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Résumés des communications – Presentation abstracts

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Session: Contexts of violence

Moderators: Sarah Chateau & Claire Nicolet, MSF France

- Erica Simons
- Thomas Roederer

High mortality and violence among refugees and returnees from West Darfur, Sudan arriving in Chad, 2023: results from three retrospective mortality surveys

Erica Simons, Epicentre, France; Emmanuel Grellety, Epicentre France

Background

Fighting erupted on 15 April 2023 in Sudan between the army and the paramilitary Rapid Support Forces. By September 2023, more than 420,000 people had fled to Chad. To describe the health status of the displaced populations in camps in eastern Chad, several surveys were realised. We describe retrospective crude and under five mortality rates, reported causes of death and frequency and type of violence events experienced by displaced populations in three camps in eastern Chad.

Methods

Cross-sectional surveys were carried out in August and September 2023 in Toumtouma, Ourang and Arkoum camps. Each survey included retrospective mortality and frequency and type of violent events experienced. All surveys considered a pre-crisis and crisis phase.

Results

In all sites, the crude mortality rate (CMR) was significantly higher in the crisis phase than in the pre-crisis phase. The CMR was particularly elevated in Ourang camp (CMR: 2.25 deaths/10,000 people/day [95% CI: 1.77 - 2.74] in the crisis phase versus CMR: 0.11 deaths/10,000 people/day [95% CI: 0.02 - 0.20] in the pre-crisis phase). Violence was the leading self-reported cause of death in all sites. Among households in Ourang, more than 90 percent originating from El Geneina, more than 1 in 10 of all men aged 30 and over died of violent causes. In Toumtouma, Ourang and Arkoum camps, the overall frequency of violence among households was 3.3%, 11.7% and 4.4% respectively, with beatings and shooting most frequently cited.

Conclusion

In the three camps investigated, excess mortality was observed among households during the crisis phase, with excess mortality primarily linked to violence among men. The population in Ourang camp, largely from El Geneina, appears to have been particularly affected by the violence, with CMR 20 times higher than in the pre-crisis period and mortality rates exceeding the standard emergency threshold (1 death/10,000 people/day).

Several cross-sectional surveys were carried out among displaced populations arriving in Chad. We provide epidemiological evidence of the high rates of mortality and violence since the start of the conflict in Sudan.



Mortality and Violence in Haiti in 2023: 2 population-based surveys

Thomas Roederer, Epicentre, France

Background

Haiti faces chronic instability for decades, but recent years have seen exacerbation following the assassination of president Juvenel Moïse in 2021. Over 95 armed gangs are battling for control of Port-au-Prince and constant clashes paralyze infrastructure and medical assistance. Data on mortality and violence are virtually non-existent. To address this information gap, we conducted two retrospective mortality surveys, one among MSF national staff and another in the Cité Soleil commune population in Port-au-Prince.

Methods

The first cross-sectional survey was conducted in April 2023 among the MSF-OCP, OCA and OCB national staff and their families. All 1545 MSF Haitian employees were eligible. The second took place in August 2023 in the Cité Soleil commune, where a spatial sample of 1400 households was randomly selected. Indicators included crude mortality rate, causes of death, and experiences of violence.

Results

The MSF staff survey interviewed 819 members representing 3977 individuals, while the Cité Soleil survey interviewed 1669 households representing 8202 individuals. Mortality was low in the MSF staff, with only 6 deaths, in Cité Soleil, 176 deaths were reported, translating into a crude mortality rate of 0.63/10000/day [95% CI: 0.54 - 0.73]. Violence accounted for 40% of deaths, with an estimated age-standardized number of homicides of 2,300. Nearly half of MSF Staff family members and Cité Soleil participants experienced some form of violence.

Conclusion

Our findings confirm the alarming levels of violence experienced by the Haitian population. In 2022-2023, Haiti was one of the most dangerous countries in the world for civilians. Urgent action is needed to strengthen humanitarian access, healthcare provision and civilian protection.

Two surveys conducted by Epicentre/MSF in 2023 in Haiti confirm the extreme violence the population is suffering. Urgent action is needed to improve healthcare access and civilian protection.



Session: Challenges and opportunities to improve access

Moderators: Farah Hossain, MSF Japan & Alain Alsalhani, Access Campaign, MSF

- Birgit Schramm & Farah Hossain
- Issaka Soumana

A concern for large-scale treatment access: High prevalence of active HCV infection among Forcibly Displaced Myanmar Nationals residing in camps, Cox's Bazar, Bangladesh

Birgit Schramm, Epicentre, France; Farah Hossain, MSF Japan

Background

Hepatitis C virus (HCV) is a major cause of liver diseases globally. Transmission is primarily bloodborne through unsafe injections or healthcare practices. Effective treatment exists, yet access to diagnosis and treatment is limited. Few data indicated high HCV exposure among Rohingya refugees/FDMN residing in crowded camps in Cox's Bazar District, Bangladesh, where Médecins Sans Frontières is pioneering HCV services. Representative information on the prevalence of active HCV infection and exposure risk factors was lacking.

Methods

A cross-sectional survey was carried out in May-June 2023, including adults (≥ 18 years) by simple random geo-sampling (one participant per household, target sample 680), in seven camps (8W, 12, 13, 16, 17, 18, 19) in Cox's Bazar District. Participants were screened with an HCV-antibody test (SD Bioline), and active infection assessed with Xpert® HCV Viral Load test (Cepheid) if seropositive. A structured questionnaire was administered to identify risk factors of exposure.

Results

Of the 641 participants, median age was 34 years [IQR 28, 46], 66.3% were female. The estimated prevalence of HCV-seropositivity was 29.7% (95%CI: 26.0-22.8), and the prevalence of active infection was 19.6% (16.4-23.2). Multivariable regression revealed higher odds of HCV-seropositivity for female (adjusted odds ratio (aOR)=1.7 (1.0-2.6)), age groups ≥ 25 years old (aORs ranging from 2.3 to 2.9), reported medical injection(s) (aOR=1.7 (95% CI: 1.0-2.6)) or surgery (aOR=4.7 (95%CI: 1.3-16.7)). Half of participants never heard about Hepatitis C, 4.0% of viremic participants reported previous HCV treatment.

Conclusion

The survey revealed a significant burden of active HCV infection among adult Rohingya camp residents, which, extrapolated may affect an estimated 86,000 individuals. Urgent action is required to expand diagnosis and treatment to prevent advanced liver disease and transmission. A collaborative task force with camp-based health stakeholders is now underway for a mass screening and treatment initiative, as well as a camp-wide HCV awareness campaign.

High prevalence of Hepatitis C infection among Rohingya refugees urges the implementation of large-scale diagnosis- and treatment initiatives, along with awareness and health promotion campaigns.



Determining whether mass vaccination campaigns with fractional dose of PCV10 (Pneumosil®) could accelerate herd protection against pneumococcal transmission in sub-Saharan Africa

Issaka Soumana, Epicentre Niger

Background

In settings with low Pneumococcal Conjugate Vaccine (PCV) coverage, mass campaigns targeting multi-age cohorts (MAC) might accelerate herd protection but would be costly. Campaigns using fractional dose PCV would decrease cost and increase access.

Methods

We conducted a cluster-randomized trial in Niger to evaluate the effect of a mass campaign targeting children aged 1-9 years on pneumococcal carriage. 63 villages were randomized in a 3:3:1 ratio to receive campaigns with a single full dose of a 10-valent PCV (Pneumosil®), a single 1/5th fractional dose, or no campaign. We conducted two independent carriage surveys among a total of 2268 households 6 months before and 6 months after vaccination, collecting a nasopharyngeal swab from a child aged 1-9 years for culture and serotyping. If the full-dose campaign was shown superior to control in carriage reduction, the non-inferiority of fractional-dose campaign was to be evaluated, with the lower bound of the 95%CI > -7.5%. Registration: NCT05175014, PACTR20211257448484

Results

Surveys were conducted between December 22, 2021, and 18 March, 2022, and December 12, 2022, and March 9, 2023. The vaccination campaign was June 15-August 2, 2022. Participant characteristics were similar between the two surveys and across arms. Pre-vaccination, vaccine-type (VT) carriage was 15.6% in the full-dose arm, 17.9% in the fractional dose arm, and 18.8% in the control arm. Post-vaccination, VT carriage was 4.6% in the full-dose arm, 8.0% in the fractional dose arm, and 16.5% in the control arm. In the primary analysis, the risk difference between the full dose and the control arms was -12.0% [-19.0; -5.0], $p=0.001$, and

between the full dose and fractional dose arms it was -3.5% [-5.8; -1.1], meeting the prespecified non-inferiority criterion. Similar results were seen after adjustment for age, vaccine coverage and other factors.

Conclusion

MAC campaigns had a marked impact on VT carriage and fractional-dose campaigns met non-inferiority criteria. Such campaigns should be considered in low-coverage settings, including humanitarian emergencies, to accelerate population protection.

Pneumococcal conjugate vaccines, vaccination campaigns, fractional dosing, humanitarian emergency, Niger

Session: Models of care

Moderators: Christopher Mambula & Etienne Guillard, MSF France

- Jihane Ben-Farhat
- Valentina Carnimeo & Pascale Lissouba
- Anca Vasiliu

Exploring patient preferences and outcomes: the example of new differentiated models of HIV care delivery in Uganda and the DRC among people living with HIV

Jihane Ben-Farhat, Epicentre, France

Background

Mobility of people living with HIV (PLWH) among urban population in Goma and the fisherfolk community in western Uganda can serve as a barrier to retention in care. To address this challenge, MSF supported MoH in deployment of WHO recommended Differentiated Services Delivery Models (DSDM), especially Community ART groups (CAG) where clients form groups and rotate drug pick-up. In these studies, we aimed to explore retention-in-care, viral load coverage and suppression among PLWH enrolled in DSDM and describe acceptability and satisfaction of these models in Goma, DRC and Kasese, Uganda.

Methods

In both contexts, we carried out a retrospective cohort analysis complemented by a cross-sectional survey in Goma and a qualitative survey in Kasese. For the cohort analysis, we examined the characteristics of PLWH enrolled in DSDM. Utilizing Kaplan-Meier survival analysis, we estimated retention in care and calculated viral coverage and suppression rates at 12 months post-model initiation. In Goma, we administered a satisfaction questionnaire to a subset of the active cohort, while in Kasese, we conducted interviews and facilitated focus group discussions to document the acceptability and relevance of DSDM.

Results

In total, 1950 PLWH in Goma and 1773 PLWH in Kasese were included in the cohort analyses. After one year of model initiation, more than 90% of PLWH enrolled in MSF-supported DSDM were retained in care (94.1% among PLWH in Goma and 97.6% in Kasese). Of PLWH who retained in care at 1-year, proportion of virally suppressed PLWH was high in both contexts (96.4% in Goma and 97.0% in Goma). PLWH and healthcare providers expressed positive sentiments towards DSDM,

acknowledging their utility in enhancing convenience and reducing transport expenses for ART access. Moreover, they noted benefits such as decreased waiting times, alleviation of overcrowding and workload at healthcare facilities, as well as the role of DSDM in mitigating stigma and fostering responsibility sharing among group members.

Conclusion

Although great progress has been made in the fight against the HIV epidemic in recent years, a one-size-fits-all approach to caring for people living with HIV is no longer appropriate. The findings from these evaluations underscore the effectiveness of tailored, differentiated services, which maintain high retention rates in care, even within mobile communities, while also garnering strong acceptability. It is imperative to consider integrating DSDM into routine programming for chronic illnesses. By adapting clinical care to suit the lifestyles of PLWH, such models can offer enhanced support to patients, ultimately improving health outcomes.

MSF's response to retention challenges among PLWH involved supporting the deployment of WHO-recommended DSDMs, including CAGs. The studies aimed to evaluate retention in care, viral load coverage, and suppression among PLWH enrolled in these DSDMs, while also investigating their acceptability and satisfaction



Challenges and lessons of implementing models of HIV Care in Carnot, Central African Republic

Valentina Carnimeo, Epicentre, France; Pascale Lissouba, Epicentre, France

Introduction

In Carnot, Central African Republic, MSF collaborates with the Ministry of Health at the District Hospital (DH), providing comprehensive care for chronic diseases, including integrated HIV services. Since 2016, HIV differentiated treatment models (DTMs) have been introduced, including multi-monthly dispensing of antiretroviral therapy, Community ART Groups (CAGs), and decentralized care. A multi-methods study was conducted to describe and understand the continuum of care of patients in the cohort, including retention indicators, treatment adherence, perceptions of DTMs and reasons for late presentation to care.

Methods

Programmatic data of the HIV cohort in Carnot between 2011 and 2022 was analysed retrospectively. A cross-sectional survey was conducted on a random sample of active patients who underwent a clinical examination, CD4, viral load (VL) and ARV resistance tests to estimate the proportion of virological failures and resistance profiles. Lastly, semi-structured interviews were conducted with key informants, health care workers, active patients, and patients late for their appointments (< 6 months).

Results

In 2023, the cohort included 4,745 patients on treatment, with 35.5% (N=1,684) lost-to-follow-up. The probability of retention in care decreased over time and adherence to care (% of late appointment to the health centre) was lower than 80%. Among the 341 patients surveyed, 96% of them were on a treatment based on dolutegravir (DTG), and 12% (N=40, 95%CI 8-16) had virological failure. Among those, nearly one third (29.6%) presented drug resistances to the class of molecules currently used and 2.4% presented resistance to DTG, indicating that lack of adherence was likely the cause of virological failure. DTMs were not optimally implemented, and perceptions were mixed. Reasons for late presentations to appointments included access and service-related barriers, stigmatisation and socio-economic vulnerability, however, patients facing these barriers were often excluded from accessing DTM.

Conclusion

Despite DTMs, patients' retention in care remains low. Strategies for better implementation and equitable access for patients are urgently needed.

In the Central African Republic, despite efforts, HIV care retention faces challenges. Differentiated models show promise but are not fulfilling their potential. Overcoming obstacles is crucial.



Community household child contact investigation for tuberculosis

Anca Vasiliu, IRD, France

Background

Globally, the uptake of tuberculosis-preventive treatment (TPT) among children with household tuberculosis contact remains low, partly due to the necessity of bringing children to health facilities for investigations. This study aimed to evaluate the effect on TPT initiation and completion of community-based approaches to tuberculosis contact investigations in Cameroon and Uganda.

Methods

We did a parallel, cluster-randomised, controlled trial across 20 clusters (consisting of 25 district hospitals and primary health centres) in Cameroon and Uganda, which were randomised (1:1) to receive a community-based approach (intervention group) or standard-of-care facility-based approach to contact screening and management (control group). The community-based approach consisted of symptom-based tuberculosis screening of all household contacts by community health workers at the household, with referral of symptomatic contacts to local facilities for investigations. Initiation of TPT (3-month course of rifampicin-isoniazid) was done by a nurse in the household, and home visits for TPT follow-up were done by community health workers. Index patients were people aged 15 years or older with bacteriologically confirmed, drug-susceptible, pulmonary tuberculosis diagnosed less than 1 month before inclusion and who declared at least one child or young adolescent (aged 0–14 years) household contact. The primary endpoint was the proportion of declared child contacts in the TPT target group (those aged <5 years irrespective of HIV status, and children aged 5–14 years living with HIV) who commenced and completed TPT, assessed in the modified intention-to-treat population.

Findings

The study included nine clusters in the intervention group (after excluding one cluster that did not enrol any index patients for >2 months) and ten in the control group. Between Oct 14, 2019 and Jan 13, 2022, 2894 child contacts were declared by 899 index patients with bacteriologically confirmed tuberculosis. Among all child contacts declared, 1548 (81·9%) of 1889 in the intervention group and 475 (47·3%) of 1005 in the control group were screened for tuberculosis. 1400 (48·4%) child contacts were considered to be in the TPT target group: 941 (49·8%) of 1889 in the intervention group and 459 (45·7%) of 1005 in the control group. In the TPT target group, TPT was commenced and completed in 752 (79·9%) of 941 child contacts in the intervention group and 283 (61·7%) of 459 in the control group (odds ratio 3·06 [95% CI 1·24–7·53]).

Community household contact tracing for tuberculosis is effective, feasible, cost-effective, and acceptable. It has the potential to timely identify contacts with tuberculosis and provide preventive treatment to children.



Session: Hepatitis E: from outbreak response to policy changes

Moderators: Iza Ciglenecki, MSF Stwitzerland & Melanie Marti, WHO

- Etienne Gignoux
- Joseph Aumuller

First mass reactive vaccination campaign against Hepatitis E: main results of observational studies

Etienne Gignoux, Epicentre, Epicentre, France

Introduction

Hepatitis E was first identified in the 1990s, but major epidemics date back to the 1950s. There is no specific treatment, and it can be fatal especially for pregnant women, causing spontaneous abortion and stillbirths. In 2011, the first vaccine was made available, and in 2015, the WHO recommended its use during epidemics, including for pregnant women. However, several major epidemics occurred without vaccine use. The first mass reactive vaccination took place in 2022 at the Bentiu camp in South Sudan, alongside operational research.

Methodology

We assessed vaccination feasibility and acceptance through coverage surveys and conducted focus group discussions on acceptance. We monitored adverse events following immunization (AEFI) for pharmacovigilance. To assess safety in pregnancy, we monitored the pregnancy outcomes of all women identified as pregnant during the vaccination campaign through a census. Despite the significant efficacy shown in a phase 3 clinical trial after three doses, we aimed to evaluate the vaccine's efficacy in South Sudan during an epidemic after administering two doses through a case-control study.

Results

Coverage of at least one dose of the Hecolin vaccine after three rounds was estimated at 86% (95% CI: 84-88), with no cases of severe AEFI. Focus groups revealed strong concern about hepatitis E and high confidence and demand for the vaccine. An emulated target trial showed a relative risk of foetal loss between vaccinated and unvaccinated pregnant women at 1.1 (95% CI: 0.7-1.8). Vaccine effectiveness after two doses was estimated at 88.3% (95% CI: 53.8-97.6) using a test-negative design.

Discussion

We found high vaccine coverage, good acceptance, and demand from the population. There was no evidence of increased risk of foetal loss among vaccinated pregnant women. Despite the small number of cases, the reduced dose regimen appeared effective in reducing disease risk in this highly exposed population.

Studies from the first mass reactive vaccination against hepatitis E demonstrated high coverage and acceptance, no safety issues among pregnant women, and good effectiveness after two doses.



Hepatitis E outbreak response in Fangak County, South Sudan: coverage and acceptance of a vaccination campaign targeting women of reproductive

Joseph Aumuller, Epicentre, France

Background

In September 2023, the South Sudan Ministry of Health declared an outbreak of hepatitis E virus in Fangak County, Jonglei State. From April to November 2023, MSF identified 169 hepatitis E cases, among them 45% pregnant women. Cases reported at the hospital were severe and the case fatality ratio (CFR) was high with 18 deaths, 53% were women of reproductive age and 42% were pregnant women. In response, MSF together with the Ministry of Health conducted the 2nd ever reactive vaccination campaign with the Hecolin vaccine. The 1st to target exclusively women of reproductive age.

Methods

This is a descriptive, cross-sectional cluster survey with a two-stage cluster sampling design. The two strata selected were the Old Fangak and Mareang/Toch Payams.

To complement the vaccination coverage estimates, understand perception of the vaccine, and the acceptance of the strategy to vaccinate only women of reproductive age, qualitative methods were utilized following the second round of vaccination.

Results

High coverage was observed of at least one dose of hepatitis E vaccine, according to recall or card, among vaccine eligible women: 94% [95% CI 92-95] in Old Fangak and Mareang /Toch Payams. Coverage of two doses was lower, with estimated coverage of 77% [95% CI 74-80%] according to recall or card. Vaccination coverage was similar in both strata, even in hard-to-reach areas.

While community members reported high acceptance of vaccine, many were critical of the vaccine strategy targeting women aged 16 to 45. This was perceived to conflict with the observed cases of Hepatitis E among the population and physical reproductive age, exclude other vulnerable groups, and not consider community priorities or decision-making structures.

Conclusion

The vaccination campaign reached high coverage despite challenging field conditions, and low acceptance of the strategy.

In response to a Hepatitis E outbreak MSF conducted the second ever reactive campaign reaching high coverage in women of reproductive age.



Session: Tuberculosis

Moderators: Cathy Hewison, MSF France & Dr Stavia Turyahabwe, Ministry of Health Uganda

- Sofia Payotte & Giulia Scarpa
- Mathieu Bastard
- Maelenn Gouillou

'You can save a life if we get those algorithms right'. A multi-country mixed-methods evaluation of new paediatric TB diagnostic algorithms

Sofia Payotte, Epicentre, France; Giulia Scarpa, Epicentre, France

Background

Under-diagnosis of tuberculosis in children remains a major concern worldwide. The World Health Organization (WHO) recommends two new treatment decision algorithms for TB in children less than 10 years presenting with presumptive pulmonary TB. The algorithms are adapted to contexts with, and without radiography, include laboratory testing if available, and aim to facilitate treatment decision by assigning scores to symptoms and radiological features. However, little is known about the feasibility and acceptability of implementing these algorithms in Sub-Saharan Africa settings

Methods

Using a qualitative study design, we conducted 45 semi-structured interviews with health workers in nine health facilities in Uganda, Niger and Guinea. We analyzed the data thematically, and using the critical discourse analysis with a deductive and inductive approach to identify contextual barriers and acceptance of the intervention among health workers.

Results

Firstly, discourse analysis shows that health workers identify various socio-cultural factors (e.g.: delays in children arriving at health facilities, stigmatization) and structural factors (e.g. high workload for health workers, lack of resources in the health centres) as the major barriers that make TB diagnosis difficult. In this context, implementation of the algorithms is positively perceived (e.g.: the scoring system was found to be useful and user-friendly) but raises some challenges (e.g.: additional paperwork). Otherwise, results shows that the implementation of the algorithms plays a role in strengthening health worker's sense of autonomy and efficiency, and some paramedical staff (nurses) express the wish to be more directly involved in applying the algorithms.

Conclusion

This study found that the new TB algorithms were perceived positively by health workers, and well accepted in the three countries. However, it illustrates the extent to which the implementation of innovative tools in healthcare structures needs to consider the existing system, potential barriers, and opportunities to ensure long-term use.

The new WHO algorithms to diagnose TB in children are user-friendly for health workers. However, several structural and socio-cultural factors influence their longer-term use.



Treatment of children and adolescents with MDR/RR-TB regimens containing bedaquiline and delamanid: results from the endTB observational study

Mathieu Bastard, WHO, Switzerland

Background

Children and adolescents with multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB) are under diagnosed and under treated. Few reports exist on the treatment of children and adolescents with newer TB drugs. We assessed the safety and effectiveness of MDR/RR-TB regimens containing bedaquiline and delamanid among children and adolescents.

Methods

The endTB observational study is a prospective, multi-site study. Children and adolescents aged 19 years and below are included in this analysis. We report the frequency and outcomes of clinically relevant adverse events of special interest (AESI) and end of treatment outcomes.

Results

A total of 190 children and adolescents from 14 countries were included (< 5 years: 4, 5-14 years: 20, 15- 19 years: 166), 47% had BMI < 18.5 Kg/m², 6% were HIV positive, 68% previously treated with second-line drugs, 52% had fluoroquinolone resistance, 71% cavity or bilateral disease on chest Xray. Initial treatment contained bedaquiline only (51%), delamanid only (39%) or both (10%) as part of a multidrug regimen. Other frequently used drugs were linezolid (82%), cycloserine (71%), clofazimine (70%) and fluoroquinolones (69%). End of treatment outcomes were 85% success, 5% death, 4% failure, 4% lost to follow and 2% not evaluated. Most common clinically relevant AEs were peripheral neuropathy, electrolyte depletion and hearing loss with 26 (16%), 24 (15%) and 11 (7%) patients experiencing at least one event respectively. Two patients (1%) experienced clinically relevant QT interval prolongation which resolved without sequelae.

Among patients experiencing hearing loss 4 (36%) resolved, 4 (36%) resolved with sequelae, 1 (9%) did not resolve, and 2 (18%) had unknown outcomes. Among patients experiencing peripheral neuropathy, 14 (54%) resolved, 9 (35%) resolved with sequelae, 3 (11%) did not resolve.

Conclusion

Treatment of MDR/RR-TB with bedaquiline and delamanid is effective and well tolerated amongst children and adolescents. All oral regimens should be scaled up as recommended by WHO for these age groups.

All oral short treatment regimens containing bedaquiline and delamanid should be scaled up in children and adolescents with drug-resistant tuberculosis.



endTB clinical trial: results in key subgroups of patients with drug-resistant tuberculosis

Maelenn Guillou, Epicentre, Epicentre

Background

endTB is a Phase 3, randomized, controlled, non-inferiority trial, comparing five 9-month experimental regimens consisting of 4-5 drugs (including bedaquiline, delamanid, clofazimine, linezolid, fluoroquinolones, and pyrazinamide) to the standard of care for rifampicin-resistant, fluoroquinolone-susceptible tuberculosis. Three experimental regimens (endTB1, endTB2, endTB3) were non-inferior to the control in the primary analysis. This analysis explores the efficacy results of the endTB clinical trial in key subgroups (HIV positive, low BMI, diabetes, severe disease) to help clinicians to make the choice between these three regimens for patients with a more difficult to treat form of disease.

Methods

For each subgroup, proportion of favourable outcome at Week 73 was calculated in each arm. Risk differences and 95% confidence intervals were estimated in the modified intention-to-treat population (mITT), which included all randomized participants who took at least one dose of study treatment and had a positive pre-randomization tuberculosis culture. Results in each arm were plotted on forest plots.

Results

In HIV-infected patients, efficacy results are consistent with the overall results in endTB1 and endTB2 while in endTB3 the effect of trt favours the control arm. No differences from the overall population were observed in any of the 3 arms in patients with a more severe disease, while treatment effect in patients with low BMI, favours the control arm in all 3 arms. Treatment effect in patients with diabetes, favours the experimental arm in all 3 arms.

Conclusion

All 3 arms could reasonably be used in patients with severe disease or diabetes. endTB1 and endTB2 appeared to be particularly efficacious in HIV positive patients. Longer or regimens with more drugs may achieve better results in patients with low BMI. Additional research is needed to confirm these findings.

endTB clinical trial main efficacy results hold in patients with severe disease or diabetes. 2 regimens could be recommended for HIV-infected patients.



Session: Outbreak I Ebola

Moderators: Prof. Steve Ahuka, INRB DRC & John Johnson, MSF France

- Sophie Meakin
- Rebecca Coulborn

Effectiveness of rVSV-ZEBOV vaccination during the 10th Ebola virus disease epidemic in the Democratic Republic of the Congo: a retrospective observational analysis

Sophie Meakin, Epicentre, Epicentre

Background

The recombinant vesicular stomatitis virus–Zaire Ebola virus (rVSV-ZEBOV) vaccine is the only vaccine recommended for use to respond to Zaire ebolavirus outbreaks by SAGE. A single ring vaccination trial found the efficacy to be 100%; however, no estimates of real-world effectiveness have yet been published.

Methods

We conducted a retrospective test-negative case-control analysis to estimate effectiveness of rVSV-ZEBOV vaccination against Ebola virus disease (EVD) during the 2018 - 2020 epidemic in the Democratic Republic of the Congo (DRC), using data on suspected cases collected at Ebola treatment centres. Missing data were imputed using multivariate imputation. Among those who reported contact with an Ebola case before symptom onset, each EVD-positive case was matched to one EVD-negative control by sex, age, health zone and month of symptom onset. Effectiveness was then estimated from the odds ratio of being vaccinated vs. unvaccinated among cases and controls, after adjusting for the matching factors.

Results

The primary study population contained 309 cases and controls each, on average, of which between 11 and 23 cases (3.6 – 7.4%) and between 48 and 80 controls (16 – 26%) were recorded as vaccinated at least ten days before symptom onset. We found rVSV-ZEBOV vaccination at least ten days before symptom onset was 84% effective against developing EVD (95% credible interval [70%, 92%]). There was no apparent difference in effectiveness by sex, age, or due to a change in vaccination protocol.

Conclusion

This study is the first to estimate real-world effectiveness of rVSV-ZEBOV vaccination EVD during the second largest EVD outbreak ever recorded. Our findings confirm that rVSV-ZEBOV vaccination is highly protective against developing EVD and support its reactive, targeted use in at-risk people during future outbreaks.

Using a retrospective test-negative study design, we estimated the real-world effectiveness of the rVSV-ZEBOV vaccine and confirmed that it's highly protective against developing the disease.



Case fatality risk among individuals vaccinated with rVSVΔG-ZEBOV-GP: a retrospective cohort analysis of patients with confirmed Ebola virus disease in the Democratic Republic of the Congo

Rebecca Coulborn, Epicentre, France

Background

The rVSVΔG-ZEBOV-GP vaccine constitutes a valuable tool to control Ebola virus disease (EVD) outbreaks. This study aimed to assess the protective effect of the vaccine against death among patients with confirmed EVD.

Methods

In this retrospective cohort analysis of patients with confirmed EVD admitted to Ebola health facilities in the Democratic Republic of the Congo between July 27, 2018, and April 27, 2020, we performed univariate and multivariate analyses to assess case fatality risk (CFR) and cycle threshold for nucleoprotein according to vaccination status, EVD-specific treatments, and other risk factors.

Results

We analysed all 2279 patients with confirmed EVD. Vaccination significantly lowered CFR (vaccinated: 25% (106/423) vs not vaccinated: 56% (570/1015); $p < 0.0001$). In adjusted analyses, vaccination significantly lowered the risk of death compared with no vaccination, with protection increasing as time elapsed from vaccination to symptom onset (vaccinated ≤ 2 days before onset: 27% [27/99], adjusted relative risk 0.56 [95% CI 0.36–0.82, $p = 0.0046$]; 3–9 days before onset: 20% [28/139], 0.44 [0.29–0.65, $p = 0.0001$]; ≥ 10 days before onset: 18% [12/68], 0.40 [0.21–0.69; $p = 0.0022$]; vaccination date unknown: 33% [39/117], 0.69 [0.48–0.96; $p = 0.0341$]; and vaccination status unknown: 52% [441/841], 0.80 [0.70–0.91, $p = 0.0011$]).

Cycle threshold values were significantly higher—indicating lower viraemia—among patients who were vaccinated compared with those who were not vaccinated; the highest difference was observed among those vaccinated 21 days

or longer before symptom onset (median 30.0 cycles [IQR 24.6–33.7]) compared with patients who were not vaccinated (21.4 cycles [18.4–25.9], $p < 0.0001$).

Conclusion

To our knowledge, this is the largest observational study describing the protective effect of rVSVΔG-ZEBOV-GP vaccination against death among patients with confirmed EVD admitted to an Ebola health facility. Vaccination was protective against death for all patients, even when adjusted for EVD-specific treatment, age group, and time from symptom onset to admission.

Among EVD-confirmed patients, vaccination reduced the risk of dying from EVD by more than half compared to being unvaccinated, even after adjusting for risk factors.



Session: Outbreak II

Moderators: Ismael Adjaho, MSF WaCA & Prof. Steve Ahuka, INRB DRC

- Céline Langendorf & Birgit Nikolay
- Catherine Eisenhauer
- Yves Amevoin & Franck Ale

Measles confirmation and seroprevalence: addressing the challenges of sample collection and laboratory procedures

Céline Langendorf, Epicentre, France; Birgit Nikolay, Epicentre, France

Background

While case confirmation is most of the time not necessary for case management decisions – the measles outbreak response relies on the timely biological confirmation of outbreaks to facilitate a vaccination response. Seroprevalence estimates, on the other hand, can help plan vaccination activities or evaluate them, by quantifying immunization levels in the population. In remote areas where transport of serum or plasma samples is challenging, we ideally would like to use dried blood spots (DBS) which are easy to collect, easy to transport, and theoretically stable in time and temperature. However, the practical use of DBS under field conditions is not as easy as we expect. Based on different examples of measles surveys in the DRC and Niger, we will describe the challenges we are facing regarding interpretation of serology results from DBS for both measles biological confirmation and seroprevalence surveys.

Results and discussion

In the DRC, for biological confirmation, the sensitivity of DBS samples compared to plasma decreases with transport delays and is lower in remote settings. Measles seroprevalence based on DBS was lower than expected, raising questions about the use of the recommended seropositivity threshold and the correlation with seroprotection after vaccination. In Niger, we found that a good quality DBS can be obtained under field conditions, and an adjustment factor for DBS compared to serum is needed but may vary between settings.

Conclusion

Serology on DBS is the most acceptable procedure so far for biological confirmation of measles cases and seroprevalence. However, additional investigations are needed to better standardize, test, and interpret DBS samples to help making the most appropriate operational decisions.

Biological confirmation of outbreaks and seroprevalence estimates are the key components of measles control. Serology on dried blood spots is the most appropriate method but raises many challenges on interpreting the results.



Multi-country validation of a simple alert system to improve measles outbreak response

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Background

Outbreak alert systems can offset the severity of measles epidemics by minimising response delays. Existing systems, however, are often too sensitive to be practical when identifying areas for reactive interventions. To redress this challenge, we present a simple alternative system that combines a weekly and triweekly suspected case threshold. First evaluated in the DRC in 2022, here we extend the evaluation of this system to the context of Niger.

Methods

A large number of threshold combinations were evaluated against indicators of cases captured by intervention and false alert risk. Combinations were evaluated against admin 2 level surveillance data from the DRC and Niger from 2015-2024. Performance was then compared to standard recommendations from the WHO and MSF.

Results

The two example countries have distinct epidemic profiles, with the DRC exhibiting mass epidemics and Niger showing strong annual seasonality. In both settings, the proposed alternative alert system outperformed the existing WHO and MSF recommendation. The WHO recommendation, which is triggered by four suspected cases occurring within one month in a given locale (here, admin level 2), performs similarly to the proposed alternative when selecting the most sensitive of threshold combinations. The MSF recommendation, which is triggered by a raw increase in number of cases for three consecutive weeks, performed markedly worse, capturing 50% or less of cases. This poor performance is predominantly attributable to the high volatility of weekly measles surveillance data.

Conclusion

This analysis presents a simple evidence based alert system to improve measles outbreak response. It has been assessed in two countries, Niger and the DRC, and found to outperform standard recommendations. At present the system is available for use in both countries via their respective surveillance dashboards. Ongoing work is being conducted to evaluate the system in settings with additional epidemic profiles, including areas with low burden and areas with poor surveillance.

Alert systems are a valuable tool to improve outbreak response but standard options are often too sensitive to be practical. Here we propose and evaluate a simple alternative that offers more balanced performance.



The surge of diphtheria in 2023: Global overview, MSF responses & challenges

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Background

Diphtheria is an infection of the upper respiratory tract characterized by the production of an extracellular toxin. Individuals with incomplete immunization or low levels of antitoxin antibodies are particularly susceptible to infection. Specific treatment relies on Diphtheria Anti-Toxin (DAT) and the disease is preventable by active immunization. Since 2019, large outbreaks have been reported in WHO African Region, but 2023 has seen an unprecedented surge in diphtheria cases in West Africa, mainly Kano State, Nigeria.

Methods

Médecins Sans Frontières (MSF) and Epicentre have been involved in response efforts but have faced several challenges due to limited hospital capacity and a global shortage of DAT. This led to the implementation of new solutions such as home-based care, adaptation of DAT dosage and strategic allocation of DAT stocks. Preliminary descriptive analysis shows the key figures from the 2023 diphtheria outbreak and summarizes critical insights from one year of MSF intervention in Kano.

Results

MSF treated around 23 thousand individuals across 14 sites in five countries. Nearly half of these patients required hospitalization, with an overall case fatality rate (CFR) of 6%. The majority of patients were under 15 years of age, and most were female.

In Kano State, Nigeria, specifically, three main centres were established at the peak of the outbreak. MSF used adaptive strategies to deal with the constraints of the response, which were phased according to the number of cases and the

availability of drugs. Centralised case management was used for severe cases, while a decentralised care model, including home-based care, was used for mild and close contacts. The primary centre, which remains operational, has received approximately 9 thousand patients.

Data indicate that the prompt administration of diphtheria antitoxin (DAT) may influence patient outcomes. Furthermore, an early immunization campaign could have potentially reduced the overall mortality rate associated with the epidemic.

Conclusion

The surge of diphtheria in West Africa highlighted numerous challenges in combating the disease in low-resource settings, particularly concerning the availability of diphtheria antitoxin (DAT). Further analyses are required to accurately assess the impact of home-based care and DAT dosage strategies. Scaling up global DAT production and enhancing routine vaccination programs could be crucial in preventing future outbreaks.

Since 2022, West and Central Africa are facing diphtheria outbreaks, with MSF treating 23,000 people globally (CFR: 6%).

Limited hospital capacity and DAT shortages emphasize the need for increased DAT production and improved vaccination programs.





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