



Two-dose vaccine effectiveness following the first reactive mass vaccination campaign against hepatitis E in Bentiu, South Sudan

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Hepatitis E

- Hepatitis E exists worldwide, large outbreaks in Africa and Asia
- Long incubation period, mean 5 – 6 weeks (range from 2-10 weeks)
- Usually self-limiting but can lead to acute liver failure and death
- Pregnant women in the second or third trimester, are at increased risk of acute liver failure, fetal loss and mortality
- No specific treatment

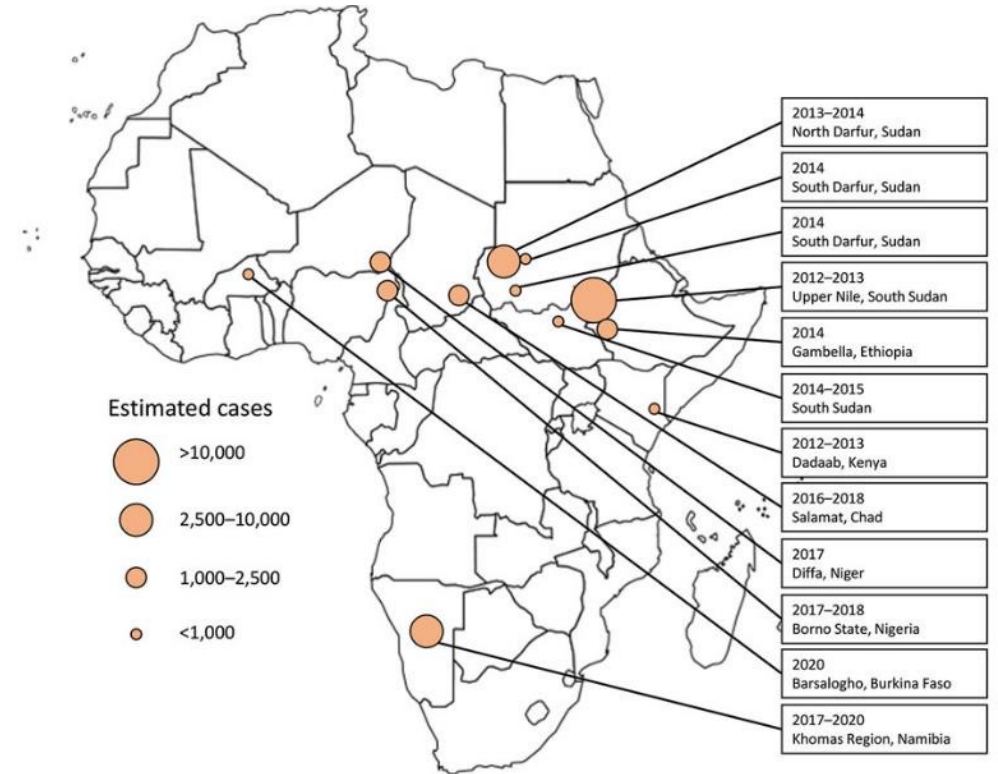
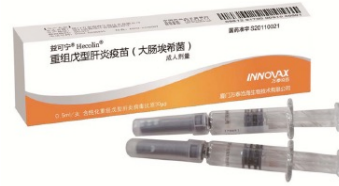
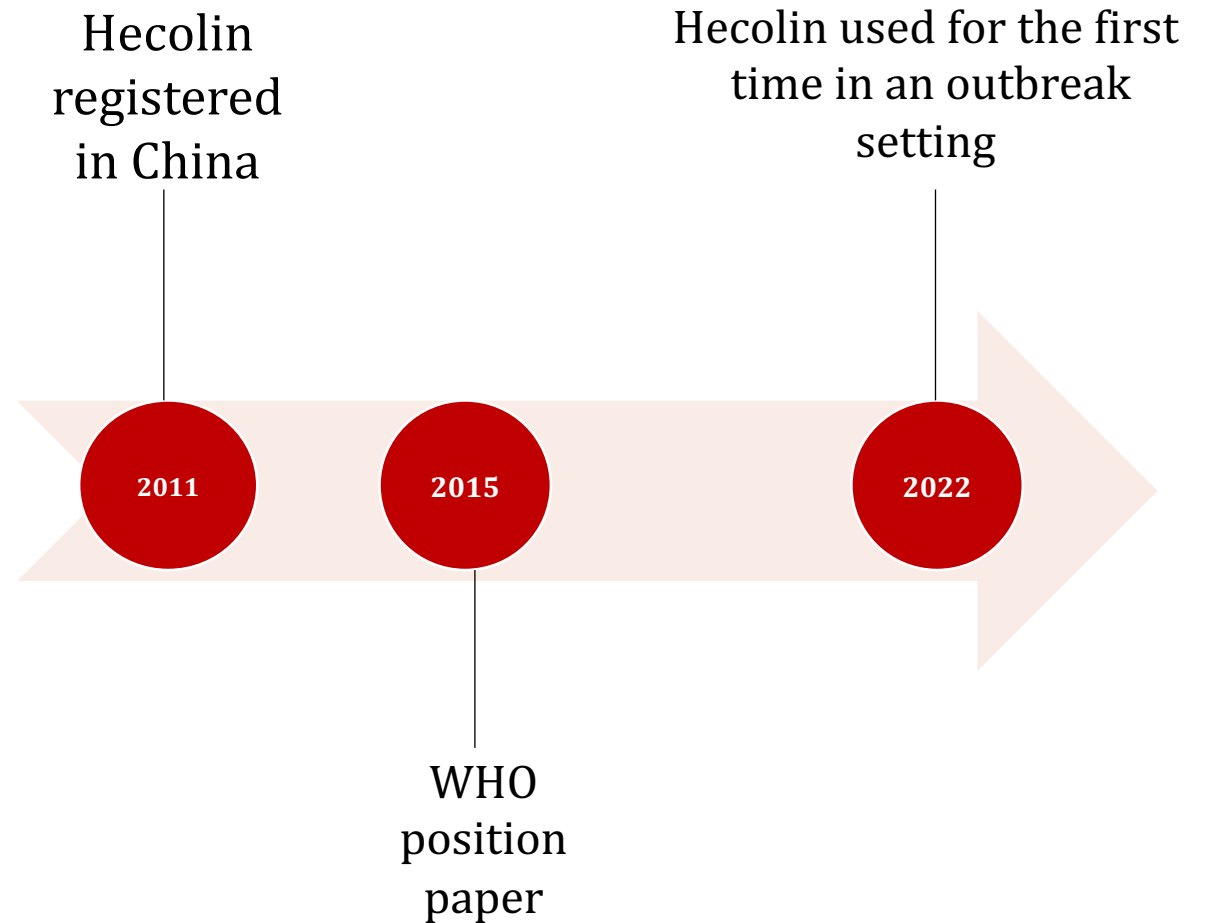


Figure. Geographic distribution of acute hepatitis E virus outbreaks reported among displaced persons in sub-Saharan Africa, 2010–2020
[Source](#) CDC Research Letter Viral Hepatitis E Outbreaks in Refugees and Internally Displaced Populations, sub-Saharan Africa, 2010–2020, May 2022

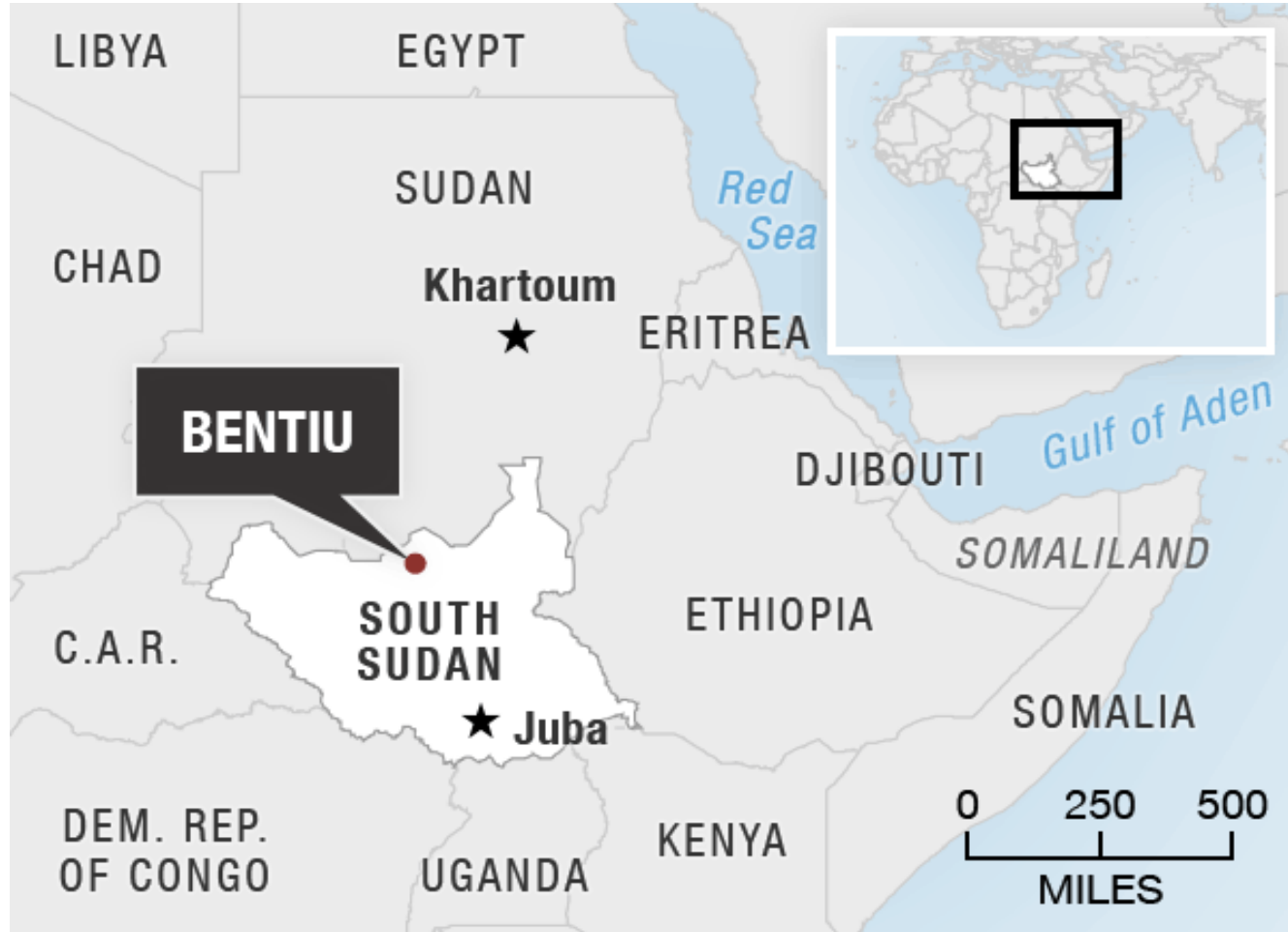
Hepatitis E vaccine



- Recombinant vaccine, Hecolin[®] (Innovax, China)
- 3 doses (0, 1, 6 mo), ≥16 yrs old
- 100% efficacy in a per protocol analysis at 1 year and 93% at 54 months
- Not WHO prequalified
- WHO 2015 recommendation for use in outbreak setting

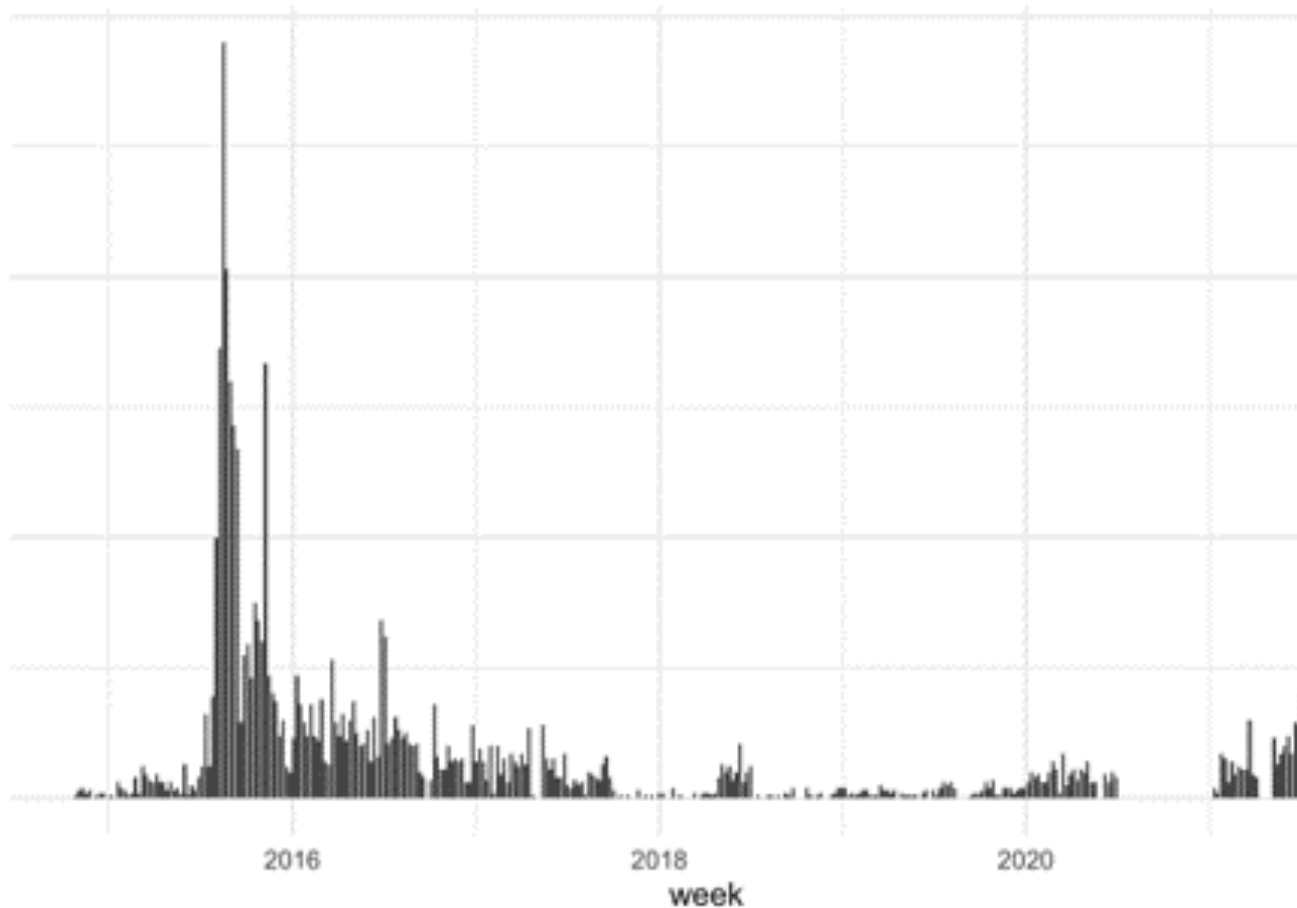


Bentiu internally displaced persons camp, South Sudan



- Established Dec. 2013
- ~112,000 residents
- Limited water and sanitation facilities

Hepatitis E in Bentiu internally displaced persons camp, South Sudan



- Large hepatitis E outbreak in 2015, with ongoing transmission after
- Increase of cases mid-2021 following floods and population influx
- Outbreak declared in August 2021
- MOH requested MSF to support integration of hepatitis E vaccination in outbreak control strategy



First mass reactive vaccination campaign

Target population:

- ✓ ~ 27'000 Bentiu IDP camp residents
- ✓ 16-40 years old, including pregnant women
- ✓ No acute illness or jaundice

- Implemented in 3 vaccination rounds: March, April and October 2022
- Vaccines delivered through fixed and mobile sites, and door-to-door strategy
- High administrative vaccination coverage >90% in each vaccination round



Objectives

1. Feasibility and acceptance

- Vaccination coverage surveys
- Focus group discussions

2. Safety

- Adverse events monitoring during vaccination
- Adverse events reported during survey
- Pregnancy cohort to monitor pregnancy outcomes

3. Two-dose vaccine effectiveness

- Enhanced surveillance acute jaundice syndrome
- Case-control study

Timeline of vaccination and study

2022

Mar

Apr

May

Jun

Jul

Aug

Sep

Oct

Nov

Dec

2023

Jan

Feb

Mar

Apr

1

2

3



Vaccination campaign



Vaccination campaign

AEFI surveillance

Enhanced acute jaundice syndrome surveillance and case-control study

Primary endpoint enrollment period

◆ Vaccination coverage survey

◆ Vaccination coverage survey

Pregnancy census

Pregnancy follow-up

Acceptance and safety

- High vaccination coverage
- Vaccine safe with few adverse events reported

Please see details in the poster

Coverage by dose	According to recall or card		Confirmed by card	
	% (n)	95 % CI	% (n)	95 % CI
One or more doses	86% (1377)	[84-88]	40% (644)	[37-43]
Two or more doses	73% (1160)	[70-75]	19% (305)	[17-21]
Three doses	58% (924)	[55-61]	10% (163)	[9-12]

Note that confirmed by card means that all doses reported were verified on vaccination card. Very few individuals retained vaccination cards or had them available at interview.

Vaccination coverage and adverse events following immunisation after the first reactive mass vaccination campaign against Hepatitis E in Bentiu, South Sudan

Introduction
Hepatitis E (HEV) is a common cause of gastroenteritis and acute liver failure. HEV infection is associated with elevated liver enzymes and hepatocellular carcinoma. HEV infection has been reported in China since 2011.

Methods
We conducted a cross-sectional study in Bentiu IDP camps. We used a household survey to assess vaccination coverage and adverse events following the first mass vaccination campaign against Hepatitis E using the Hecoloid vaccine.

Results
A total of 1377 individuals were included. Coverage according to recall was 86% (1377) and confirmed by card was 40% (644). Adverse events were reported in 1.7% (24) individuals.

Conclusion
The vaccine was well accepted and well tolerated in the Bentiu IDP camp community and should be considered for use in future outbreak response.

Acknowledgements
We thank the Ministry of Health and the Bentiu IDP camps for their support and participation.

Methods: Enhanced surveillance

All cases with acute jaundice seeking care at MSF hospital referred from clinician to study team

- ✓ Written consent
- ✓ Questionnaire
- ✓ Vaccination status
- ✓ Follow-up visit 2-4 weeks later

- ✓ Lab testing in Bentiu
 - Assure HEV IgM RDT
 - Hepatitis C, B, malaria
 - Liver function tests (**ALT, AST, Bilirubin**)

- ✓ Lab testing in Geneva
 - ELISA IgM
 - ELISA IgG
 - PCR

Suspected HEV case: An individual presenting with an acute (i.e., recent, new or sudden) onset of jaundice, dark urine or pale clay stools.

Probable HEV case: A suspected case with a serum alanine aminotransferase (ALT) concentration ≥ 2.5 times the normal range limit with

- 1) a positive IgM test (ELISA and/or RDT) test or;
- 2) a ≥ 4 -fold rise in IgG titers (ELISA) in paired samples collected 2 to 4 weeks after initial blood draw.

Confirmed HEV case: A suspected or probable HEV case with PCR-detected HEV RNA isolated from a plasma sample.

Methods: Case-control study

Vaccine eligible cases with acute jaundice seeking care at MSF hospital enrolled in surveillance

- ✓ Written consent
- ✓ Questionnaire
- ✓ Vaccination status
- ✓ Follow-up visit 2-4 weeks later
- ✓ 6 controls per case recruited in the community

- ✓ Lab testing in Bentiu
 - Assure HEV IgM RDT
 - Hepatitis C, B, malaria
 - Liver function tests (**ALT**, *AST*, *Bilirubin*)

- ✓ Lab testing in Geneva
 - ELISA IgM
 - ELISA IgG
 - PCR

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Confirmed HEV case: A suspected or probable HEV case with PCR-detected HEV RNA isolated from a plasma sample.

Results: case enrolment

- Enhanced surveillance: all suspect cases seeking care at MSF hospital
- Case-control study : vaccine eligible suspect cases

Status	All suspect cases	Vaccine-eligible suspect cases
Enrolled	1,186	354
Admitted to hospital	137	26
Died	18	3

Results: case enrolment by vaccine eligibility

Vaccine-eligible cases

- Reside in Bentiu IDP camp
- Age 16 – 40 years

Non-eligible cases

- Children <16 years
- Adults >40 years
- Reside outside Bentiu IDP



Results: case enrolment by vaccine eligibility

17 (5.6%) out of 287 vaccine-eligible cases were probable or confirmed hepatitis E

	Eligible (N=287)	Not-eligible (N=625)
Sex		
Female	161 (56.1%)	252 (40.3%)
Male	126 (43.9%)	373 (59.7%)
Age Group		
0-5	0 (0%)	219 (35.0%)
6-10	0 (0%)	137 (21.9%)
11-15	0 (0%)	100 (16.0%)
16-39	277 (96.5%)	100 (16.0%)
40+	10 (3.5%)	69 (11.0%)
Effective Doses		
0	97 (33.8%)	612 (97.9%)
1	49 (17.1%)	3 (0.5%)
2	113 (39.4%)	3 (0.5%)
3	11 (3.8%)	0 (0%)
Missing	17 (5.9%)	7 (1.1%)
Study Classification		
Suspected	270 (94.0%)	542 (86.7%)
Probable	1 (0.3%)	14 (2.2%)
Confirmed	16 (5.6%)	66 (10.6%)
Missing	0 (0%)	3 (0.5%)

*Preliminary analysis results may change

Results: preliminary* vaccine effectiveness estimate

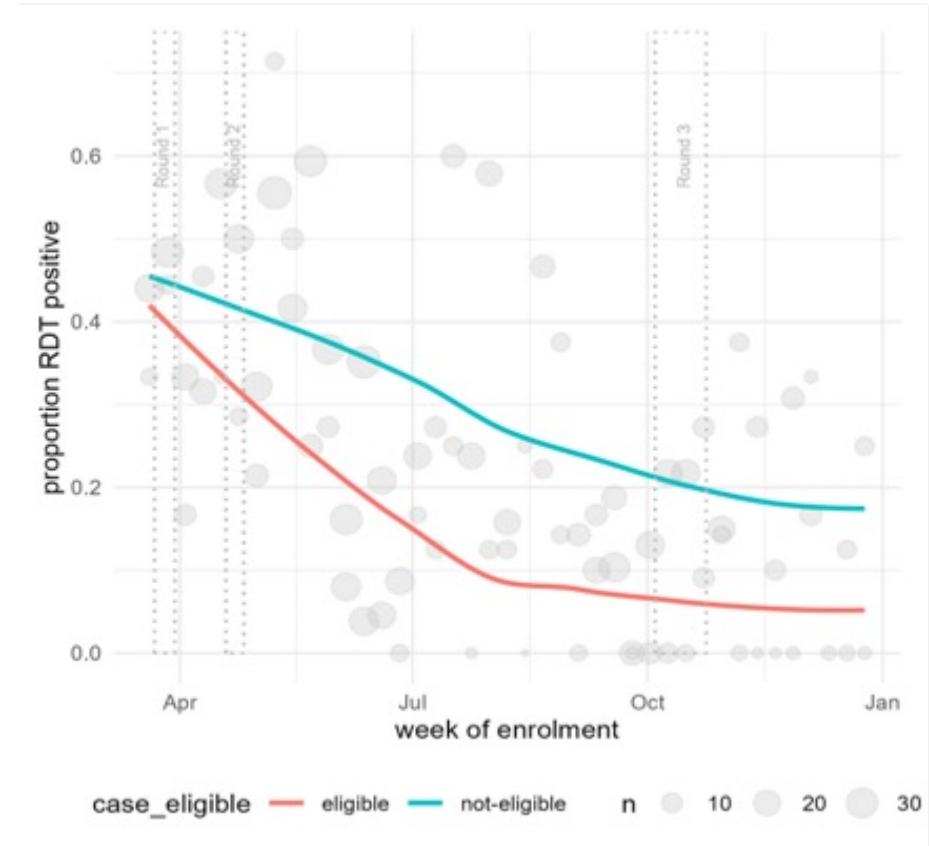
Two doses of Hecolin vaccine provides **83.9%** (-33.1–98.1) effectiveness against probable or confirmed cases

	Cases	Controls	Crude VE (95% CI)
1 Dose	15	48	87.9% (0.8–98.5)
2 Doses	13	44	83.9% (-33.1–98.1)
≥1 Dose	17	99	86.5% (36.3–97.1)

*Preliminary analysis results may change

Results: reduction in incidence after vaccination

2.6-fold decrease in the incidence rate of RDT positive hepatitis E cases **before** and **after** the second dose campaign in Bentiu (including those not eligible for vaccination)



Discussion

Limitations

- Results are preliminary, analysis and confirmatory PCR testing is ongoing
- Low number of confirmed cases leads to large confidence intervals
- Specific Bentiu context
 - Population movement
 - Prior exposure to hepatitis E virus

Strengths

- Bias indicator analysis shows null vaccine effectiveness against non-hepatitis E jaundice
 - 2 dose VE: 9.8% (-34.6–39.5)
- Large amount of clinical data generated which will help us understand vaccine, diagnostics and general HEV epidemiology

Conclusions

- Vaccine was well accepted and tolerated in Bentiu IDP camp community
 - Preliminary estimates suggest short-term two-dose protection to be strong and potentially sufficient for outbreak response
 - Reduction in case incidence overall after vaccination
- Vaccination one of the interventions in outbreak response



Elizabeth Nyaruon Thon, the Chairperson of Bentiu IDP camp is exasperated over the sanitation conditions in the camp. © Peter Caton / MSF

Thank you to the South Sudan Ministry of Health, World Health Organisation, Health partners in Bentiu, MSF OCA and OCG in Bentiu, Juba, Amsterdam and Geneva

Thank you to the CHC and the entire population of Bentiu IDP camp



MSF staff member, Doki Simon, working on the Hepatitis E vaccination study. © Peter Caton / MSF

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