningitis surveillance in the other African meningitis belt countries through standardized protocols, tools, and technical assistance [15, 16]. One of MenAfriNet's biggest accomplishments has been the successful formation of a consortium of international partners and Ministries of Health committed to fighting meningitis in the region. This consortium has promoted country ownership, collaboration, communication, data sharing, and curation of best practices, and it supported the professional development of local public health leaders. Through MenAfriNet support, in-country laboratory capacity to test and confirm suspected meningitis cases improved. Before MenAfriNet, there was no direct rt-PCR capacity in the 5 countries; all MenAfriNet countries now have the capacity to perform direct rt-PCR to test CSF specimens for *N meningitidis*, *S pneumoniae*, and *H influenzae* and to conduct serogroup testing for specimens that are positive for meningococcus [14].

MenAfriNet support has resulted in improvement in the quality and availability of meningitis surveillance data to measure impact of MACV and guide public health efforts to reduce meningitis disease burden [13]. For example, this case-based surveillance platform has enabled estimating population-based incidence of confirmed meningitis and better quantification of meningitis disease burden in the region [17], filling an important information gap that previously was not possible. High-quality laboratory MenAfriNet data have also been used by countries with outbreak response measures including their application to the International Coordinating Group on Vaccine Provision for Meningitis for obtaining access to meningitis vaccines for outbreak response. The case-based surveillance data from Burkina Faso has been instrumental for monitoring the epidemiology of bacterial meningitis post-MACV, as well as to detect and confirm 5 NmA cases, including the first documented case of MACV failure [18]. These data accelerated Burkina Faso's timeline for conducting a catch-up campaign for children born after the initial MACV campaign and introducing MACV into the Expanded Programme on Immunization (EPI) for young children in an effort to halt NmA transmission.

The MenAfriNet network has also facilitated partner organizations and Ministry of Health staff in supporting each other, both in providing routine technical assistance for surveillance and in responding to several epidemics in the region. In 2014, scientists from the Burkina Faso National Reference Laboratory for meningitis hosted and trained laboratory scientists from Mali on direct rt-PCR and supplied them with necessary reagents and materials to do their own in-country testing for meningitis. In 2015, MenAfriNet personnel, including epidemiologists and laboratory scientists from Burkina Faso, aided Niger in responding to the first large-scale epidemic of *N meningitidis* serogroup C (NmC) meningitis [19]. In addition, in 2016, a NmC meningitis outbreak was detected in Ouelessebougou, a MenAfriNet district in Mali. Strong relationships between MenAfriNet partners and Mali health officials allowed rapid confirmation of the outbreak as NmC and implementation of an early vaccination campaign [20]. Also in 2016, AMP's mobile laboratory was deployed in Togo to help confirm and characterize an *N meningitidis* serogroup W meningitis outbreak [21]. MenAfriNet provided Togo with CSF collection kits, TI media, and other

laboratory reagents to aid in testing. In 2017, Burkina Faso staff conducted a data validation workshop and then led data validation workshops with their counterparts in Niger, and officials from Niger then led a data validation workshop in Mali. These collaborations were characteristic examples of the intercountry "south-south" collaboration that has been fostered through the MenAfriNet consortium.

The MenAfriNet surveillance platform has also been effectively leveraged to answer priority research questions. To assess the long-term impact of MACV on the prevalence, serogroup distribution, and molecular characteristics of asymptomatic nasopharyngeal carriage of *N meningitidis*, particularly NmA, meningococcal carriage evaluations were conducted in Burkina Faso in 2016-2017. MenAfriNet data have contributed to cost-effectiveness studies of possible vaccination strategies for multivalent meningococcal conjugate vaccines. Burkina Faso's case-based surveillance system has also proven to be a valuable platform for monitoring pneumococcal meningitis epidemiology [22] and evaluating the introduction of pneumococcal conjugate vaccine [23], and the strong collaboration among MenAfriNet partners in Burkina Faso laid the foundation for a nationwide vaccination coverage survey after MACV introduction into the routine immunization program [24].

## CHALLENGES

The progress made through MenAfriNet did not come without challenges. Maintaining and promoting consistent communication between partners, especially communication between MenAfriNet countries to share lessons learned and coordinate regional meningitis activities proved to be a challenge from the outset. To address this, MenAfriNet work groups held regular teleconferences and in-person meetings to discuss technical issues and facilitate discussions between countries. The annual MenAfriNet partners' meeting was also used as an opportunity to foster communication and coordination between all partners and countries.

Given the limited internet connectivity in the region, consistent transmission of case-based surveillance data at all levels along with a standardized system that could efficiently receive and merge data from all MenAfriNet countries posed a significant challenge. To that end, MenAfriNet partners worked with individual countries to develop plans for transmitting and compiling data at regular intervals. A standardized database management system was also developed that allowed data from all MenAfriNet countries to be harmonized and stored into a single database for analysis. The roll out of the database had its own challenges including delays in developing the system and database versions that required in-person installation in each country. To tackle these challenges and ensure that high-quality data were collected, MenAfriNet staff held annual data validation workshops to harmonize all data collected through the MenAfriNet network. In addition, an end-of-project data validation workshop was held to finalize data collected throughout the course of the project.

Another challenge was establishing and maintaining a functioning CSF specimen transport and tracking system. The limited resources, frequent stock out of CSF collection and transport materials, poor infrastructure, and long distances led to temporary interruption of specimen collection and led to long delays in the specimen getting to a reference laboratory for confirmatory testing. To address this issue, MenAfriNet partners designed and

implemented STELAB, first piloted in Burkina Faso. STELAB is a real-time specimen and data tracking system that facilitates specimen transport and data transfer from the diagnosing health facility to the national level with the ability to track specimen and data in real-time at all levels [25].

An unexpected challenge was the 2014-2016 Ebola virus disease epidemic in West Africa [26]. This unprecedented crisis necessarily diverted public health personnel, funds, and attention away from other health problems and disrupted travel to West Africa just as MenAfriNet was launching. Although the Ebola epidemic temporarily deprioritized MenAfriNet activities, the consortium's partnerships were strengthened, and it continued to achieve planned milestones. Another challenge encountered was the geopolitical situation in MenAfriNet countries, complicating country priorities and partner travel. In response, MenAfriNet leveraged the in-country capacity it had built, relied upon regional partners to implement and support MenAfriNet activities, and rescheduled activities as needed.

## CONCLUSIONS

The MenAfriNet model is a successful and expandable platform for implementing and strengthening high-quality, case-based meningitis surveillance, evaluating vaccine impact, responding to meningitis epidemics, and monitoring the changing epidemiology of bacterial meningitis in the African meningitis belt. Although the MenAfriNet consortium was established to specifically address meningococcal meningitis and evaluate the impact of MACV, it is also a valuable platform for evaluating the effectiveness of MACV integration into EPI programs, pneumococcal conjugate vaccines, and the potential future deployment of a multivalent meningococcal conjugate vaccine. Moving forward, MenAfriNet will leverage the surveillance and research platform and the strong international and intercountry partnerships established during its tenure to continue providing high-quality meningitis data and technical assistance to inform immunization policies in the region. In addition, it will make the standardized surveillance tools publically available to further strengthen surveillance and contribute to understanding the evolution of meningitis in the African meningitis belt [27].

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments.

The MenAfriNet consortium (www.menafrinet.org) is an international consortium led and implemented by Ministère de la Santé du Burkina Faso, Ministère de la Santé et de l'Hygiène Publique du Mali, Ministère de la Santé Publique du Niger, Ministère de la Santé Publique du Tchad, Ministère de la Santé et de la Protection Sociale du Togo, Agence de Médecine Préventive, Centers for Disease Control and Prevention (CDC), and World Health Organization (WHO), with support and collaboration from other international and nongovernmental organizations. We thank all MenAfriNet partners, including participating national health systems, health centers, and laboratories.

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**Figure 1.**
Countries in the African meningitis belt (in light gray) and the 5 MenAfriNet countries (in orange).

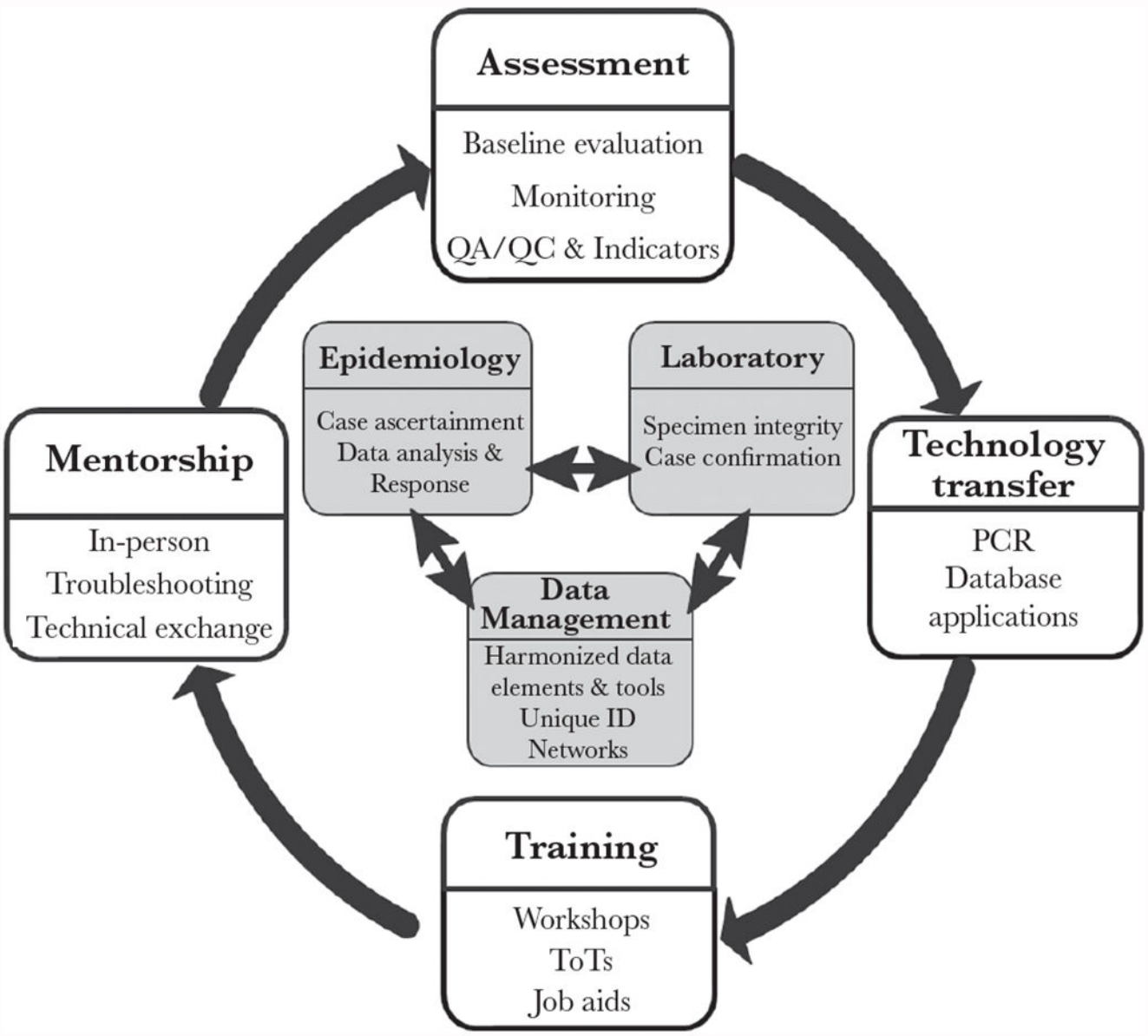


**Figure 2.**
The MenAfriNet model for surveillance strengthening. ID, infectious diseases; QA, quality assurance; QC, quality control.

**Table 1.**

MenAfriNet Countries, Number of Included Districts, and Total Population in Each Country Under Surveillance by 2017

| | | | Districts Included in MenAfriNet | Population Under MenAfriNet Surveillance |
|---|---|---|---|---|
| **Country** | **Year of MACV Mass Campaigns** | **Year Country Invited to Join MenAfriNet** | **n/N (%)[a]** | **n (%)[a]** |
| Burkina Faso | 2010 | 2014 | 70/70 (100) | 19 632 397 (100) |
| Mali | 2011–2011 | 2014 | 12/73 (16) | 4 027 829 (22) |
| Niger | 2010–2011 | 2014 | 24/64 (38) | 7 347 840 (37) |
| Chad | 2011–2012 | 2015 | 4/100 (4) | 811 414 (5) |
| Togo | 2014 | 2014 | 5/40 (13) | 963 411 (13) |
| Total | - | - | 115/347 (33) | 32 782 641 (40) |

Abbreviations: MACV, meningococcal serogroup A conjugate vaccine.

[a]Data as of January 1, 2017. Districts and population under MenAfriNet continued to grow throughout the course of the project.