

Epidemiological study of cholera hotspots and epidemiological basins in East and Southern Africa

In-depth cholera epidemiological report for South Sudan

April 2018



**PROSPECTIVE
COOPERATION**
laboratoire d'idées



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SUMMARY

Cholera continues to represent a major public health concern in the East and Southern Africa region. From 2007 to 2016, approximately 634,000 cases and 14,303 cholera-related deaths were reported in the region with an average case fatality rate of 2.3%. To guide cholera control and prevention strategies, UNICEF established epidemiological studies in the countries of two geographical regions: the Greater Horn of Africa and the Zambezi Basin. The current assignment aims to better understand the dynamics of the disease in South Sudan. Identification of cholera hotspots as well as high-risk populations and practices will serve to guide the decision-making processes and advocacy initiatives.

South Sudan has recently gained independence from the North in 2011. Inter-ethnic warfare and politic rivalries has led to a civil war that has been ongoing since December 2013. As a direct consequence of the prolonged conflict, approximately one third of the total population (3.5 of 12 million) has been displaced.

From 2006 to 2017, suspected cholera cases were first detected in the Eastern Equatoria State, either in counties close to the Ugandan border or the capital city Juba. The state of Eastern Equatoria and Juba city in particular seem to play a role in amplification and diffusion of cholera outbreaks towards the east along the border with Uganda and Kenya and along the Nile River up to the city of Malakal. Outbreak patterns changed over time, with outbreak onset during the dry season (January-February) and during the rainy season (April-June). A high case fatality rate was registered in the Sudd, a vast swamp that stretches between Bor and Malakal, in areas where access is limited either due to conflict or difficult geographical terrain.

Cholera foci are located in major cities that host large IDP camps and settlements, along the border with Uganda and Kenya, and in the Sudd Swamp along the Nile River. In the past years, specific groups of population were affected such as internal displaced peoples in camps or settlements as well as military or armed groups. During the 2016/2017 epidemic, cholera outbreaks heavily affected displaced and host communities living in the Sudd Swamp and communities in cattle camps.

Cholera transmission was often observed during funeral rituals, around affected households and in facilities that received cholera cases. Open defecation has often been reported as a contributing factor for cholera outbreaks over the past years. Since the onset of the ongoing conflict, the already low WASH indicators have further declined with increases in the cost of safe water in urban areas, damage to water facilities, and continued population displacement.

To control cholera outbreaks in the country, nearly two million doses of oral cholera vaccine were administered since December 2012. Nevertheless, little has been done to substantially improve access to basic services in cholera hotspots. Twelve counties, which host approximately 2,280,000 people (18% of the total estimated population), account for two-thirds of the total number of cases. High priority counties should be assessed and targeted for longer-term WASH, Health and social mobilization improvements taking into account the protracted nature of the conflict in some parts of the country.

South Sudan is situated between two major cholera transmission zones, the Great Lakes Region in the south and the Horn of Africa in the east. Evidence of cross-border spread from and to neighboring countries has been reported, especially involving Uganda and to a lesser extent Kenya, Ethiopia and Sudan. Additional genetic studies of *Vibrio cholerae* strains circulating in the East and Central Africa region would confirm these initial but limited observations and promote a concerted effort to eliminate cholera.

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ABBREVIATIONS

AMREF	African Medical and Research Foundation
ARC	American Refugee Council
AWD	Acute Watery Diarrhea
C4D	Communication for development
CATS	Community Approaches to Sanitation
CLTS	Community-Led Total Sanitation
CFR	Case Fatality Rate
CHF	Common Humanitarian Funds
CMD	Christian Mission for Development
CTC	Cholera treatment centre
DRC	Democratic Republic of the Congo
EPR	Emergency, Preparedness and Response
ESAR	East and Southern Africa region
EWARN	Early warning alert and response network
GIS	Geographical Information System
GTFCC	Global Task Force on Cholera Control
HDK	Household disinfection kit
HLSS	Health Link South Sudan
ICG	International Coordinating Group
IDD kit	Interagency diarrheal disease kit
IDP	Internally displaced persons
IDSR	Integrated disease surveillance and response
IPC	Infection prevention and control
IRC	International Rescue Committee
JMP	Joint Monitoring Programme
KAP	Knowledge Attitudes and Practices
MSF-E	Médecins Sans Frontières Espagne
MSF-CH	Médecins Sans Frontières Suisse
MSF-H	Médecins Sans Frontières Hollande
NFI	Non-food items
OCHA	United Nations Office for the Coordination of Humanitarian Affairs
OCV	Oral cholera vaccine
ORP	Oral rehydration point
ORS	Oral rehydration salts
SCI	Save the Children International
UN PoC	United Nations Protection of Civilians <i>site</i>
<i>V. cholerae</i>	<i>Vibrio cholerae</i>
WASH	Water, Sanitation and Hygiene

INTRODUCTION

Cholera is contracted by consuming food or water contaminated with toxigenic *Vibrio cholerae* or by accidental ingestion of contaminated faeces following direct contact with a cholera patient. This ancient disease continues to represent a major public health concern in the East and Southern Africa region. To guide cholera control and prevention strategies, UNICEF developed a regional cholera framework in May 2017 (1). Implementation of the framework hinges on epidemiological studies focused on identifying areas regularly affected by cholera outbreaks (termed “hotspots”) in the countries of two geographical regions: the Greater Horn of Africa (South Sudan, Kenya, Somalia) and the Zambezi Basin (Angola, Malawi, Mozambique, Zambia and Zimbabwe).

South Sudan is located in Central-East Africa, bordered by Sudan to the north, Ethiopia to the east, Kenya to the southeast, Uganda to the south, the Democratic Republic of the Congo (DRC) to the southwest, and the Central African Republic to the west. South Sudan recently gained independence from the North in 2011 (2). Inter-ethnic warfare and politic rivalries has led to a civil war that has been ongoing since December 2013 (2). In July 2016, a second outburst of violence erupted in Juba, the capital, and subsequently spread to the Greater Equatoria Region (2). As a direct consequence of the prolonged conflict, approximately one-third of the total population (3.5 of 12 million) were displaced, with approximately two million of those internally displaced and over 1.5 million finding refuge in neighboring countries, especially Kenya, Sudan and Uganda (2). Due to the precarious living conditions of many South Sudanese, cholera represents a major public health concern. From 2014 to 2017, epidemics have been declared every year, during which time the country reported 28,677 cases and 650 deaths due to cholera (case fatality rate (CFR)≈2.3%) (3).

The current report provides an overview of the cholera outbreak dynamics, contributing factors, as well as high-risk populations and practices in South Sudan. Following an in-depth analysis of the databases obtained, cholera hotspots were identified and classified. Furthermore, the report covers recommendations regarding effective control measures (prevention, preparedness and emergency response). These findings will serve to better guide the decision-making process and advocacy initiatives in South Sudan to put an end to cholera as outlined in the Global Roadmap to 2030 (4).

STUDY BACKGROUND AND OBJECTIVES

BACKGROUND

Cholera continues to represent a major public health concern in East and South Africa. From 2007 to 2016, approximately 634,000 cases and 14,303 cholera-related deaths were reported in the region with an average CFR of 2.3% (5). Seventy-six percent of cases and 85% of deaths were notified by Somalia, Kenya, South Sudan, Malawi, Mozambique, Zambia, Zimbabwe and Angola combined, with an average CFR of 2.5% (5). However, the cholera burden in the study region is markedly heterogeneous, with Somalia reporting 37.2% of cases (179,693 cases) from 2006 to 2015. During the same ten-year period, Zimbabwe reported 27% (130,537 cases) of cases. From 2006 to 2015, Mozambique reported 52,715 cases, Angola declared 42,407 cases, Kenya recorded 38,176 cases, Zambia reported 16,381 cases and Malawi declared 11,004 cholera cases. From 2009 to 2016, 12,534 cases were registered in South Sudan (5).

The epidemiological understanding of cholera dynamics at various administrative levels provide insight into the mechanisms of cholera diffusion both geographically and over time. While cholera cases are regularly reported in the majority of countries in the study region, repeated and persistent outbreaks affect only a limited number of specific zones and populations termed “cholera hotspots”. Cholera outbreaks often amplify and spread from cholera hotspots via the movement of vulnerable and highly mobile populations, regardless of boundaries. Thus, to control and prevent cholera outbreaks, it is critical to identify and characterize cholera hotspots, often affected populations, and major drivers of cholera transmission. Such information is critical to strengthen cholera control and preparedness efforts in each country as well as cross-border collaborations.

Cholera is preventable as long as access to safe water, proper sanitation facilities, and satisfactory hygienic conditions are ensured and sustained for the entire population. Unfortunately, the cost of the universal coverage strategy often exceeds the available funds and capacities of countries affected by cholera. Thus, targeted strategies based on an epidemiology-driven approach significantly alleviate cost constraints, while effectively controlling and preventing outbreaks.

OBJECTIVE

To establish effective strategies to combat cholera in South Sudan, the current assignment aims to better understand the local dynamics of the disease at a national and sub-regional level. To identify cholera hotspots as well as high-risk populations and practices for targeted humanitarian and development programs, this study applies a comprehensive approach combining field research and epidemiological analysis. Study outcomes also include strategic recommendations for enhanced epidemiological surveillance, particularly for cross-border collaboration, targeted preparedness activities, as well as evidence-based emergency and prevention programs in the Health, Water, Sanitation and Hygiene (WASH), Health and Communication for Development (C4D) sectors. These findings will serve to guide the decision-making process and advocacy initiatives to control and prevent cholera in the Central-East Africa region.

METHODS

Cholera surveillance

Cholera surveillance and response is led by the Epidemic, Preparedness and Response (EPR) unit of the Ministry of Health with the support of the WHO country office and the Health cluster. Cholera surveillance and response is implemented within the context of the integrated disease surveillance and response (IDSR) and the early warning alert and response network (EWARN) (6). The latter operates in conflict-affected areas with the support of specific partners.

The following standardized suspected cholera case definition is acknowledged by the Ministry of Health in South Sudan:

- a patient aged five years or more who develops severe dehydration or dies from acute watery diarrhea (AWD) in an area where cholera is not known to be present
- or
- a patient aged two years or more that develops AWD, with or without vomiting, in an area where cholera has been confirmed

A case of cholera is confirmed when *Vibrio cholerae* is isolated from any patient with diarrhea.

The identification of a single suspected cholera case warrants an investigation by the outbreak response team, which includes stool sample collection and the implementation of immediate control measures (6). Since 2014, cholera confirmation has been conducted by the National Public Health Laboratory in Juba.

Cholera data

The total number of cases per county (admin. 2 unit) for 2006 and 2007 (yearly data) was retrieved from a report on cholera preparedness and response prepared by the WHO Emergency Response team in July 2014. Weekly time series of cholera cases and deaths per county between week 17 of 2014 (outbreak start) and week 38 of 2017 (outbreak ongoing) were generated from the line lists of suspected and confirmed cholera cases provided by the WHO Data Management team. The names of the administrative units were corrected to match the names in the reference map file. The number of administrative units was derived from the map file (10 states and 79 counties).

Cholera line lists from 2014 to 2017 included patients of all ages. For the epidemiological analysis, we removed cases that did not meet the standardized case definition.

Population data

The population data per county was extrapolated from the South Sudanese 2008 census by OCHA for humanitarian planning purposes. Population projections were calculated by applying a population growth factor of 1.03 each year between 2008 and 2017. The 2008 population was used for the 2006 and 2007 epidemiological factors. The OCHA population dataset contains 10 states and 80 counties. To match the number of administrative units of the reference map file (10 states and 79 counties), Akoka County was merged with Baitet County.

Rainfall data

Precipitation levels were estimated from daily TRMM Multi-Satellite Precipitation Analysis remote sensing products [1]. Three-hour estimates were totaled to daily estimates. The estimated daily value was aggregated weekly by county (district administrative level).

Geographic information system (GIS) data

Geographic thematic information were made available by OCHA. These layers correspond to the administrative units, main populated places, road networks, rivers, lakes and other major bodies of water.

Oral cholera vaccine campaign data

Oral cholera vaccine (OCV) data was primarily provided by John Hopkins University and the WHO South Sudan Emergency Response Team. Missing information such as the type of population, the type of campaign (pre-emptive/reactive), the number of doses (single dose versus two-dose regimen), vaccine coverage and timing were retrieved from scientific publications, the cholera response situation report [\[2\]](#) and the OCV risk assessment completed in April 2017 (3).

Cholera hotspot classification

The cholera hotspot classification method was derived from a classification algorithm developed for the countries of West Africa [\[3\]](#). The method is based on a distribution threshold of the following epidemiological criteria: the number of outbreaks, the outbreak duration and the attack rate throughout the study period. In the specific case of South Sudan, a temporal profile of cholera transmission was not available for 2006 and 2007 (only the yearly sum of cases was available); however, the algorithm was adapted based on the available data (i.e., outbreak recurrence).

To define an outbreak event (start and end week), polynomial smoothing was applied to the time series. The method was used to smooth sharp increases during outbreak onset and end events (potential notification bias). Observed and smoothed values were manually verified, and the smoothing parameters (same for each outbreak episode) were optimized to avoid inflating the length of outbreak episodes. Patterns of sporadic cases were removed (e.g., a single case or two to three cases without reported cases during the two weeks before and after). Two successive outbreaks separated by an inter-epidemic period equal to or greater than six weeks were considered as two separate events. Outbreak characteristics were extracted for each time series, and the derived epidemiological parameters were computed (unique outbreak ID, number of cases, variance of weekly case count, start and end date, duration, cumulative incidence, standardized outbreak cumulative incidence (i.e., proportional to outbreak length)). Counties were classified into four cholera hotspot types according to the criteria displayed in Table 1. Thresholds were defined considering the values used for West African countries as well as data quality and quantity in South Sudan (p42). The software used includes a spreadsheet program for data management, QGIS for management of geographic information files and R for statistical computing, graphics and cartography.

Type	Interpretation	Frequency (percentile)	Frequency (number of outbreaks)	Duration (percentile)	Duration (number of weeks)
T1	Highest Priority Area	>90	>3	≥40	≥10.5
T2	High Priority Area	between 60 and 90	between 2 and 3	≥40	≥10.5
T3	Medium Priority Area	>90	>3	<40	<10,5
T4	Low Priority Area	between 60 and 90	between 2 and 3	<40	<10,5

Table 1: Frequency and duration of cholera outbreak thresholds per hotspot type

Ethical considerations

The study has been approved by the South Sudan Ministry of Health. Only secondary data and anonymized line lists of suspected cholera cases were analyzed. No ethical review board was required from the Ministry of Health.

STUDY FINDINGS

PART 1 – CHOLERA EPIDEMIOLOGY IN SOUTH SUDAN

I. History of cholera from the 17th to 20th century

Sudanese territories first reported cholera in **1831**, which was likely to have originated from Ethiopia (7). The next recorded outbreak occurred in **1856** and heavily affected the border with Ethiopia (7).

During the seventh pandemic, cholera reached Sudan in **1971** when infected Ethiopian refugees fled their homes to settle in neighboring Sudan due to civil unrest (8). Cholera was then officially reported in the south in 1979, likely introduced by Ugandan refugees (8,9). In May **1985**, a cholera outbreak erupted among Ethiopian refugees in Western Sudan in the aftermath of the historical 1984 famine in Ethiopia, during which farming communities walked long distances to access international aid in Sudan (8,10).

No official reports of cholera cases in Sudan were released during the 1990s and early 2000s. However, a 2001 WHO South Sudan health update mentioned confirmed outbreaks of cholera in a number of locations in Upper Nile State during the three previous years (11). Furthermore, molecular analyses of isolates from the **1998-1999** epidemic in the East and Southern Africa region included 16 strains from Sudan, which provided clear evidence that cholera was circulating during this period. These analyses showed that the isolates clustered into two separate genetic groups, one in Sudan, Kenya and Tanzania and one in Ethiopia, Somalia and along the Southeastern border of Kenya with Somalia (12).

II. Epidemiology of cholera between 2005-2017

a. Dynamics of recent cholera outbreaks

The 2005 cholera outbreak

Between 2005 and 2009, cases of cholera were reported every year. In early April **2005**, a first outbreak emerged in various locations in Kenya, affecting Kakuma Camp. The site, which hosted Sudanese refugees, is located close to the border with Southern Sudan and Uganda. In late April 2005, cholera was confirmed in Southern Sudan. Three months later, in June 2005, the disease was observed in Uganda among Sudanese refugees in Arua Camp at the border with Southern Sudan. Genetic analysis of clinical isolates from Kenya, South Sudan and Arua in Uganda showed that outbreaks were caused by genetically similar strains, thus indicating regional circulation of this strain (13). Introduction of the disease in Southern Sudan in 2005 was most likely linked to outbreaks in Kenya associated with migration of infected individuals.

The 2006 cholera outbreak

On January 28, **2006**, cholera cases were reported in the city of Yei, Southern Sudan, close to the border with Uganda, and then rapidly spread to the city of Juba (14). The disease was then reported 500 km northeast of Juba in the region of Gambella, Ethiopia in April (15,16). During the course of the outbreak, cholera cases were laboratory-confirmed in several locations (Torit, Kapoeta, Bor and Malakal) (17). During this year, 19,277 cases of cholera (CFR=2.9%) were reported, of which 63% were notified in Central Equatoria State. Juba and Yei counties accounted for 49.6% and 13.5% of the total number of cases reported nationwide, respectively. Eastern Equatoria State was also heavily affected with 22% of cases registered in the counties of Lafon, Magwi, Torit and Ikotos. Cases were also reported in Jonglei State (4.56%), Bor South and Pibor counties, further north in Unity State (8.22%), Panyijiar and Rubkona counties and in Upper Nile State (2.13%), Luakpiny-Nasir county ([Figure 1](#)).

Observations indicated that the outbreak followed the route of the river south-north, which was probably favored by the displacement of populations via ferries, boats and ships on the Nile River (14).

The 2007 cholera outbreak

There is no evidence of cholera transmission carried over from 2006 into 2007; nevertheless, cases were reported in January 2007 (14,15). During the **2007** cholera outbreak, 22,412 cases (CFR=1.8%) were notified. Most of the cases were reported in Central Equatoria, in Juba (41.72%) and Yei (11.77%) counties. Cases in Juba primarily came from Muniki and Kator Payams (18). Few cases were reported in Magwi County (2.17%), Eastern Equatoria State and Jonglei State (6.4%). The outbreak extended to the following counties: Rumbek centre (Lake State), Malakal (Upper Nile State), Tonj (Warrap State) and Wau (Western Bahr el Ghazal State) ([Figure 1](#)).

The 2008/2009 cholera outbreak

Unfortunately, no cholera case/death numbers at the state or county levels were available for the 2008-2009 cholera outbreak. Qualitative information was retrieved through investigation reports shared by the Ministry of Health and the WHO.

Cholera cases were first suspected in February **2008** in military barracks in Owinykibul payam, Magwi County, close to the Ugandan border (19). In March, the Yei civil hospital started to register patients with cholera-like disease, including some returnees who returned home to find few basic services such as clean drinking water and sanitation facilities (20). In Juba, the first suspected cholera case occurred in the army barracks in New Site on April 28th. The most affected areas were Muniki (Nyakuron, Jebel Kujur and Customs Market), and Kator (Central and Lologo) Payams¹, where open defecation is widely practiced and the population drinks water from pools during the dry season (18).

In May 2008, an upsurge in cholera cases was observed in Magwi County (21). The first cases were a returnee from Uganda and three relatives who later attended his funeral, a good number of his neighbors contracted cholera as well (21). An investigation conducted in June in three payams revealed that a considerable number of patients had attended a funeral or visited a patient in the hospital where no appropriate infection prevention and control (IPC) measures were implemented (21). Sharing of communal meals and the local brew with limited adequate hand washing capacities was observed (21).

By June 2008, the outbreak spread further north and reached the city of Bor in Jonglei State (22). Cholera cases were recorded in July in Aweil County with no indication concerning the manner by which the epidemic reached the northwestern part of the country (23). Communities that were affected by cholera were displaced by floods and found refuge on some densely populated islands such as Toich (24) and Peth along the Lol River (25,26). The disease also spread within the army barracks in Pariath (26).

In early January 2009, the outbreak extended to neighboring Gogrial West County (Warrap State) (27). An abnormal number of deaths was observed as patients were delayed in reaching health facilities, which was probably due to the geographical characteristics of this swampy area (Alek west Payam) with no roads between villages (27,28). Overall, 27,017 cholera cases (CFR=0.57%) were registered in 2008, while 48,035 cases (CFR=0.13%) were reported in 2009 (29).

¹ A payam is the second-lowest administrative division below county.

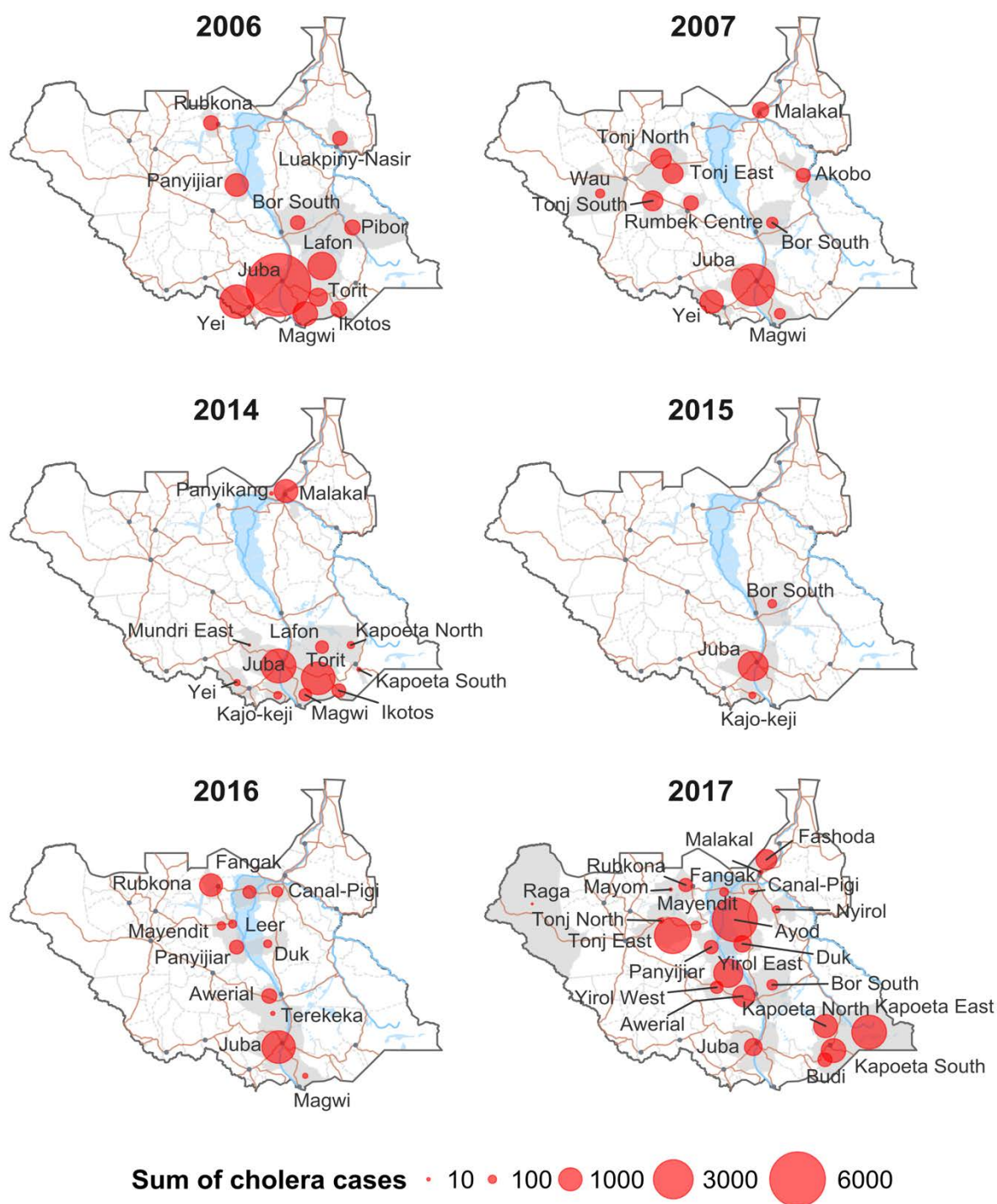


Figure 1: Cholera burden in South Sudan during 2006-2007 and 2014-2017. The yearly total number of cholera cases by county are indicated by red circles; the key indicates the relative number of cases represented. Counties with reported cases are displayed in light grey.

The 2010-2014 period

Information is not available concerning confirmed cholera cases **between January 2010 and April 2014**. It should be noted that at that time, Southern Sudan separated from Sudan following the 2011 referendum and became an independent country, the Republic of South Sudan. Given the limited laboratory capacity in South Sudan during this period, the marked number of AWD cases reported and the fact that Kenya and Uganda were reporting cases (5), sufficient evidence is lacking to consider this timeframe a lull period.

The 2014 cholera outbreak

The next recorded outbreak started on April 29, **2014** in Juba, at the United Nations House Protection of Civilians (UN PoC) 3 camp (30), a few month after the onset on the conflict (December 2013) ([Figure 3](#)). Although the origin of the epidemic is uncertain, cases of cholera were reported on April 23, 2014 in Obongi County, which is located along the White Nile River in Northern Uganda (31). The “index case”, a 28-year-old internally displaced person (IDP) had left the camp and eaten in Gudele 2 market (30). Two of the contacts in the household where the index case stayed overnight in Gudele and one neighbor developed symptoms consistent with cholera over the following days. The disease then spread within Juba City with cases associated with household transmission, transmission in health facilities managing cholera cases, and unsecured funeral rituals (32). By May 19, the cholera outbreak had reached the military barracks (Kaka and Panyagor) (32). During the same period, an increased number of AWD cases was observed outside of Juba at the Owiny Kibul military base (Magwi County) (32) and in Melut County (Upper Nile State), where nine men died of cholera-like symptoms (33). At that time, the water treatment plant in Melut was not functioning and the community was consuming water from the Nile River.

In late May (weeks 21 and 22), cases of cholera were reported along major commercial roads towards Kadjo-Keji and Yei at the border with Uganda and further north in Mundri East County. In each case, the index case had traveled from Juba (32). In late June (week 24), the disease was notified in Nimule (Magwi County) at the Ugandan border. An epidemiological investigation revealed that the index case had attended a funeral (32). Neighboring counties such as Torit and Lafon were affected during the same period. In Torit, the community practiced open defecation along the same river where they obtain drinking water (34) ([Figure 1](#)).

June 30 (week 27) marked the extension of the disease among IDPs in Wau shilluk (Malakal County) as well as the peak of the epidemic. Cholera cases were also notified in Kapoeta North County (week 27), Ikotos County (week 28) at the border with Kenya, and Panyikang County (week 29), which neighbors Malakal ([Figure 1](#)).

The epidemic ended in mid-November (week 46) with a total of 6,421 cholera cases and 167 deaths (CFR 2.6%) reported from 13 counties (35) ([Figure 2](#)). Juba, Torit and the Wau shilluk IDP site were the most affected areas with 35%, 33% and 11% of the total number of cholera cases registered at the national level, respectively ([Figure 3](#)).

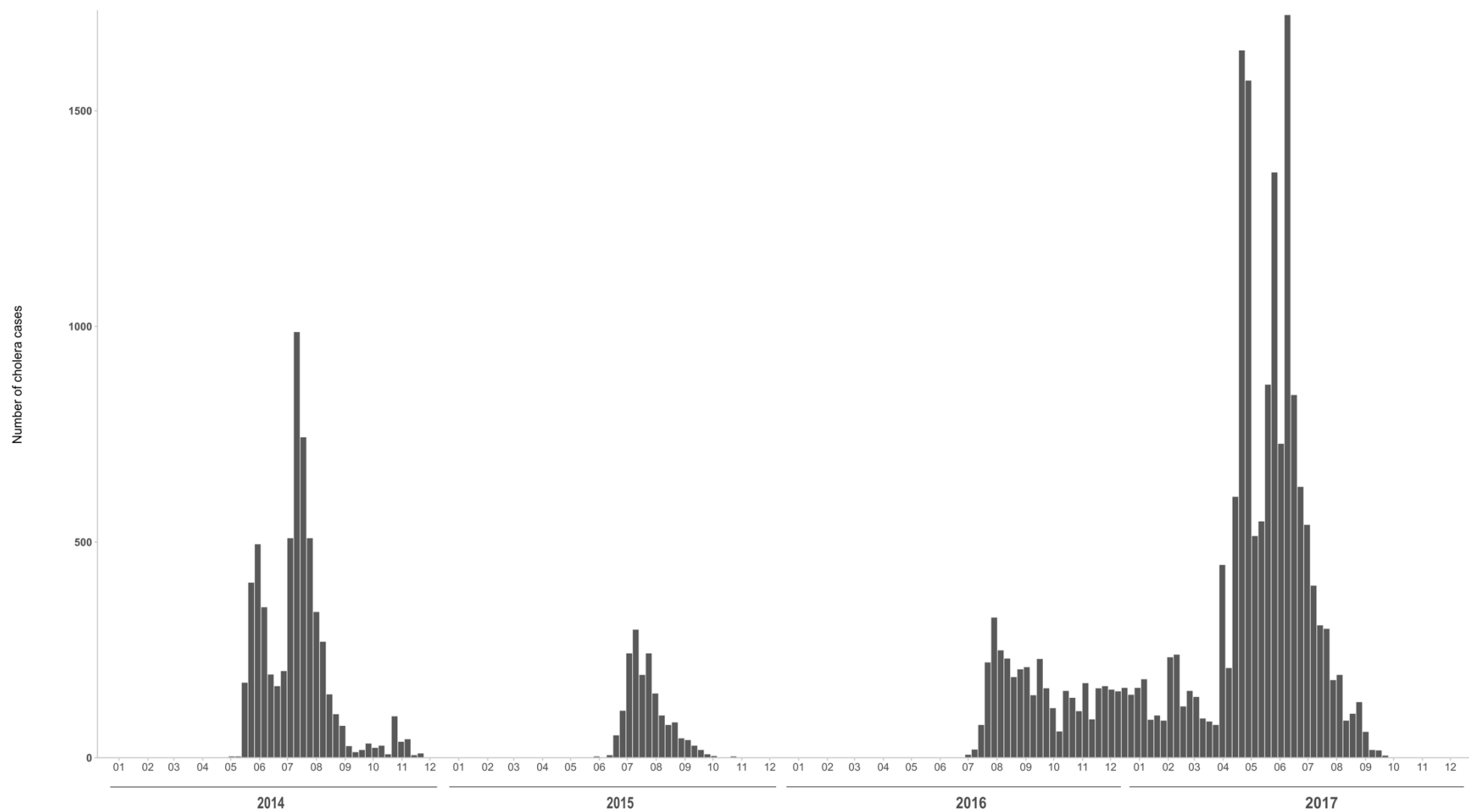


Figure 2: Epidemiological histogram of cholera cases in South Sudan during 2014-2017. Cholera outbreak pattern by county and ISO week are displayed in grey.

The 2015 cholera outbreak

The following year, cholera reappeared during the rainy season at the same IDP camp in Juba (UN House PoC camp 3) on May 18, **2015** ([Figure 3](#)). The retrospective investigations of outbreak onset during both 2014 and 2015 indicated that the epidemic may have started earlier in the host communities of Juba (36). The outbreak extended to Kajo-Keji at the border with Uganda by mid-June (week 22) and two weeks later to Bor (week 25). The epidemic peaked in early July (week 26) and ended mid-October (week 41).

The 2015 cholera event was limited in space and scale compared to previous outbreaks with three counties reporting 1,818 cases and 47 deaths (CFR 2.6%) ([Figure 2](#)) (37). Juba notified 89% of the cases, while Bor South and Kadjo-Kedji reported 8% and 3% of cases, respectively ([Figure 1](#)) ([Figure 3](#)).

The 2016/2017 cholera outbreak

Like 2014 and 2015, the **2016** cholera epidemic started in Juba during the rainy season ([Figure 3](#)). On June 18 (week 24), cases of cholera were observed in host communities in Juba and eventually reached IDPs (UNMISS Tongping, UN House PoC 3 camp, Mahad, Mangatain, Gumbo), refugees (Gorom) and military barracks (Giada, Newsite). From Juba, the outbreak quickly spread among islands along the Nile in Duk (week 26) and Terekeka (week 28) counties. In mid-August (week 32), cases of cholera were reported in Fangak (Jonglei State) and Awerial (Lakes State) counties. The disease was confirmed in the Mingkaman IDP camp (Awerial County) on August 24 (week 34). Meanwhile, the Nimule Hospital at the border with Uganda (Magwi County) registered patients affected by cholera coming from Uganda and Nimule ([Figure 3](#)).

In late September, the outbreak expanded into Unity State, first to Leer (week 39) and then to Mayendit (week 40) and Panyijiar (week 42) among the River Nile islands or at the edge of the Sudd Swamp². Around the same time, an outbreak quickly spread within the Bentiu UN PoC camp (week 41) with clusters of cases in sectors surrounding the pond (38), while sporadic cases were registered in Bentiu town (Rubkona county) in June. In late October, Haat Islands in Ayod County (Jonglei State) was affected, although cases were not reported in the national cholera line lists ([Figure 3](#)) (39).

The 2016 epidemic continued during the dry season with a resurgence of cases in Juba UN House PoC 3 camp during week 52. Outbreaks occurred in new counties such as Yirol East (Lakes State) in early January 2017 (week 1). In Yirol East, cholera cases were mainly observed in Shambe (40), Langmatot (41) at the edge of the Sudd Swamp and on the islands of Lake Shambe (42). In Bor County, patients with cholera-like symptoms from the Kwei Islands were hospitalized in Jalle on January 29th (week 4) (43). Following cattle raids in December 2016, people were displaced from Jalle Payam to the Kwei Islands, where they used swamp and Nile river water for drinking purposes. In early February (week 5), the number of cases increased in Awerial IDP informal settlements (44) ([Figure 3](#)).

February marked a turn in the pattern of the epidemic, cholera cases initially occurred among the population (host communities and IDPs) living in the Sudd Swamp (i.e., islands, swampy areas) and among IDPs temporally settled in urban areas (UN PoC camps, formal camps, informal settlements) with a sharp increase in cases among pastoralists in hard to reach areas ([Figure 2](#)). During the dry season, cattle herders gravitated and converged on the remaining water sources, usually in the swampy areas along rivers or ponds where affected IDPs and host communities are settled.

² The Sudd is a vast swamp in South Sudan formed by the White Nile river, which covers an area of 500 kilometers (310 miles) south to north and 200 kilometers (120 miles) east to west. The swamp stretches from Bor to Malakal and is one of the world's largest wetlands.

In late February (weeks 8 and 9), cholera cases came from the Guthom cattle camps in Yirol East County. In this area, an investigation revealed that patients either originated or visited the islands on the Nile River (41). At the same time, cattle camps in Awerial were also affected (Panguan, Dor).

Towards the end of March (week 13), the outbreak in Ayod dramatically intensified in cattle camps of Pajiek payam (45) and quickly spread to other surrounding cattle camps (e.g., Buol, Torch and Tar) (46). Around 1,600 cases were registered during week 16. Around the same period, a large number of cases and deaths were reported at the neighboring Mamour cattle camp (Duk county) (47) ([Figure 3](#)).

While cattle camps in various counties were affected, hundreds of patients with cholera-like symptoms were received in MSF treatment centers in Aburoc, Fashoda County in late March (week 13). The area hosts thousands of IDPs who fled the conflict ([Figure 3](#)).

In late April 2017 (week 16), the outbreak extended to Kapoeta Counties near Uganda and Kenya affecting nomadic communities in hard to reach areas ([Figure 3](#)). In this area, access to drinking water is severely restricted as the rock substrate renders borehole drilling impossible, thus forcing humans and animals to consume surface water from ponds along the road during the dry season (48). Difficult terrain, poor road network, and very poor phone network coverage were also major limitations for health workers conducting response (49). Cholera transmission has also been facilitated due to a lack of adherence to the dead body management procedures and IPC in treatment centers. Furthermore, patient conditions were worsened by the food crisis prevailing in the area (48).

On May 18th (week 20), a number of cholera-related deaths in facilities (eight deaths) and in the community (20 deaths) were reported in Tonj East among cattle herders (50) ([Figure 3](#)). The outbreak was probably amplified by inadequate infection control measures and case management as well as the delayed response given the poor road network and insecurity (50). In early June, the outbreak followed the displacement of cattle herders in Ayod who were returning to Pieri in Urol County (51).

On July 28, 2017, an outbreak started in a gold mining area in Ngauro (Budi County) and spread to Nagishot following the displacement of miners (52).

Between June 18, 2016 and December 18, 2017, a total of 20,438 cholera cases and 436 deaths (CFR 2.14%) were reported in 10 states and 26 counties (3). The outbreak peaked in April (week 16) ([Figure 2](#)). Unlike previous outbreaks, the majority of cases was registered outside of Juba in Ayod County, representing 18.7% of the total number of cases. Tonj East and Kapoeta South were also heavily affected with 11.9% and 10.23% of cases, respectively. Juba notified 12.3% of the total number of cases; the most affected payams were Rajaf, Northern Bari, Mununiki and Kator in areas closer to the river Nile, not serviced by the public water utility (53) ([Figure 1](#)).

The highest attack rates were registered in the counties of Yirol East, Awerial and Ayod, where the outbreaks took place in nomadic communities ([Figure 3](#)). A high CFR was reported from Nile River islands and swampy areas bordering the Sudd Swamp in Terekeka, Duk, Yirol East, Bor, Panyijiar and Leer counties as well as cattle camps in Awerial, Yirol East, Bor, Duk, Uror, Ayod, Kapoeta South, Kapoeta North and Kapoeta East (39). In those hard to reach areas, access to healthcare is limited, especially during the onset of the outbreak. In Budi County, a high CFR (7%) was recorded with a high number of deaths occurring in the community. The humanitarian response in this county was hampered by insecurity and poor road conditions during the rainy season (54).

The 2016-2017 cholera epidemic probably spread to refugee camps in neighboring Uganda in July 2016 (55) and to Sudan in August 2016 (56).

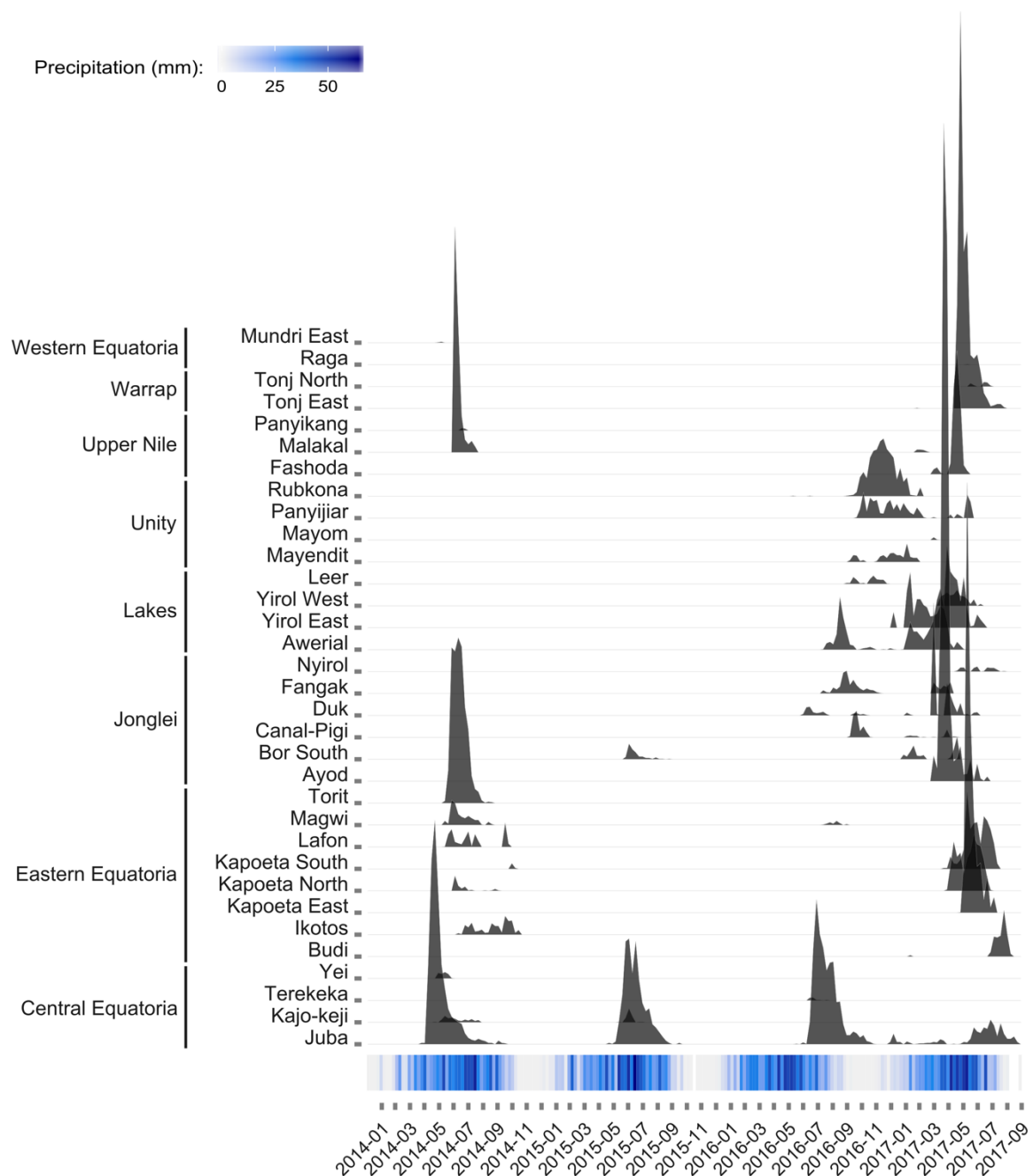


Figure 3: Epidemiological histogram of cholera cases by county and estimated weekly precipitation in South Sudan for the period 2014-2017. The cholera outbreak pattern by county and by ISO week are displayed in grey.

b. Epidemiological parameters

During the study period, Central Equatoria State had the highest cholera caseload, with 19,985 cases (40%). Juba County reported one third (16,825 cases) of the total number of cases and was affected every year; outbreaks lasted an average of nine months (37 weeks). Yei County, which is located close to the border with the DRC and Uganda, was affected by outbreaks three times with a short average duration of six weeks ([Table 2](#)).

Eastern Equatoria State reported 21% (10,707 cases) of the total number of cholera cases; outbreaks lasted an average of four months (17 weeks). Magwi County was affected four times. The counties of Torit and Kapoeta East reported the highest number of cases, 2,521 and 2,090 cases, respectively. A high CFR was registered in Budi (7%) and Lafon (6.4%) ([Table 2](#)).

The State of Jonglei reported 12% (6,201 cases) of the total number of cholera cases. Bor South and Duk were the most regularly affected counties, they were affected five and three times, respectively, by outbreaks of short duration ranging from eight weeks to 12 weeks. Ayod County registered the highest number of cases (3,578 cases/7%), although it was only affected once (i.e., 2017). A high CFR of 6.7% was reported in Duk ([Table 2](#)).

In Upper Nile State, Malakal County was affected three times; outbreaks lasted six weeks on average. The states of Warrap, Unity and Lakes were affected twice during the period with an average outbreak duration of 16, 39 and 49 weeks, respectively. The most frequently affected counties include Tonj East, Tonj North (Warrap), Panyijiar and Rubkona (Unity). The counties of Panyijiar (Unity) and Yirol East (Lakes) reported a high CFR of 4.7% and 4.6%, respectively ([Table 2](#)).

The county of Wau (Western Bahr El Ghazal), which hosts the second most populated city, was affected once in 2007 by a small outbreak (112 cases) ([Table 2](#)).

c. Overview of cholera outbreak dynamics

From 2006 to 2017, suspected cholera cases were first detected in Eastern Equatoria State, either in counties close to the Ugandan border (Yei in 2006 and Magwi in 2008) or the capital city Juba (2014, 2015 and 2016). The state of Eastern Equatoria and Juba City in particular seem to play a role in amplification and diffusion of cholera outbreaks towards the east along the border with Uganda and Kenya and along the Nile River up to the city of Malakal. Outbreak patterns changed over time, with outbreak onset during the dry season (January-February) in 2006 and 2008 and during the rainy season (April-June) from 2014 to 2017 ([Figure 3](#)). Cholera cases were reported during the dry season (November to February) in 2006-2007, 2008-2009 and 2016-2017 ([Figure 3](#)).

The states of Central Equatoria, Eastern Equatoria, Jonglei and Unity were frequently affected by cholera outbreaks; they were affected at least four times during the study period and represented 78% of the total number of cases. A high CFR was registered mainly in the Sudd, in areas where access is limited either due to the conflict or difficult geographical terrain ([Figure 1](#)) ([Table 2](#)).

Overall, the country appeared to be affected by sub-regional outbreaks implicating border countries such as Uganda (9,13,21,31,55), Kenya (12,13), Ethiopia (8,14,57) and Sudan (56). However, additional evidence, such as genetic analysis of *V. cholerae* isolates, are required to confirm the origin and spread of cholera to and from neighboring countries.

STATE / COUNTY	Cases / Deaths	% of total cases	Cumulative incidence rate (per 10,000 inhab.)	Case Fatality Ratio (%)	Recurrence (No. of outbreaks)	Outbreak duration (average in weeks)	Median onset week [min-max]
CENTRAL EQUATORIA	19 985 / 80	39.6	136.7	1.3	5	37	20 [16-26]
JUBA	16 827 / 75	33.4	336.1	1.2	5	37	20 [16-26]
YEI	3 007 / 0	6.0	114.9	0.0	3	6	20 [20-20]
KAJO-KEJI	136 / 0	0.3	5.4	0.0	2	9.5	23 [22-24]
EASTERN EQUATORIA	10 707 / 74	21.2	91.0	1.0	5	17	22 [16-32]
TORIT	2 521 / 0	5.0	186.5	0.0	2	15	23 [23-23]
KAPOETA EAST	2 090 / 25	4.1	98.9	1.2	1	12	21 [21-21]
LAFON	1 621 / 16	3.2	118.4	6.4	2	20	23 [23-23]
MAGWI	1 460 / 1	2.9	66.6	0.4	4	10.5	27.5 [23-32]
KAPOETA SOUTH	1 026 / 10	2.0	100.1	1.0	2	10.5	29 [16-42]
KAPOETA NORTH	1 017 / 1	2.0	76.6	0.1	2	14.5	21 [17-25]
IKOTOS	671 / 0	1.3	60.2	0.0	2	20	27 [27-27]
BUDI	301 / 21	0.6	23.6	7.0	1	8	29 [29-29]
JONGLEI	6 201 / 93	12.3	35.1	1.9	5	22	25 [3-26]
AYOD	3578 / 39	7.1	199.4	1.1	1	19	12 [12-12]
BOR SOUTH	768 / 6	1.5	26.5	2.3	5	8	18 [3-25]
DUK	534 / 36	1.1	63.2	6.7	3	12	26 [5-41]
PIBOR	373 / 0	0.7	19.5	0.0	1	n/a	n/a
FANGAK	364 / 5	0.7	24.8	1.4	2	13	22 [12-32]
AKOBO	314 / 0	0.6	17.7	0.0	1	n/a	n/a
CANAL-PIGI	200 / 5	0.4	15.2	2.5	2	11.5	22.5 [5-40]
WARRAP	4 493 / 43	8.9	35.0	1.8	2	16	19 [19-19]
TONJ EAST	3 062 / 43	6.1	204.6	1.8	2	16	19 [19-19]
TONJ NORTH	731 / 0	1.4	34.3	0.0	2	7	24 [24-24]
TONJ SOUTH	700 / 0	1.4	62.4	0.0	1	n/a	n/a
UNITY	3 333 / 50	6.6	40.3	2.4	2	39	39 [39-39]
RUBKONA	1 509 / 10	3.0	103.4	0.9	2	24	39 [39-39]
PANYIJAR	1 503 / 28	3.0	221.6	4.7	3	14.5	30 [18-42]
MAYENDIT	225 / 5	0.4	27.7	2.2	1	21	40 [40-40]
LAKES	3 193 / 80	6.3	35.1	2.8	2	49	32 [32-32]
YIROL EAST	1 454 / 67	2.9	160.4	4.6	1	29	52 [52-52]
AWERIAL	1 171 / 13	2.3	193.2	1.1	1	43	32 [32-32]
RUMBEK CENTRE	332 / 0	0.7	16.6	0.0	1	n/a	n/a
YIROL WEST	236 / 0	0.5	17.4	0.0	1	14	14 [14-14]
UPPER NILE	2 422 / 11	4.8	18.6	0.7	4	12.5	16.5 [8-25]
MALAKAL	1 375 / 0	2.7	75.4	0.0	3	6.5	16.5 [8-25]
FASHODA	716 / 11	1.4	141.4	1.5	1	12	12 [12-12]
LUAKPINY-NASIR	322 / 0	0.6	11.7	0.0	1	n/a	n/a
WESTERN BAHR EL GHAZAL	113 / 0	0.2	2.5	0.0	1	n/a	n/a
WAU	112 / 0	0.2	5.3	0.0	1	n/a	n/a

Table 2: Epidemiological parameters of cholera outbreaks by main affected states and counties during the periods 2006-2007 and 2014-2017. Case fatality ratio, outbreak duration and median onset week are calculated over the 2014-2017 period. Counties that account for less than 100 cases of cholera during the period are not displayed.

d. Risk factors

Conflict and population displacement

During the 1970s and 1980s, upsurges in cholera cases in Southern Sudan were linked to refugee displacement from Uganda and Ethiopia due to political turmoil and famine (8). In the twentieth century, following the end of the civil war with North Sudan in 2005, displaced residents began returning to Southern Sudan. Furthermore, returnees from Kenyan, DRC and Ugandan refugee camps settled among local communities, thus likely reintroducing the disease in the country (14).

Two years after the independence of South Sudan in July 2011, an internal conflict erupted in Juba between political factions (December 2013) and expanded countrywide; the states of Jonglei, Unity and Malakal were the most affected. Despite the signing of a peace agreement in August 2015, another major crisis erupted in July 2016 in Juba and intensified in the Greater Equatoria region, an area that was previously not affected. Since 2013, the country has been experiencing some of the world's most significant population displacement events, with the number of IDPs topping two million during the first half of 2017 (58). Furthermore, many people have been moving back and forth between South Sudan and neighboring countries, particularly Uganda, which harbors large refugee camps. Multiple and unpredictable population movement in and out of crowded IDP and refugee camps increases the risk of exportation and importation of outbreak-prone diseases such as cholera. Security concerns continue to be a major obstacle hindering timely and comprehensive response efforts to public health emergencies and cholera outbreaks in particular. Humanitarian interventions in conflict areas have been either limited or hampered in affected communities such as those in Leer, Mayendit, Panyijiar, Yirol East and West, Ayod, and Torit Counties during the 2016-2017 outbreak (39,59,60).

Structural factors

Since the onset of the crisis in December 2013, humanitarian aid has focused on life saving activities in a highly volatile environment; limited investments have been made to substantially improve social services. In Juba, the public water system only supplies approximately 17% of the city's population (53). With the dramatic increase in the cost of fuel, the cost of safe water delivery via water trucks in urban areas has topped out, and water vendors have turned towards river water, thus rendering households less likely to consume safe water (51,57). Additionally, the destruction of infrastructure including water points and the closure of health facilities were a direct consequence of the conflict (61).

Major population displacement towards river islands or swampy areas has forced communities to rely on surface water with limited capacity to ensure that water is safe for consumption. Straying from homes and villages also had an impact on the severity of the disease, when sick individuals were forced to walk for hours or days to reach a health facility, such as those who found refuge on the Sudd islands (43,44).

South Sudan has a largely underdeveloped road network with the current interstate and international road network consisting of approximately 5,000 km of gravel roads and 300 km of asphalt roads (62). During the rainy season many roads are largely inaccessible, which thus isolates large areas of the country. Poor road conditions and limited access to healthcare contributed to relatively high CFRs in hard to reach areas along the Nile River and the border regions with Uganda and Kenya. This was further exacerbated during the 2016/2017 outbreak in the Sudd islands and cattle camps (44,49,59).

Inadequate pre-positioning of materials and limited technical capacity for proper isolation of cholera cases have been observed multiples times in the past years, which has certainly played a role in amplifying cholera transmission within treatment centers, thus facilitating the spread of the disease (21,26,27,32–34,43,48–51,63). Restricted access to basic services, such as appropriate healthcare, safe drinking water and adequate sanitation facilities, are a direct effect of the conflict and major drivers of cholera outbreaks in the country.

The protracted crisis coupled with drought has led to serious food shortages in the country. In October 2016, serious food insecurity coupled with cases of cholera was reported in Ayod County (64). In February 2017, famine was declared in the northern part of the country in Leer and Mayendit Counties (65). In June, food security crisis and cholera were observed in Kapoeta (60). Severe malnutrition favors cholera infection by lowering the gastric acid levels of individuals (66), and diarrhea is considered more severe among patients suffering from malnutrition (67).

Environmental factors

The Sudd, which is one of the world's largest swamps, formed by the White Nile River and stretching from Bor to Malakal, seems to be the scene of recurrent cholera outbreaks (14,68). Since the onset of the conflict, thousands of IDPs have temporally settled on large, solid floating vegetation islands or at the edge of the swamp in overcrowded conditions (69). An assessment conducted in the Southern Jonglei islands in December 2015 has indicated that inhabitants use the swampy water surrounding the islands for drinking, cooking, bathing and defecating. Due to the low water table in some areas, it is impossible to build pit latrines (70). With the large influx of IDPs, the environmental conditions in the Sudd seem to be particularly prone to the spread of diarrheal diseases including cholera, as observed during the 2016-2017 outbreak that largely affected this area. Proximity to bodies of water has also been highlighted as a risk factor during the 2016-2017 epidemic in the Bentiu IDP camp. Cholera incidence was higher in sectors surrounding the water retention pond (38).

High-risk practices

Open defecation has been often reported as a contributing factor to cholera outbreaks over the past years (18,21,34,38,43,50,68,71). A 2015 Knowledge Attitude and Practice (KAP) survey conducted in Kadjo-Keji, Torit and Magwi Counties revealed that 76% (n=81) of respondents in rural settings performed open defecation, which also reduces the possibility to then wash hands with soap (71). An assessment performed by the social mobilization sector in 2014 also mentioned a high rate of open defecation in Torit, especially along the river (34) where the population can hide behind vegetation. Regarding the perception of water for drinking purposes, the 2015 survey highlighted that 70% (n=110) of respondents in Kajo Keji believe that clear water is safe (71), while the 2014 assessment stated that the community in Torit prefer drinking river water compared with borehole water, which tastes salty (34). The survey also explored community behaviors associated with medical care and showed that 18% (n=35) of respondents in Torit used traditional medicine and 26% (n=54) in Magwi urged patients to drink less liquids (71).

Case control studies investigating individual high-risk behaviors were conducted in Juba during the 2007 and 2014 epidemics. The results showed that using a water source close to the place of residence (72), eating outside of the home (29), and traveling (29) or living in Juba for less than one year (72) were significant risk factors for cholera. While individuals that consumed a hot meat or hot fish meal (72), treated drinking water or received OCV were less likely to contract the disease (29). Case investigations during the 2006 – 2017 period sited cholera transmission during funeral rituals (21,32) and around affected households (21,30,32,43,48). Being in a facility that receives cholera cases was also noted as a risk factor (21,26,32,33,51).

e. High risk populations

In the past years, outbreaks have been reported among IDPs (6,73) as well as military or armed groups (6,32,60,74) in various counties (Table 3). During the 2014 outbreak only, cholera incidence was higher among IDPs compared with non-IDPs outside of Juba (Wau Shilluk) (36).

During the 2016 and 2017 epidemics, reports from the Ministry of Health highlighted additional high-risk populations. The cholera outbreak heavily affected displaced and host communities living on islands of the Sudd Swamp (38–44,63,68) (Table 3). In February 2017, an increase in cholera cases was observed in cattle camps and communities living in hard to reach villages at the end of the dry season in the states of Jonglei and Lakes. Thereafter, cholera outbreaks broke out among pastoralists in various parts of the country (46,48,51,75,76) (Table 3). It was found that pastoralists gathered around the remaining water sources usually in the swampy areas along rivers or water bodies. Communities in cattle camps live in overcrowded conditions with limited capacity to practice hygienic behaviors. The unpredictable movement of cattle herders also rendered a rapid response a major challenge (68). In July 2017, cholera transmission was high in gold mining sites in Kapoeta and Budi County (Ngauro). The outbreak followed the displacement of miners in Budi (52,77).

POPULATION GROUP	STATE	COUNTY	LOCATION
IDPs IN CAMPS / SETTLEMENTS	CENTRAL EQUATORIA	JUBA	UN PoC; Tongping; Don Bosco; Mahad; Mangatain; Gumbo
	JONGLEI	BOR SOUTH	Mingkaman
	UNITY	PANYIJAR	
		RUBKONA	Bentiu UN PoC
	UPPER NILE	FASHODA	Aburoc
MILITARY / ARMED GROUPS		MALAKAL	Wau Shiluk
	CENTRAL EQUATORIA	JUBA	Kaka; Panyagor; Giada; New site; Luri; Nesitu; Gondokoro; Bilpam
	CENTRAL EQUATORIA	TEREKEKA	Magri; Mangala
		YEI	
	EASTERN EQUATORIA	MAGWI	Owinykibul
POPULATION IN ISLANDS / SWAMPS	NORTHERN BAHR EL GHAZAL	AWEIL	Pariath
	UPPER NILE	MALAKAL	
	CENTRAL EQUATORIA	TEREKEKA	
	JONGLEI	AYOD	Haat
		BOR SOUTH	Kwei, Twic East, Pajatriei and Wutnathel islands; Dhiam Dhiam (port)
POPULATION IN CATTLE CAMPS		DUK	Kawer; Long; Moldova; Koyom
	LAKES	YIROL EAST	Pabulek and Kaduwaw Islands; Shambe at the border of the Sudd; Langmatot
	UNITY	LEER	
		PANYIJAR	Ganyliel and Tayar Islands; Nyal at the edge of the Sudd
	EASTERN EQUATORIA	KAPOETA EAST	Jie
POPULATION IN CATTLE CAMPS		KAPOETA NORTH	
		KAPOETA SOUTH	
	JONGLEI	AYOD	Buol; Torch; Tar; Pagil; Mogok
		BOR SOUTH	Jalle; Pieri
		DUK	Mamour; Padiet; Amiel; Dorok
POPULATION IN CATTLE CAMPS	LAKES	AWERIAL	Dor
		YIROL EAST	Guthom; Tharnuar
POPULATION IN CATTLE CAMPS	WARRAP	TONJ EAST	

Table 3: Population or group affected by cholera outbreaks during the period 2006-2014.

III. Hotspot classification

The hotspot classification algorithm has been initially developed and applied for 12 West African countries in 2014/2015 as part of a West and Central Africa Cholera Platform project lead by UNICEF Regional Office [3]. The main principle is to classify cholera-affected areas based on epidemiological characteristics (recurrence, intensity and length of epidemic). The method has been refined to the South Sudan context due to heterogenous epidemiological data and is based on a distribution threshold of the following epidemiological criteria: the number of outbreaks and the median outbreak duration over the 2006-2007 and 2014-2017 periods (Figure 4). Detailed information regarding the methods used to classify hotspots and the limitations of the analysis are described on p8 and p42, respectively.

In South Sudan, 18 cholera hotspots were identified and classified as follows (Figure 4) (Figure 5):

- **Type 1 - hotspots characterized by high frequency (≥4 outbreaks) and extended duration (≥10.5 weeks) of cholera outbreaks**

Two locales reporting one third of the total number of cases (36%) were defined as highest priority areas: **Juba** (Central Equatoria), the capital of South Sudan, and **Magwi** (Eastern Equatoria) at the border with Uganda.

- **Type 2 - hotspots characterized by moderate frequency (between 2 and 4 outbreaks) and extended duration of cholera outbreaks (≥10.5 weeks)**

Twelve counties reporting 27% of the total number of cases were defined as high-priority areas: **Ikotos** (Eastern Equatoria) at the border with Uganda; **Torit** (Eastern Equatoria), **Lafon** (Eastern Equatoria), **Kapoeta North** (Eastern Equatoria) and **Kapoeta South** (Eastern Equatoria) close to Juba and/or Uganda; **Rubkona** (Unity), which hosts the Bentiu PoC camp; **Panyijiar** (Unity) and **Fangak** (Jonglei) along the River Nile; **Canal-Pigi** (Jonglei) close to Malakal and **Tonj East** (Warrap State) along the road between major cities Malakal and Wau.

- **Type 3 - hotspots characterized by high frequency (≥4 outbreaks) and short duration (<10.5 weeks) of cholera outbreaks**

One county reporting 1,5% of the total number of cases was defined as a medium-priority area: **Bor South** (Jonglei), which hosts the major city of Bor located along the Nile river between Juba and Malakal.

- **Type 4 - hotspots characterized by moderate frequency (between 2 and 4 outbreaks) and short duration of cholera outbreaks (<10.5 weeks)**

Five counties reporting 11% of the total number of cases were defined as low-priority areas: **Yei** (Central Equatoria) at the border with the DRC; **Kajo-Keji** (Central Equatoria) at the border with Uganda; **Duk** (Jonglei), and **Malakal** (Upper Nile) along the Nile River; and **Tonj North** (Warrap).

Some counties with high attack rates (≥100 per 10,000 pop) were not classified as hotspots as they were only affected once (during the 2016/2017 large-scale outbreak). Nevertheless, specific groups of populations vulnerable to cholera outbreaks were identified in those counties such as nomadic pastoralist communities (Kapoeta East, Yirol East, Awerial and Ayod counties), IDPs (Awerial county) and refugees (Fashoda county) (Figure 4). Those high risk populations should be considered for preparedness and early response when anticipating the occurrence of a large-scale outbreak.

Overall, the regularly affected communities are located in major cities (e.g., Juba, Yei, Nimule, Bor, Bentiu, Malakal), counties bordering Uganda and Kenya, and the vast marshland of the Sudd region, as represented in the situation map below (Figure 5). The cholera hotspots (Type 1 – Type 4) accounted for 76% of the disease burden throughout the study period. Twelve counties affected by outbreaks of extended duration (Type 1 and Type 2) reported two thirds of the total number of cases.

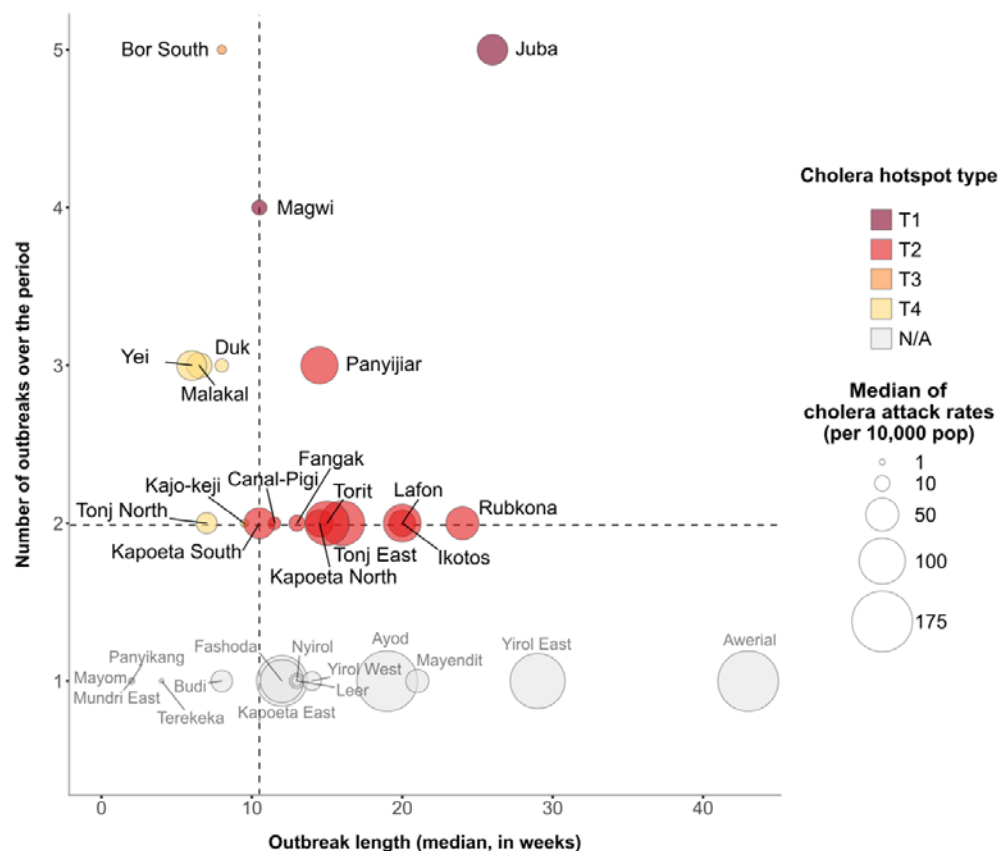


Figure 4: Cholera hotspot classification chart.

T1: Highest-priority area with high frequency (>90th percentile; >3 outbreaks) and extended duration (≥40th percentile; ≥10.5 weeks) of cholera outbreaks; T2: High-priority area with moderate frequency (between 60th and 90th percentile; between 2 and 3 outbreaks) and extended duration of cholera outbreaks; T3: Medium-priority area with high frequency and short duration of cholera outbreaks (<40th percentile; <10.5 weeks); T4: Low-priority area with moderate frequency and short duration of cholera outbreaks.

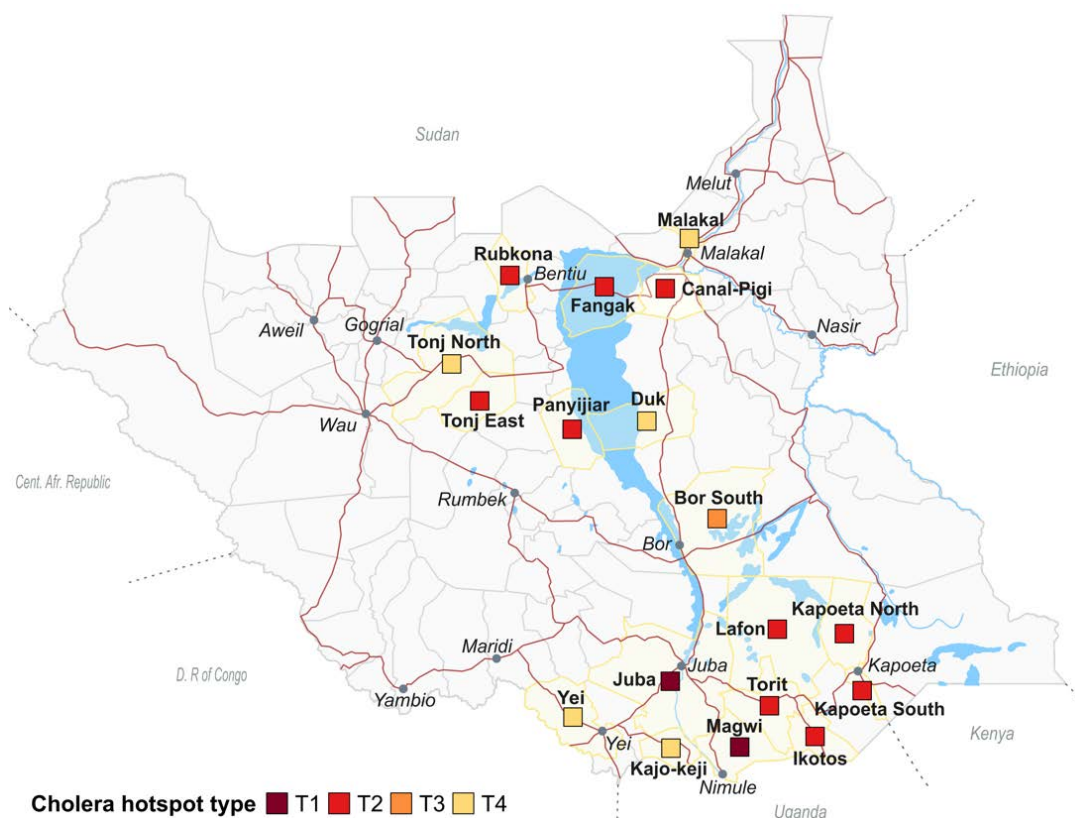


Figure 5: Cholera hotspot map of South Sudan for the periods 2006-2007 and 2014-2017.

PART 2 – CHOLERA CONTROL AND PREVENTION IN SOUTH SUDAN

I. General WASH statistics

In 2010, before the onset of the current crisis, the official statistics indicated that 68% of the population had access to improved drinking water and that only 13% use sanitary means of excreta disposal (78). No recent accurate estimate of the national WASH situation is available due to the restricted access in the field, which hampers the systematic collection of key indicators. The last survey conducted by the Joint Monitoring Programme (JMP) in 2015 indicates that nationwide access to improved drinking water sources (i.e., improved source, provided collection time is not more than 30 minutes for a round trip, including queuing) dropped to 50% since 2010 with 48% and 60% in rural and urban settings, respectively (79). However, the prolonged conflict has further reduced access to water infrastructures. An estimated 40% of WASH infrastructures are likely to be either inaccessible due to insecurity or non-functional due to destruction of equipment and poor operation and maintenance (61). Additionally, the rapid inflation in fuel costs has led to a dramatic increase in the cost of water delivered by truck as well as a reduction in the quantity of water supplied by networks (53). Thus, the proportion of populations relying on surface water, which stood at 7% in 2015 (79), has probably increased, especially for households living in urban areas and displaced populations hiding in bushes and/or swampy areas.

In 2015, according to JMP estimates, only 10% of the population have access to at least basic sanitation (79). The percentage is even lower in rural settings with approximately 6% of the population using improved facilities that are not shared with other households (79). In that context, 61% of the population must resort to open defecation (79). The practice is widespread in rural settings with approximately 70% of the population; these numbers have dropped to 22% in urban settings (79). Since 2015, the number of IDPs have continued to increase in the country, reaching two million (16% of the national population) by May 2017 (58). Thus, sanitation coverage has most likely decreased.

The 2015 JMP survey does not include national hygiene estimates for South Sudan. KAP surveys were conducted by Oxfam in 2016 and 2017 in Juba. The results show that a large proportion (67%) of households do not have washing facilities and that 16% do not wash their hands with soap, citing the cost of soap as the main reason (53). In rural settings, given the high rate of open defecation (70%), the majority of the population most likely does not wash their hands with soap after excreta disposal.

II. Health, WASH and C4D interventions

In South Sudan, cholera control and prevention interventions at the national and local levels are coordinated by a Task Force chaired by the Ministry of Health (80). The Cholera Task Force includes representatives of the Ministry of Water, United Nations agencies, Non-Governmental Organizations (NGO) and community-based organizations from the Health and WASH clusters. The Task Force is organized into five sub-committees corresponding to the following themes: 1) coordination; 2) logistics and security; 3) surveillance, laboratory, case management, and oral cholera vaccine; 4) water, sanitation and hygiene; and 5) social mobilization and health education (80).

The strategy promoted by the Cholera Task Force focuses on emergency interventions during outbreaks and preparedness activities during the inter-epidemic period in all states. The approach is based on the delivery of an integrated package of services to affected households, communities, institutions and public places during outbreaks. When the outbreak is already widespread throughout the community, the response strategy is based on targeting areas with active cholera transmission (80).

The outbreak threshold has been defined as one suspected cholera case according to the following standard case definition:

- a patient aged five years or more who develops severe dehydration or dies from AWD in an area where cholera is not known to be present (6)
- or
- a patient aged two years or more that develops AWD, with or without vomiting, in an area where cholera has been confirmed (6).

The draft version of the Cholera Response and Prevention Plan for 2018-2020 has integrated the notion of hotspots developed in the present study following the presentation of the preliminary results in December 2017. Additionally, sustainable Health, WASH, social mobilization improvements in cholera hotspots are now planned (6).

Since 2014, lessons learnt exercises have been conducted each year, in which strengths, weaknesses, lessons learnt, recommendations and follow-up actions are identified per sector. Outcomes of the outbreak response review is then integrated into the Cholera Response and Prevention Plan, which is updated on a yearly basis (80). In December 2017, the Ministry of Health together with its partners has decided to expand the yearly cholera plan to a multiyear plan.

Cholera surveillance and response is led by the Epidemic Preparedness and Response (EPR) unit of the Ministry of Health with the support of WHO and the Health cluster. The identification of a single suspected cholera case warrants an investigation by the outbreak response team, which includes stool sample collection and the implementation of immediate control measures (6). Since 2014, cholera confirmation has been conducted by the National Public Health Laboratory in Juba. Culture sensitivity and specificity has been performed at the Pasteur Institute in Paris, since 2015. Once the alert threshold is reached, the cholera Task Force is activated at the national and state levels, line lists are updated on a daily basis, situation reports are produced regularly, and community health workers are trained in active case finding (6). Task Force meetings are held twice a week during the acute phase of the disease. Sharing of information on the epidemiological situation with neighboring country is limited and happens mainly at the agency level; nevertheless, a two-day cross-border meeting was held in February 2018 between the Ministries of Health of South Sudan and Uganda with the support of the WHO and UNICEF to improve the surveillance of cholera and other epidemic diseases in border areas.

Health cluster meetings, which are led by the WHO, are held once a week during the acute phase of the epidemic. Beyond the surveillance component, the Health Cluster implementing partners are in charge of medical care for cholera patients including community management through oral rehydration points (ORPs), IPC in healthcare facilities through training and provision of adequate supplies, and support for the practice of safe and dignified burials (80).

WASH cluster cholera technical group meetings were held on a weekly basis during the acute phase of the outbreak. WASH cluster implementing partners are responsible for water trucking, hygiene promotion, distribution of hygiene kits, solid waste disposal, construction of latrines and support provided to WASH facilities in Cholera Treatment Centers (CTCs) and ORPs (80). The social mobilization working group lead by the UNICEF C4D section is a component of the WASH cluster. C4D implementing partners are responsible for supporting mass media, house-to-house hygiene promotion, public demonstrations of good practices, distribution of soap, and mobilizing local and religious leaders as well as persons of influence (80).

The OCV working group members conduct cholera risk assessments, secure and procure the vaccines, implement OCV campaigns and run coverage surveys (80). The Shanchol® vaccine was introduced for the first time in South Sudan in 2012 (81).

Since then, approximately two million doses of OCV have been administered either during preemptive or reactive campaigns targeting different groups/populations (IDPs, refugees, host populations, etc.) in various settings (open, camps, hard to reach sites, conflict settings, etc.).

III. Oral cholera vaccine uses

a. OCV strategy

In South Sudan, OCV is used in combination with other control measures to either prevent cholera outbreaks among specific populations (i.e., refugees, IDPs) or limit the spread of the disease in areas with active transmission (80). The first OCV campaign was conducted preemptively in four refugee camps and the host population in Maban County (Upper Nile State), which targeted approximately 160,000 persons between December 2012 and February 2013 (81). Since then, the Shanchol® vaccine has been deployed in the country based on WHO prequalification.

From 2012 to 2016, approximately one million doses of OCV were used in South Sudan; 81% of the total number of doses were administered in refugee and IDP formal settlements as a preemptive measure ([Table 4](#)). The vaccine was also deployed during cholera outbreaks in Juba in military camps and in areas with active transmission applying the ring vaccination strategy. The approach aimed at stopping residual transmission in an open setting by administering a single dose of the vaccine to patient contacts and neighbors of affected households (39). In total, 19% of doses were administered during reactive campaigns ([Table 4](#)).

Between March and June 2017, the Ministry of Health (with the support of the WHO and the Global Task Force on Cholera Control (GTFCC), together with participants from the Health and WASH clusters) and the Ministry of Water developed a plan for rational use of OCV (74). The deployment of approximately four million doses of OCV over the next two years targeting at least two million people aged one year and above was proposed to the International Coordinating Group (ICG) and the GTFCC (74,82). The two-year plan foresees the implementation of WASH and social mobilization emergency intervention such as distribution of non-food items and hygiene promotion during cholera outbreaks (39,74).

From January to October 2017, approximately one million doses were delivered; 97% of the total number of doses were administered during reactive vaccination campaigns targeting twelve counties ([Table 4](#)). During that period, the vaccine was used for the first time during an outbreak outside of Juba and was expanded towards different groups of the population such as hard to reach villages, cattle herders and IDP informal settlements.

In 2015 and 2016, given the vaccine shortage and high population mobility, the Ministry of Health together with the WHO and Health partners chose to pilot single-dose campaigns either preemptively or reactively ([Table 4](#)) (83). The results of a case-cohort study conducted in Juba indicated a rather good short-term protection of 87.3% (95% CI 70.2–100.0) (84). In 2017, the strategy evolved towards multiple, one-round campaigns in areas reporting cases, followed by administration of a second dose within six months. The administration of a second dose aimed at preventing cholera upsurge during the next outbreak (85), given the lack of evidence regarding long-term efficacy of the vaccine (beyond six months) (86).

b. OCV campaign information

Between December 2012 and October 2017, approximately two million doses of OCV were used, of which 59% were administered during reactive campaigns and 41% during preemptive campaigns. Twenty-three campaigns were conducted with a two-dose regimen (either preemptively or reactively), while ten campaigns involved a single dose ([Table 4](#)).

In 2017, vaccination coverage (based on population census data) after the first round of OCV varies from 52% in Kapoetha North to 91% in the Aburoc IDP camp (52). Vaccination coverage was suboptimal in Kapoetha Counties with limited access to some areas due to insecurity, community mobility (cattle camps) and poor road networks (52).

Overall, the mobilization of Health cluster partners in deploying the cholera vaccine to control cholera outbreaks is noteworthy. In 2017, a dozen NGOs implemented vaccination campaigns (ARC, CMD, HLSS IOM, IRC, Medair, MSF-E, MSF-CH, MSF-H, SCI), while the Ministry of Health together with the WHO secured and planned the deployment of OCV doses and UNICEF provided logistical support for cholera vaccine handling and cold chain.

c. OCV campaign timing

In 2017, all reactive vaccination campaigns conducted outside of Juba and Bor South were carried out after the epidemic peak either in IDP camps and open settings (left column) or hard to reach areas (right column) ([Figure 6](#)). In Bor South, a small-scale outbreak, in which case numbers decreased rapidly, occurred after the second vaccination round. However, it remains unclear whether the outbreak affected the population that received the vaccine. The delayed delivery of the OCV, in the aftermath of the cholera outbreak raises questions concerning the impact of the intervention.

YEAR	STATE	COUNTY	Community type	Doses used	Reactive / Pre-emptive	Single dose / 2-dose
2012	UPPER NILE	MABAN	refugees camp; open setting	258 925	pre-emptive	2-dose
2014	LAKES	AWERIAL	IDP camp/settlement	110 997	pre-emptive	2-dose
2014	CENTRAL EQUATORIA	JUBA	IDP camp/settlement	43 257	pre-emptive	2-dose
2014	UPPER NILE	MALAKAL	IDP camp/settlement	30 108	pre-emptive	2-dose
2014	JONGLEI	BOR SOUTH	IDP camp/settlement	5 809	pre-emptive	2-dose
2014	UNITY	RUBKONA	IDP camp/settlement	35 596	pre-emptive	2-dose
2015	UNITY	RUBKONA	IDP camp/settlement	140 971	pre-emptive	2-dose
2015	CENTRAL EQUATORIA	JUBA	IDP camp/settlement	50 670	pre-emptive	2-dose
2015	UPPER NILE	MALAKAL	IDP camp/settlement	80 079	pre-emptive	2-dose
2015	CENTRAL EQUATORIA	JUBA	open setting ; military camp	170 355	reactive	single dose
2016	UPPER NILE	MALAKAL	IDP camp/settlement	14 964	pre-emptive	single dose
2016	UPPER NILE	MELUT	IDP camp/settlement	16 970	pre-emptive	single dose
2016	CENTRAL EQUATORIA	JUBA	IDP camp/settlement; military	10 098	reactive	single dose
2017	UNITY	LEER	IDP settlement	30 772	pre-emptive	single dose
2017	UPPER NILE	MALAKAL	open setting	10 499	reactive	pending 2nd dose
2017	JONGLEI	BOR SOUTH	IDP camp/settlement	3 811	reactive	2-dose
2017	LAKES	AWERIAL	IDP camp/settlement	110 808	reactive	2-dose
2017	UNITY	RUBKONA	IDP camp/settlement	150 117	reactive	2-dose
2017	JONGLEI	AYOD	hard to reach	19 592	reactive	single dose
2017	UPPER NILE	FASHODA	IDP camp/settlement	10 723	reactive	pending 2nd dose
2017	UNITY	RUBKONA	open setting	70 296	reactive	2-dose
2017	JONGLEI	AYOD	hard to reach	23 093	reactive	2-dose
2017	CENTRAL EQUATORIA	JUBA	IDP camp/settlement	7 845	reactive	2-dose
2017	EASTERN EQUATORIA	KAPOETA EAST	hard to reach	85 058	reactive	pending 2nd dose
2017	EASTERN EQUATORIA	KAPOETA NORTH	hard to reach	154 603	reactive	2-dose
2017	EASTERN EQUATORIA	KAPOETA SOUTH	hard to reach	78 863	reactive	pending 2nd dose
2017	WARRAP	TONJ EAST	hard to reach	160 862	reactive	pending 2nd dose
2017	CENTRAL EQUATORIA	JUBA	open setting	105 925	reactive	pending 2nd dose

Table 4: Summary of oral cholera vaccination campaigns conducted in South Sudan during the period December 2012-October 2017.

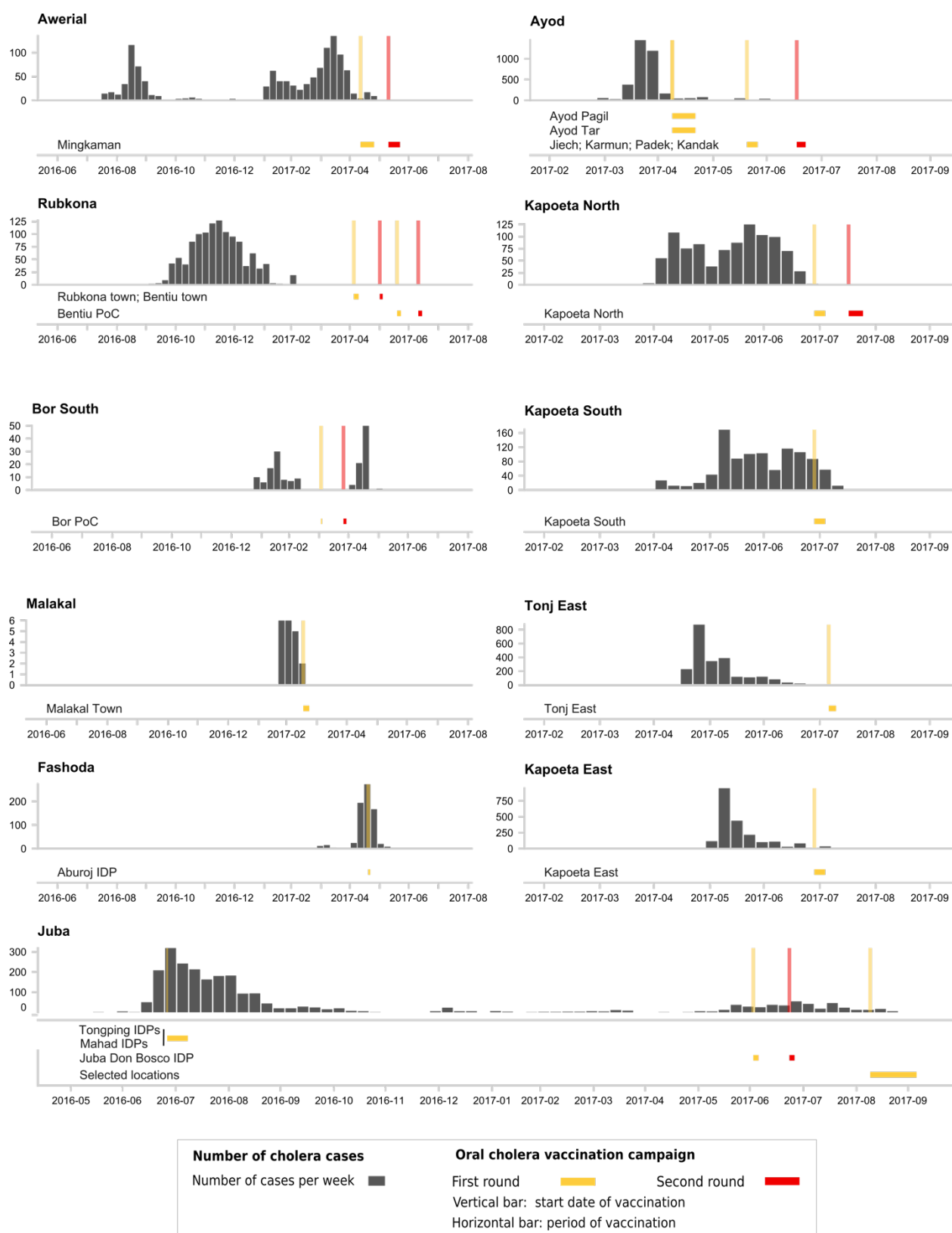


Figure 6: Epidemiological histogram and period for reactive oral cholera vaccine campaigns by county during the period June 2016-October 2017.

d. Discussion and outlook

In South Sudan, stakeholders face multiple challenges to maintain appropriate vaccination coverage. The primary challenge includes continued and massive population displacement with no clear pattern since December 2013. In the Bentiu UN PoC camp, the registration of individuals (who were not vaccinated during the previous campaign) coming from surrounding counties experiencing recurrent community clashes (87) led to a drop in vaccination coverage from 82% (31) to 40% (38) between June 2015 and December 2016. The same observation was made in April 2015 in the Juba UN PoC camp, where vaccination coverage fell from 60% to 17% 14 months after an OCV campaign was conducted (37). In 2017, the restricted number of available OCV doses and the willingness to quickly maximize the number of persons living in an affected county resulted in the delayed application of a second dose (within six months). Given the rapid drop in vaccination coverage in IDP sites, the 6-month delay in carrying out a second round among IDPs or cattle herders (highly-mobile population) raises the question of feasibility of reaching an acceptable two-dose vaccination coverage.

In 2017, reactive OCV campaigns were postponed or hampered due to vaccine shortages and/or access constraints (52,55,88,89) ([Figure 6](#)). Indeed, this was the first time the vaccine was deployed in South Sudan at such scale in a complex humanitarian environment combining recurrent inter-communal conflicts, hard to reach areas and mobile population groups. The decision to vaccinate one area might have occurred with delay (44,68), once the duration of the epidemic, the number of cases, and/or the death toll were already alarming (i.e., IDP camps, cattle camps). Finally, timely use of the vaccines seemed to be limited by the attempt to systematically respond with the OCV in highly-affected sites even after the outbreak peaked. To improve the readiness of future campaigns, an assessment should be undertaken to identify the multiple causes behind the delay observed in the implementation of the reactive OCV campaign in 2017.

While multiple uses of the vaccine (single-dose/double-dose, preemptive/reactive) in various settings (e.g., open setting, hard to reach site, camp) targeting different types of populations (e.g., refugees, IDPs, host communities, military, cattle herders) by various implementing partners have taken place over the past five years, there is an opportunity to draw a comprehensive analysis of the integration of OCV in controlling cholera in South Sudan. Feasibility and effectiveness to vaccinate highly mobile populations could be re-assessed (i.e., number of doses, time of delivery, target immunization level). Given the high rate of population displacement, the option of administering a second vaccine dose during preemptive or reactive campaigns with minimum delay in cholera hotspots could be discussed. Eventually, common targets (populations of interest) between various sectors (OCV and social mobilization working groups, and the WASH Cluster) could be reflected to control and prevent outbreaks in an integrated manner. Together with the preemptive delivery of the vaccine, more sustainable access to drinking water and sanitation facilities as well as behavioral change strategies (where realistic) should be considered in cholera hotspots to end cholera (4).

IV. Control and prevention gaps

To assess the cholera control and prevention measures in South Sudan, we conducted several interviews ([Annex 1](#)) and performed a comprehensive review of relevant documents. The identified weaknesses and gaps in cholera control and prevention are outlined by sector below.

Epidemiological and Laboratory Surveillance

- Significant delays between detection and notification of the disease sometimes occurred especially in hard to reach and insecure areas. Due to challenges in sample conditioning and transport, some samples that reached the laboratory in Juba were non-viable samples.
- There is no regular household level/high scale mapping of cholera cases nor identification of related clusters in urban areas to guide the implementation of response activities.
- Joint Health and WASH IPC activities targeting affected households are not conducted.
- Administrative constraints have delayed a cross-border meeting planned with Kenya and Uganda, and there is no systematic alerts and regular sharing of information between border countries at national and district levels regarding cholera outbreaks.
- While sample results are regularly shared via situation reports, there is no systematic feedback of results in the field.
- The reference laboratory does not currently have the capacity to conduct further strain analysis, such as antibiogram.
- In past years, the storage of isolates did not meet the quality management criteria for bio banking, which led to the loss of previous outbreak strains.

Case management and Infection, Prevention and Control

- Beyond security constraints and poor road network in some areas, the delays between alert and field response could have been reduced with enhanced preparedness of implementing partners (especially for development actors in Jonglei and Yei, who do not have the technical knowledge and financial capacity to respond to cholera outbreaks).
- The Ministry of Health and partners had limited IPC capacity in terms of technical knowledge and required equipment (i.e., tents, beds, etc.) mainly due to the frequent turnover of personnel, the focus on routine Public Health Care activities and the fact that County Health Department funds rarely cover public health emergency such as cholera. The situation improved during mid-2017 with the training of partners conducted by UNICEF and the WHO, especially in Kapoeta and Budi counties.
- Information regarding the number of cholera-related deaths in the community during cholera outbreaks is limited due to challenges in community surveillance and cultural barriers in some areas. Proper management of dead bodies either during burials or funerals was reported as lacking.
- Although significant guidance and materials have been developed to address the management of cholera patients suffering from malnutrition, information on SAM and cholera co-morbidity in line lists was lacking. Hence, little is known about case management practices concerning SAM patients during outbreaks.
- In the Bentiu PoC camp, the case-centered approach entails administration of a single dose of azithromycin or doxycycline to household contacts aged one year and above. This strategy may have a protective effect among household contacts, but the impact on cholera transmission has not been demonstrated (90).

Water, Sanitation and Hygiene

- The emergency WASH response was underfunded and lacked flexibility for Rapid Response Mechanism with a maximum deployment length of three months in hard to reach areas. Additionally, the 2017 Humanitarian Response Plan did not cover the cholera response in counties outside of Equatoria states.
- There is currently no strategic document for cholera response, prevention and preparedness for the WASH sector nor a technical guideline and training module to build partner capacities before and during outbreaks.
- Beyond security constraints in some areas, the delay between alert and field response could have been reduced with better preparedness of implementing partners (especially for development actors in Yei, which lack the technical knowledge and financial capacity to respond to cholera outbreaks). Additionally, a shortage of WASH supplies in the core pipeline occurred around March/April 2017.
- The water and sanitation interventions were limited to the distribution of soap and water treatment products to households as well as the repair of water points in affected communities. There was no systematic intervention targeted affected households such the distribution of household disinfection kit (HDK) and sensitization to prevent further transmission, and limited contribution to IPC in health facilities receiving cases.
- Interventions such as household kit distribution in urban areas do not target affected households or case clusters. This weakness is further exacerbated by challenges in accessing high scale epidemiological data especially for Juba.
- WASH partners have limited funding opportunities, strategic guidance and plans outside of Juba and other major towns for prevention activities in regularly affected areas (cholera hotspots).

Social Mobilization

- There is currently no strategic document for cholera response, prevention and preparedness for social mobilization and communication beyond the document developed for cattle camps.
- The social mobilization response seems to be limited to controlling ongoing outbreaks with little longer-term intervention with the objective of modifying high risk behaviors where realistic.
- There is no guidance on community mobilization and communication concerning IPC in health facilities receiving cholera cases (i.e., sensitization of caretakers) and affected households (i.e., stigmatization), although both sites play an important role in disease spread.
- Beyond security constraints in some areas, the delay between alert and field response could have been reduced with better preparedness of implementing partners. Furthermore, the response mechanism needs to be flexible and follow the quickly evolving epidemiological situation on the ground, focusing on areas reporting increasing or sustained high transmission.

Oral Cholera Vaccine

- While an OCV plan has been issued for the next two years, there is no clear mid- to long-term strategy especially for preemptive vaccination together with sustainable WASH improvements in cholera hotspots.
- A significant delay in implementing reactive OCV campaigns outside of Juba and UN PoC camps in Bor was observed, thus it is unclear what impact they may have had on cholera transmission.

- The feasibility of providing two doses of OCV to mobile populations (cattle camps and IDPs in formal and informal settlements) is a concern, especially when administered at six-month interval.
- OCV campaigns have been planned and carried out by various partners based on different risk assessments.

Cross-sectorial issues

- While response activities during an outbreak are rather well planned between Health, WASH and social mobilization teams, there is a lack of common targets, such as hotspots and high-risk populations, regarding formulation and implementation of preparedness efforts and more sustainable interventions.
- There is no clear integrated guidance concerning cross-sectorial activities such as IPC in health facilities and affected households for WASH, social mobilization and Health implementation partners.
- While Health and WASH cluster teams regularly meet during Task Force or working group meetings and discuss the epidemiological and response situation, there is a lack of in-depth discussion on cross-sectorial issues between cluster leads.
- Common Humanitarian Funds (CHF) for IPC of cholera in health facilities are channeled to Health cluster partners, which restricts access to interagency diarrheal disease (IDD) kits for some implementing partners.
- While Hygiene promotion messages promoted by Health cluster, WASH cluster and social mobilization working group mention the importance of drinking oral rehydration solutions at the onset of the disease, and large quantities of oral rehydration salts (ORS) are handled by Health cluster partners including UNICEF Health section, there is no ORS in the household kits dispatched via the core pipeline handled by the WASH cluster (UNICEF/IOM).

PART 3 - RECOMMENDATIONS

I. Recommended WASH, Health and C4D measures in cholera hotspots

The priority strategic actions in the 17 identified cholera hotspots (Type 1 to Type 4), include early detection, community-based surveillance, cross-border activities, and preparedness plans and actions ([Table 5](#)).

Mid-term WASH and social mobilization activities (1-3 years) should be implemented in priority in counties regularly affected by cholera and characterized by extended-duration outbreaks (Type 1 and Type 2) ([Table 5](#)). In such hotspots, hard to reach areas should be identified and targeted for enhanced access to health care to reduce the CFR. Given the protracted nature of the crisis and the environment in South Sudan, hotspots should be first characterized according to local constraints such as security or road access. Additionally, the specificity of each hotspot should be taken into account when designing mid-term and long-term interventions. An in-depth understanding of community beliefs and practices to inform behavioral change program as well as assessment of water access, sanitation facilities, and hygiene practices are required to conceive high-impact interventions. While preventive measures are planned, designed and implemented, OCV campaigns may be conducted to reduce the likelihood of cholera epidemics in cholera foci and in high-risk population identified (p23). To enhance integration of OCV use with preventive WASH and social mobilization intervention, a mapping highlighting the areas targeted by the present classification and/or OCV plan would be useful.

The priority hotspots (Type 1 and Type 2) comprise 12 counties with both urban and rural features which account for two-third of the disease burden. Those cholera foci host approximately 2,280,000 people (18% of the total estimated population) ([Table 5](#)). These figures should be assessed with caution given the baseline population (2008 population census) and the high rate of population displacement in the country. This study proposes a classification of cholera hotspots at the county level, although, this scale might not be the most cost-efficient approach when implementing preventive measures, especially expensive interventions such as water and sanitation infrastructure. An identification of transmission foci at a finer geographical scale (e.g., city section, boma, village) within the priority counties is necessary to better target the at-risk population, thus mainstreaming resources and maximizing the impact of WASH, health and social mobilization interventions (91).

STATE	COUNTY	Population estimate 2017	Recurrence (No. of outbreaks)	Outbreak duration (median, in weeks)	Median onset week [min-max]	Attack rate (median, per 10,000 inhab.)	Case Fatality Ratio (%)	Border	Hotspot type	Preparedness	Early Detection	Prevention (WASH, C4D, Health)	Role of Oral Cholera Vaccine
CENTRAL EQUATORIA	JUBA	579 778	5	26	20 [16-26]	43.17	1.3	No	T.1	☐	☐	☐	☐
EASTERN EAQUATORIA	MAGWI	249 724	4	10.5	27.5 [23-32]	9.66	0.4	Yes	T.1	☐	☐	☐	☐
EASTERN EAQUATORIA	IKOTOS	127 976	2	20	27 [27-27]	32.45	0	Yes	T.2	☐	☐	☐	☐
EASTERN EAQUATORIA	KAPOETA NORTH	151 125	2	14.5	21 [17-25]	33.81	0.1	No	T.2	☐	☐	☐	☐
EASTERN EAQUATORIA	KAPOETA SOUTH	116 695	2	10.5	29 [16-42]	44.01	1.0	yes	T.2	☐	☐	☐	☐
EASTERN EAQUATORIA	LAFON	155 833	2	20	23 [23-23]	66.23	6.2	No	T.2	☐	☐	☐	☐
EASTERN EAQUATORIA	TORIT	156 877	2	15	23 [23-23]	93.2	0	No	T.2	☐	☐	☐	☐
JONGLEI	CANAL-PIGI	150 800	2	11.5	22.5 [5-40]	6.71	2.5	No	T.2	☐	☐	☐	☐
JONGLEI	FANGAK	168 947	2	13	22 [12-32]	10.99	1.3	No	T.2	☐	☐	☐	☐
UNITY	PANYIJAR	78 020	3	14.5	30 [18-42]	64.27	4.9	No	T.2	☐	☐	☐	☐
UNITY	RUBKONA	171 192	2	24	39 [39-39]	50.2	0.9	Yes	T.2	☐	☐	☐	☐
WARRAP	TONJ EAST	170 430	2	16	19 [19-19]	96.11	1.8	No	T.2	☐	☐	☐	☐
JONGLEI	BOR SOUTH	331 611	5	8	18 [3-25]	3.23	2.0	No	T.3	☐	☐		☐
CENTRAL EQUATORIA	KAJO-KEJI	289 826	2	9.5	23 [22-24]	2.49	0.7	Yes	T.4	☐	☐		
CENTRAL EQUATORIA	YEI	298 865	3	6	20 [20-20]	40.6	0.0	Yes	T.4	☐	☐		☐
JONGLEI	DUK	96 259	3	8	26 [5-41]	7.36	6.6	No	T.4	☐	☐		
UPPER NILE	MALAKAL	214 679	3	6.5	16.5 [8-25]	29.2	0	Yes	T.4	☐	☐		☐
WARRAP	TONJ NORTH	242 616	2	7	24 [24-24]	19.48	0	No	T.4	☐	☐		

Table 5 : Cholera hotspot classification table, South Sudan (period : 2006-2007 and 2014-2017). Outbreak duration, median onset week and Case Fatality Ratio are calculated over 2014-2017 period. The counties of Yeï and Malakal which host refugees and IDPs identified as high risk population are considered for pre-emptive vaccination, although those counties are classified as low priority areas (Type 4).

II. Use of study results to guide control and prevention strategies

PREPAREDNESS & PREVENTION - Strategic documents to develop or update

1. Cholera Prevention and Response Plan for South Sudan, 2018 - 2020 (to include)

- Complete the part on cholera epidemiology which could benefit from this study.
- Include timeline and location for preparedness activities.
- Mention the role of each sector for cross-sectorial intervention (infection prevention and control in health centers and affected households, safe burial practices for suspected and confirmed cases).
 - o Given the limited number of partners, if anyone has the technical (and possibly financial) capacity to conduct an activity that is not managed by its reference cluster, he/she should be able to do so in coordination with the alternate cluster.

2. WASH Cluster cholera control and prevention strategy (to develop)

- WASH Cluster to develop a document (around 5 pages) defining the WASH strategy for cholera response, preparedness and prevention:
 - o Build on existing strategic document: Ending Cholera - A Global Road map to 2030 (GTFCC, Oct 2017), Overview of the strategy to control and prevent cholera in West and Central Africa (The West and Central Africa Cholera Platform, ECHO/UK Aid/UNICEF, May 2017), cholera framework for East and Southern Africa region (UNICEF, April 2017).
 - o Base the approach on the Shield and Sword strategy, which implies risk-informed preparedness, targeting emergency response, sustainable health, WASH and social mobilization interventions and pre-emptive OCV in cholera hotspots.
 - o Include preliminary results from the cholera epidemiological study (hotspot classification, seasonal patterns, high risk population, etc.).
 - o Consider a section that explores delivering WASH with Health and Social mobilization, encouraging a joint response and comprehensive approach to cholera control and prevention.
- WASH cluster to develop technical notes on emergency interventions and, if time allows, a training module.

3. Cholera OCV strategy (to develop)

- Integrate mid-term WASH and social mobilization intervention and preventive OCV campaign in cholera hotspots.
- Refer to Ending Cholera - A Global Road map to 2030 (GTFCC, Oct 2017).

4. UNICEF Country Office WASH program strategy Note - 10 Sept 2017 (to include)

- Add targets based on epidemiological study findings for cholera preparedness and prevention (cholera hotspots, high risk population).
- Detail intervention on cholera preparedness and prevention such as behavior change, Community-Led Total Sanitation (CLTS), Community Approaches to Sanitation (CATS) and sustainable water access in cholera hotspot.

5. UNICEF Country Office Health program strategy Note (to include)

- Add targets based on epidemiological study findings for cholera preparedness and prevention (cholera hotspots, high risk population).
- Consider support for strengthening IDRS and EPR in these areas with a focus on cholera and other epidemic prone diseases.

III. Areas of improvement for cholera preparedness, prevention and response

The below indications do not cover the entire emergency, preparedness and prevention effort, only relevant areas which would benefit for an improvement

RESPONSE – Implement early and targeted emergency response based on the epidemiological features of cholera outbreaks

- Improve early detection of cases through enhancement of community-level surveillance as well as health facility level surveillance in counties located close to the Ugandan border and in Juba, especially during the rainy season or when outbreaks are reported in neighboring countries that may spread to South Sudan.
- Share regularly information on the epidemiological situation with neighboring countries and/or border districts to anticipate the introduction of the disease in the country and trigger early detection and targeted response around the first cases.
- At the onset of the outbreak, in hard to reach areas where access to health facility is restricted and CFR is high, strengthen active case finding together with distribution of ORS or sensitization on how to make home-made rehydration solution and set up of ORPs.
- Conduct systematic and early infection, prevention and control interventions at the household level of cholera-affected patients.
 - o Train affected households on prevention focusing on safe food handling, safe disposal of excreta, hand hygiene, safe water, care-seeking behaviors, as well as disinfection of infected materials and surfaces (e.g., clothes, beddings, floor, etc.) using household disinfection kits (HDKs)
 - o If stigmatization or security does not allow the team to visit the premises of the patient, the training and distribution of HDKs can be carried out within the CTC compound
 - o The team in charge of IPC should link with personnel in charge of case management and/or surveillance.
- Improve the response strategy in urban areas (e.g. Juba) 1) by mapping the cholera-affected households during the coming outbreak by any means (paper map, geographical information system (GIS), mobile phone) and conduct targeted control interventions around clusters of cases.
 - o The objective is to mainstream resources and to improve the effectiveness of the interventions implemented in the community by targeting cluster of cases (92–94)
 - o A strong collaboration between the personnel of surveillance, case management and WASH is required.
- Improve the strategy in rural areas by systematically investigating cholera cases/cluster and unexplained community death during outbreaks. Pay attention to the specificity of cholera epidemiology in identifying the transmission context such as transmission associated with health facilities, during funeral rituals, within households, in public places or during socio-professional gatherings. The investigation should be done over the course of an outbreak as various drivers of transmission can intervene successively. Reorient the response measures according to epidemiological findings to reduce the disease burden and stop the transmission.
- Ensure infection prevention and control in the health facilities receiving cases (training and supplies).
 - o When a person is allowed onto the premises to care for the patient, ensure that he has access to the necessary information and supplies to protect against cholera, especially when washing clothes, emptying buckets, feeding the patient, etc.
 - o Restrict entry and exit of both people and materials.
 - o Build separate sanitation facilities in health facilities receiving cases of cholera.

- The social mobilization WG could include Health and WASH to limit challenges associated with integrated response.
- Mobilize financial and technical resources to stop the transmission when it is low (October to January).
- During low transmission, advocate emergency donors to fund cholera response and mobilize implementing partners (from October to January).

PREPAREDNESS - Be ready before the rainy season

- Update or develop strategic documents as per the above lists.
- Plan the prepositioning of materials based on cholera hotspot mapping and the core pipeline prepositioning sites:
 - o Include ORS in the core pipeline (UNICEF – IOM) given the severe dehydration status of patients when they reach a health facility (conflict and hard to reach areas) or streamline resources by using ORS in the IDD kits or in routine supplies.
 - o Order IDD kits with case isolation and laboratory module (laboratory sample media transport kit and rapid diagnostic tests)
- Strengthen social mobilization, Health and WASH partner's capacities:
 - o Train partner on early response activities in the community through setting up ORPs and active case findings with the objective of reducing CFR at the onset of an outbreak while larger scale response is being prepared.
 - o Train partners in Infection Prevention and Control in health facilities and affected households.
 - o Train partners on a targeted strategy in urban and rural settings (shield and sword strategy).
 - o Orient health workers on proper use of rapid tests as well as conditioning and transport of samples for confirmation.
- Initiate cross-border collaboration between neighboring countries (government, agency, NGO, civil society, etc.):
 - o Start regular sharing of data and information (cholera situation and response updates, investigation reports, etc.) between UNICEF country offices (Uganda, Sudan, Ethiopia and Kenya) and border field offices (Health section) to anticipate potential cross-border cholera threat
 - o Financial and technical support to enhance cross-border collaboration between Ministries of Health of South Sudan and neighboring countries with the objective of anticipating cross-border spread and triggering an early response
 - o IDSR focal points within the framework of International Health Regulation 2005 application should be nominated for cross-border alert and sharing of information in South Sudan and neighboring countries

PREVENTION - Plan, mobilize donors and implement prevention activities in cholera hotspots when security allows it

- Highlight areas targeted by the present classification and/or the OCV two-year plan and define common targets for the health, WASH and social mobilization sectors.
- Characterize hotspots according to local constraints (security, access during the rainy season) and define a package of interventions according to the hotspot type and local constraints (be flexible).
- Mobilize donors for prevention activities in cholera hotspots using existing strategic documents, such as the cholera road map to end cholera, the regional cholera elimination framework and results from the study.

- Implement mid-term WASH and social mobilization programs (1-3 years) such as behavior change, CLTS or CATS, social marketing of soap and household water treatment solutions, and sustainable water access in cholera hotspots together with pre-emptive OCV if relevant.

STUDY LIMITATIONS

Cholera outbreak patterns

The one-week mission in South Sudan was not sufficient to conduct field visits in regularly affected counties and communities. Hence, the information concerning risk factors, and high-risk populations and practices was primarily derived from field investigation reports and cholera situation reports collected in Juba. Little information and evidence of cross-border outbreak spread and related transmission drivers was available in the grey literature despite recurrent pattern of regional epidemic over the past decades. Genetic analysis of clinical isolates of *Vibrio cholerae* will be of primary importance to enhance the understanding of cross-border cholera dynamics between South Sudan and neighboring countries, particularly Uganda, the DRC, Kenya and Ethiopia.

Cholera hotspot classification and characterization

Several context-specific limitations were encountered during the classification of cholera hotspots in South Sudan, including a likely significant inaccuracy of the population denominator. Overall, 15% of the population are IDPs that were displaced multiple times during the study period with no clear pattern. Significant population movement had an impact on cumulative incidence, which was initially used to characterize the Type 3 and Type 4 hotspots. Additionally, time series were only available for the 2014-2017 period. The recurrence and incidence parameters were determined using the 2006-2007 and 2014-2017 epidemiological data. Meanwhile, outbreak length was analyzed exclusively for the 2014-2017 period. The limited number of time series influenced the calculation of the median recurrence and the median incidence, as the 2017 outbreak involved significantly high incidence and widespread geographic reach. The classification framework, which is based on the assessment of cholera outbreaks in West African countries, has been revised and refined to the South Sudan context to mitigate the risk associated with data quality and quantity. Hence, the threshold for high recurrence was increased (from 80th to 90th percentile) to enhance discrimination between spatial units and the median incidence was not considered to characterize Type 3 and Type 4 hotspot.

While preliminary results were shared with some of the key stakeholders (Ministry of Health (Emergency, Preparedness and Response), WHO (Emergency unit), UNICEF (WASH, Health and C4D sections), Health and WASH clusters, IOM and MEDAIR), time was insufficient for an in-depth discussion concerning the list of counties identified and the ranking results. The short duration of the field mission was inadequate to investigate local constraints, such as security and access, as well as environmental, cultural and socio-economic conditions in the pre-identified hotspots. Those firsthand data coupled with an assessment of access to healthcare and safe water, improved sanitation facilities, and hygiene practices are required to conceive high-impact interventions.

Genetic analysis of clinical isolates of V. cholerae

The reference laboratory in Juba stores 162 *V. cholerae* isolates from the 2016/2017 outbreaks only, of which 35 were shipped in November 2017 for genetic sequencing, typing, and antimicrobial sensitivity to the Institute Pasteur in Paris. Few isolates between 2014 and 2015 were sent to the Pasteur Institute and AMREF in Nairobi. In South Sudan, genetic analysis is contingent on multiple laboratory partnerships.

CONCLUSION

Since the eruption of the civil war in December 2013, the country has declared cholera outbreaks every year. Recently, a large-scale cholera outbreak, which lasted 16 months (June 18, 2016 – December 18, 2017), resulted in 20,438 cholera cases and 436 deaths in one third of all counties (3). In this war-torn country, access to improved drinking water sources stands at 50% and open defecation is widespread (approx. 65% of the population) (79). The already low WASH indicators have further declined with continued population displacement, particularly for those who found refuge on islands and swampy areas along the Nile River. Additionally, the protracted crisis coupled with drought has led to serious water and food shortages in the country, which has forced people, especially cattle herders, to gather around the remaining water points, thus rendering them more vulnerable to the disease.

To control cholera outbreaks in the country, the Ministry of Health, together with the UN agencies and the humanitarian community, has scaled up the use of oral cholera vaccine. Between December 2012 and October 2017, nearly two million doses were administered either reactively or preemptively. Nevertheless, little has been done to substantially improve access to basic services in regularly affected areas. Twelve counties which host approximately 2,280,000 people (18% of the total estimated population) account for two-third of the total number of cases. Those cholera foci are located in major cities that host large IDP camps and settlements, along the border with Uganda and Kenya, and in the vast swamp that stretches along the Nile River between Bor and Malakal. High priority counties should be assessed and targeted for longer-term WASH, Health and social mobilization improvements taking into account the protracted nature of the conflict in some parts of the country. Identification of hotspots at a finer geographical scale would better define the target population and thereby reduce the investment needed to scale up social services, while efficiently impacting the disease burden (91).

South Sudan is localized between two major cholera transmission zones, the Great Lakes Region in the south and the Horn of Africa in the east. Since cholera was first imported into the Sudanese territories in 1831, evidence of cross-border spread from and to neighboring countries has been reported, especially involving Uganda and to a lesser extent Kenya, Ethiopia and Sudan. Additional genetic studies of *V. cholerae* strains circulating in the East and Central Africa region would confirm these initial but limited observations and promote a concerted effort to eliminate cholera.

REFERENCES

1. UN Children's Fund. UNICEF Strategic Framework for Cholera in Eastern and Southern Africa: 2018-2022 [Internet]. 2017 Apr. Available from: <https://reliefweb.int/report/ethiopia/unicef-strategic-framework-cholera-eastern-and-southern-africa-2018-2022>
2. South Sudanese civil war. In: Wikipedia, the free encyclopedia [Internet]. Available from: https://en.wikipedia.org/wiki/South_Sudanese_Civil_War
3. South Sudan Tribune. South Sudan officially declares end of cholera outbreak. South Sudan Tribune. 2018 Feb 7;
4. GTFCC. Ending Cholera - A Global Roadmap to 2030. 2017.
5. World Health Organization. Cholera, number of reported cases (data by country) [Internet]. Global Health Observatory Data Repository [Internet]. Available from: Available from: http://www.who.int/gho/epidemic_diseases/cholera/en/
6. Ministry of Health, South Sudan. Cholera Prevention and Response Plan, 2018 - 2020. 2017 Dec.
7. Pankhurst R. The history of cholera in Ethiopia. *Med Hist.* 1968 Jul;12(3):262–9.
8. Malholland K. Cholera in Sudan: An account of an epidemic in a refugee camp in eastern Sudan, May-June 1985. *Disasters.* 1985 Dec;9(4):247–58.
9. Wren CS. Thousands of Ugandans Flee to the Sudan [Internet]. 1979 [cited 2017 Aug 24]. Available from: <https://www.nytimes.com/1979/06/18/archives/thousands-of-ugandans-flee-to-the-sudan-former-amin-minister-talks.html>
10. Swerdlow DL, Malenga G, Begkoyian G, Nyangulu D, Toole M, Waldman RJ, et al. Epidemic cholera among refugees in Malawi, Africa: treatment and transmission. *Epidemiol Infect.* 1997 Jun;118(3):207–14.
11. World Health Organization. WHO SOUTHERN SUDAN HEALTH UPDATE. 2001 Dec.
12. Pugliese N, Maimone F, Scarscia M, Materu SF, Pazzani C. SXT-related integrating conjugative element and IncC plasmids in *Vibrio cholerae* O1 strains in Eastern Africa. *J Antimicrob Chemother.* 2009 Mar;63(3):438–42.
13. Mugoya I, Kariuki S, Galgalo T, Njuguna C, Omollo J, Njoroge J, et al. Rapid spread of *Vibrio cholerae* O1 throughout Kenya, 2005. *Am J Trop Med Hyg.* 2008 Mar;78(3):527–33.
14. Karsany MS, Elshayeb AA, Salih KMA. Epidemiology and Recent outbreak of Cholera in Sudan. *Advances in Bioresearch.* 2012 Mar;3(1):23–5.
15. ProMED-mail. Cholera, diarrhea & dysentery update 2006 (34). Archive Number: 20060818.2312 [Internet]. 2006 Aug. Report No.: 20060818.2312. Available from: www.promedmail.org
16. ProMED-mail. Cholera, diarrhea & dysentery update 2006 (36). Archive Number: 20060904.2520 [Internet]. 2006 Sep. Report No.: 20060904.2520. Available from: www.promedmail.org
17. World Health Organization South Sudan ERT. Current Situation update and transmission risk to guide preparedness and response. 2014 Jul.
18. MSF-Spain. MSF-SPAIN intervention May -July 2008, Juba Cholera Outbreak, Southern Sudan. 2008.
19. IFRC. DREF Operation Sudan: Acute Watery Diarrhoea Epidemic. 2008 Jun.
20. ProMED-mail. Cholera, diarrhea & dysentery update 2008 (24). Archive Number: 20080425.1446. Cholera - Sudan (Yeï) [Internet]. 2008 Apr. Report No.: 20080425.1446. Available from: www.promedmail.org

21. Ministry of Health, Southern Sudan. Cholera outbreak in Magwi County, Eastern Equatorial State (EES). 2008 May.
22. ProMED-mail. Cholera, diarrhea & dysentery update 2008 (28). Archive Number: 20080617.1896. Cholera - Sudan (South) [Internet]. 2008 Jun. Report No.: 20080617.1896. Available from: www.promedmail.org
23. Southern Sudan Medical Journal. Reports from Southern Sudan. 2009 Jan;
24. ProMED-mail. Cholera, diarrhea & dysentery update 2008 (40). Archive Number: 20081014.3253. Cholera - Sudan [Internet]. 2008 Oct. Report No.: 20081014.3253. Available from: www.promedmail.org
25. Ministry of Health, South Sudan. Acute Watery Diarrhea in Malual Bai Payam, Peth village in Aweil East County. 2009 Feb.
26. MSF-France. Week 43 Acute Watery Diarrhea Epidemiological Report, Northern Bahr el Ghazal, 19th to 25th October 2008. 2008 Oct.
27. Mayout A. Investigation report of Acute Watery Diarrhea in Alek West Payam. Ministry of Health, Warrap State, South Sudan; 2009 Jan.
28. MEDAIR. Watsan and Health assessment and intervention report, Akon - Alek West Payam, Warrap State. 2009 Jan.
29. Ujjiga TTA, Wamala JF, Mogga JJH, Othwonh TO, Mutonga D, Kone-Coulibaly A, et al. Risk Factors for Sustained Cholera Transmission, Juba County, South Sudan, 2014. *Emerg Infect Dis*. 2015 Oct;21(10):1849–52.
30. Ministry of Health, South Sudan, WHO, South Sudan. Cholera Outbreak Investigation Report. 2014 May.
31. Abubakar A, Azman AS, Rumunu J, Ciglenecki I, Helderman T, West H, et al. The First Use of the Global Oral Cholera Vaccine Emergency Stockpile: Lessons from South Sudan. *PLOS Med*. 2015 Nov 17;12(11):e1001901.
32. Ministry of Health, South Sudan. Cholera Alert South Sudan. 2014 Jun.
33. MSF-Spain. MSF-Spain Initial Assessment Kaka. 2014 May.
34. UNICEF South Sudan. Social Mobilization and Communication Cholera Response in Lopa and Torit Counties of Eastern Equatoria State. 2014 Jun.
35. World Health Organization. South Sudan Emergency Response. 2014 Dec. Report No.: 44.
36. Wamala F J, Mpairwe M A, Boateng K, Maleghemi S, Ujjiga T. A. T, Mutebi M, et al. Outcomes of Management of Cholera Outbreak among IDPs and Non-IDPs in a Complex Emergency Setting of South Sudan. *American Journal of Infectious Diseases and Microbiology*. 2016;4(6):123–8.
37. Iyer AS, Bouhenia M, Rumunu J, Abubakar A, Gruninger RJ, Pita J, et al. Immune Responses to an Oral Cholera Vaccine in Internally Displaced Persons in South Sudan. *Sci Rep*. 2016 Oct 24;6:35742.
38. Republic of South Sudan. Situation report on cholera in South Sudan, 29 December 2016. 2016 Dec.
39. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 28 October 2016. 2016 Oct.
40. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 10 February 2017. 2017 Feb.
41. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 3 March 2017. 2017 Mar.
42. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 17 March 2017. 2017 Mar.
43. Ministry of Health, South Sudan. Cholera Outbreak Investigation Report, Jalle payam - Bor South county. 2017 Jan.
44. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 3 February 2017. 2017 Feb.

45. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 24 March 2017. 2017 Mar.
46. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 21 April 2017. 2017 Apr.
47. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 7 April 2017. 2017 Apr.
48. World Health Organization South Sudan. Suspected Cholera outbreak, Investigation in Greater Kapoeta counties, May 2017. 2017 May.
49. UNICEF South Sudan. Report on cholera field monitoring and support mission to Kapoeta, South Sudan. 2017 Jun.
50. Dr. Tut M. Tonj East Cholera Outbreak - Field Report. 2017 Jun.
51. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 7 June 2017. 2017 Jun.
52. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 25 August 2017. 2017 Aug.
53. Urban WASH Technical Working Group. Juba Cholera Response 2018 - Roadblocks and Ways Forward. 2017 Nov.
54. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 8 September 2017. 2017 Sep.
55. ProMED-mail. Cholera, diarrhea & dysentery update 2016 (30). Archive Number: 20161014.4548860 [Internet]. 2016 Oct. Report No.: Archive Number: 20161014.4548860. Available from: www.promedmail.org
56. ProMED-mail. Cholera, diarrhea & dysentery update 2016 (28). Archive Number: 20160917.4495868 [Internet]. 2016 Sep. Report No.: Archive Number: 20160917.4495868. Available from: www.promedmail.org
57. Echenberg M. Africa in the Time of Cholera: A History of Pandemics from 1817 to the Present. 1st ed. New York: Cambridge University Press; 2011. 232 p.
58. IDMC » South Sudan [Internet]. [cited 2017 Aug 25]. Available from: <http://www.internal-displacement.org/countries/south-sudan>
59. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 28 April 2017. 2017 Apr.
60. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 30 June 2017. 2017 Jun.
61. UNICEF South Sudan. Program Component Strategy Note, Water, Sanitation and Hygiene (WASH). 2017.
62. Logistic Cluster, South Sudan. South Sudan Road Network. 2013.
63. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 24 February 2017. 2017 Feb.
64. Unknown. Ayod County situation update: suspected Cholera cases from mid August to early October, 2016. 2016 Oct.
65. UN News Centre. Famine declared in region of South Sudan – UN [Internet]. 2017. Available from: <http://www.un.org/apps/news/story.asp?NewsID=56205#.WmW6CK3pO8V>
66. Nalin D. CHOLERA, NON-VIBRIO CHOLERA, AND STOMACH ACID. The Lancet. 1978 Oct;312(8095):856–9.
67. Palmer DL, Koster FT, Alam AKMJ, Islam MR. Nutritional Status: A Determinant of Severity of Diarrhea in Patients with Cholera. J Infect Dis. 1976 Jul 1;134(1):8–14.
68. Republic of South Sudan. Situation report on cholera in South Sudan, 5 May 2017. 2017 May.
69. IRINnews. Worsening food crisis in South Sudan's swamplands [Internet]. 2014. Available from:

<http://www.irinnews.org/news/2014/03/03/worsening-food-crisis-south-sudan's-swamplands>

70. REACH. Situation Overview: Southern Jonglei Islands, South Sudan. 2015 Dec.
71. Forcier consulting. Cholera Knowledge, Attitudes and, Practices Assesment. 2015 Oct.
72. Centers for Disease Control and Prevention (CDC). Cholera outbreak - Southern Sudan, 2007. MMWR Morb Mortal Wkly Rep. 2009 Apr 10;58(13):337–41.
73. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 7 July 2017. 2017 Jul.
74. Ministry of Health, South Sudan. Rapid Risk Assesment and Oral Cholera Vaccine Recommandations for Cholera Control in South Sudan. 2017 Apr.
75. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 27 October 2017. 2017 Oct.
76. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 9 July 2017. 2017 Jul.
77. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 19 August 2017. 2017 Aug.
78. Ministry of Health - Government of Southern Sudan, National Bureau of Statistics - Government of Southern Sudan. South Sudan - Household Health Survey 2010 [Internet]. 2010. Available from: <http://microdata.worldbank.org/index.php/catalog/2588>
79. WHO/UNICEF Joint Water Supply and Sanitation Monitoring Programme, World Health Organization, UNICEF. Progress on sanitation and drinking water. 2015.
80. Ministry of Health, South Sudan. Cholera Prevention and Response Plan, 2017. 2017.
81. Porta MI, Lenglet A, de Weerd S, Crestani R, Sinke R, Jo Frawley M, et al. Feasibility of a preventive mass vaccination campaign with two doses of oral cholera vaccine during a humanitarian emergency in South Sudan. Trans R Soc Trop Med Hyg. 2014 Oct 13;
82. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 11 June 2017. 2017 Jun.
83. Parker LA, Rumunu J, Jamet C, Kenyi Y, Lino RL, Wamala JF, et al. Adapting to the global shortage of cholera vaccines: targeted single dose cholera vaccine in response to an outbreak in South Sudan. Lancet Infect Dis. 2017 Jan 18;
84. Azman AS, Parker LA, Rumunu J, Tadesse F, Grandesso F, Deng LL, et al. Effectiveness of one dose of oral cholera vaccine in response to an outbreak: a case-cohort study. Lancet Glob Health. 2016 Nov;4(11):e856–63.
85. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 17 November 2017. 2017 Nov.
86. SAGE Working Group on OCV. Conclusions of the SAGE Working Group on oral cholera vaccines and proposed recommendations. 2017 Apr.
87. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 3 November 2016. 2016 Nov.
88. Ministry of Health, South Sudan. Situation report on cholera in South Sudan, 14 April 2017. 2017 Apr.
89. Ministry of Health, South Sudan WSS. Cholera Response - Oral Cholera Vaccination Campaign in Tonj East. 2017 Aug.
90. WHO. Prevention and control of cholera outbreaks: WHO policy and recommendations [Internet]. 2014. Available from: http://www.who.int/cholera/prevention_control/recommendations/en/index4.html
91. Lessler J, Moore SM, Luquero FJ, McKay HS, Grais R, Henkens M, et al. Mapping the burden of cholera in sub-Saharan Africa and implications for control: an analysis of data across geographical scales. The Lancet

[Internet]. 2018 Mar [cited 2018 Mar 4]; Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0140673617330507>

92. Dunoyer J, Sudre B, Rebolledo J, Cottavoz P. Le choléra transfrontalier en Sierra Leone et Guinée en 2012 et les stratégies d'intervention associées [Internet]. Action Contre la Faim – France. UMR 6249 Laboratoire Chrono - Environnement, Université de Franche - Comté. Étude financée par le Service d'aide humanitaire à la Commission Européenne (ECHO).; 2013 Feb [cited 2016 Feb 26] p. 91. Available from: https://www.humanitarianresponse.info/system/files/documents/files/RapportCholera_2013.pdf

93. Bi Q, Azman AS, Satter SM, Khan AI, Ahmed D, Riaj AA, et al. Micro-scale Spatial Clustering of Cholera Risk Factors in Urban Bangladesh. Ryan ET, editor. PLoS Negl Trop Dis. 2016 Feb 11;10(2):e0004400.

94. Finger F, Bertuzzo E, Luquero FJ, Naibei N, Touré B, Allan M, et al. The potential impact of case-area targeted interventions in response to cholera outbreaks: A modeling study. von Seidlein L, editor. PLOS Med. 2018 Feb 27;15(2):e1002509.

ANNEX 1 - INTERVIEWEE LIST

Id	Country	Agency/GoV	Name	Position
1	South Sudan	Health cluster	Andrew Mballa	Public Health Officer
2	South Sudan	Health cluster	Magdalene Nana Araba Asakwor Armah	Health cluster coordinator
3	South Sudan	Health cluster	Penn Kmah	Health cluster coordinator Equatoria state
4	South Sudan	IOM	Baudouin Luce	WASH officer
5	South Sudan	IOM	Daniel Kuria	Information management officer
6	South Sudan	Medair	Alicia Morcombe	Emergency Response Team Health
7	South Sudan	MOH	Dr. Mathew Tut	Director Emergency, Preparedness and response
8	South Sudan	OCHA	Frank Nyakairu	Head of communication and information management
9	South Sudan	OCHA	Mohamud Halake Dida	Communication and information management specialist
10	South Sudan	Public Health Laboratory	Angelo Ngor	Infectious Disease Consultant
11	South Sudan	Public Health Laboratory	Dr. Lul Ojok	General Director
12	South Sudan	Public Health Laboratory	Robert Lubajo	Laboratory Technologist
13	South Sudan	UNICEF	Abdallah Abdel Rassoul	WASH emergency officer
14	South Sudan	UNICEF	Aping Kuluel Machuol	Communication for development officer
15	South Sudan	UNICEF	Gopinath Durairajan	Chief of Communication for development section
16	South Sudan	UNICEF	Joseph Kambale Wavungire	WASH cholera focal person
17	South Sudan	UNICEF	Lillian Okwirri	Deputy Representative
18	South Sudan	UNICEF	Marine Mosnier	Emergency specialist Greater Equatoria region
19	South Sudan	UNICEF	Penelope Campbell	Chief of Health section
20	South Sudan	UNICEF	Viktor Kinyanjui	Chief of WASH section
21	South Sudan	WASH cluster	Karolina Rasinska	WASH cluster co-coordinator (NRC)
22	South Sudan	WHO	Dr. Joseph Wamala	Epidemiologist
23	South Sudan	WHO	Dr. Mpairwe M. Allan	Emergency coordinator