

2022 Annual Report

Epicentre is a unique place where the problems faced by MSF's medical teams are transformed into research questions, in order to adapt practices to contexts where access to care and innovation are major challenges. With 2/3 of its funding coming from MSF's own fundraising activities, Epicentre has the ability to set its own research priorities.

Closer to MSF

Epicentre's 3 centers in Maradi, Niger, Mbarara, Uganda, and Paris, France, combine a wide range of skills and experience, in addition to decentralized epidemiologists in MSF sections and offices. This network ensures responsiveness and agility in line with MSF's missions, which will be further strengthened by the new Field Epidemiology Training in Humanitarian Contexts (FETCH) starting in October 2022 with a cohort of 7 epidemiologists. At the end of this one-year training course, the epidemiologists will be able to autonomously lead outbreak investigations, conduct surveillance and population surveys within the framework of MSF operations and in complex emergency contexts. This epidemiological expertise will increase Epicentre's capacity to support MSF response to epidemics, describe and analyze population health situations to better guide programs, and pursue its research to propose solutions adapted to populations living in unstable conditions or with inadequate access to healthcare. In 2022, Epicentre's epidemiologists carried out more than a hundred projects, mainly in Africa.



Coping with epidemics

Being there to respond to emergencies...

MSF's areas of intervention are characterized by a high prevalence of infectious diseases and large-scale epidemics. At the end of 2022, Uganda faced an Ebola epidemic. MSF mobilized alongside the Ministry of Health to support patient medical care. At the same time, Epicentre's epidemiologists collaborated in surveillance activities, documenting cases and their contacts to ensure a comprehensive understanding of the epidemic and conducted qualitative research to understand the social context in which the epidemic was occurring and adapt the response. Their action was facilitated by the knowledge acquired during previous Ebola epidemics.

... Improving response to epidemics

A collaboration between the National Program for Emergencies and Humanitarian Actions, the Ministry of Health of the Democratic Republic of the Congo (DRC), INRB Kinshasa and Epicentre laid the foundations for an algorithm to identify people most at risk of developing Ebola disease in the presence of clinical signs suggestive of infection by the virus, published in November 2022 in *The Lancet Infectious Disease* (1). It is based on data from over 24,000 suspect cases during the Ebola epidemic in the DRC between August 1, 2018 and August 28, 2019. It appears important to determine both the exact moment when symptoms appeared and also the exposure history to assess the risk of infection. Contact with a person infected with the Ebola virus remains the most important predictive factor of the disease, independently of the patient's symptomatology, particularly in the first two days after the onset of symptoms.

Developing appropriate tools

A "line list" is a data collection tool which records the information needed to monitor sick people and implement control measures during an epidemic. Until now, each structure opened by MSF during an epidemic created its own "line list". In 2022, at the request of MSF-OCP, Epicentre's Data Science team developed a standardized tool that can be deployed in all MSF facilities: the "outbreak tool". It facilitates the work of the teams, ensures rapid implementation of a "line list" and improves the quality of the data collected. It requires no technical knowledge and is currently being upgraded to make it compatible with DHIS2, the most widely used data collection and analysis tool.

Reducing response times

Epicentre's UrgEpi project in the DRC aims to develop an algorithm for prioritizing measles epidemic alerts. Analysis and experience of previous epidemics in the DRC have led to the definition of a more sensitive alert threshold. However, in light of initial experience, early detection using the sensitive threshold in high-risk areas does not always enable us to intervene before the epidemic has progressed substantially. Our aim for 2023 is to assess whether the integration of rapid diagnostic tests could enable more reliable and earlier detection of cases, and hence intervention.

Cholera: a 360° approach to containing epidemics

The Case-Area Targeted Intervention (CATI) strategy deployed by MSF in DRC to contain cholera epidemics combines antibiotic chemoprophylaxis, hygiene promotion interventions, distribution of hygiene kits and a dose of oral vaccine within a 100-meter radius of index cases. An Epicentre study aims to assess the impact of different CATI interventions, depending on their combination, sequencing and timing, on the spread of an epidemic.



Vaccination: a public health weapon that still faces many difficulties

Deploying vaccines for the most vulnerable populations remains a challenge, due to logistical difficulties, accessibility and cost. Research therefore appears to be a way to break the deadlock and facilitate access to vaccines.

Cholera vaccination: When to administer the 2nd dose?

The optimal interval between the two doses of cholera vaccine remains a matter of debate. In collaboration with the Ministry of Health and representatives of the Guinean health authorities, MSF-OCB with the support of Epicentre is conducting a clinical trial to assess whether the immune response with an extended interval of 6 months or 12 months between two doses of oral cholera vaccine is at least as good as that obtained by administering the second dose of vaccine according to the manufacturer's instructions, i.e. two weeks after the first dose. The aim is to define the optimal conditions for administering the vaccine, and to be able to propose a vaccination schedule that could provide a solution, at least temporarily, to the problems of vaccine shortages.

Pneumococcus: are split doses of PCV vaccine feasible?

Dose splitting of vaccines is another solution for coping with shortages or reducing the cost of vaccination campaigns. To facilitate access to the 10-valent pneumococcal vaccine in low-and middle-income countries, Epicentre is conducting an EDCTP-funded trial, in collaboration with several partners, to assess the impact and feasibility of mass single-dose and split-dose campaigns of this vaccine in Niger.

First hepatitis E vaccination campaign in an epidemic context

Research in emergency situations is necessary for innovative response and should not require compromise to our high standards of work. In 2022, Epicentre worked with MSF-OCG



to document the first use of hepatitis E vaccine in response to an epidemic in Bentiu camp in Unity state, South Sudan. The only vaccine available has proved highly effective in preventing the disease in clinical trials but had never been evaluated in epidemic conditions. Epicentre's study will add to the data on the effectiveness of this vaccine, and on its safety in pregnant women, who pay the heaviest price for this disease.

Enable Lassa: laying the foundations for a vaccine trial against Lassa Fever

The Coalition for Epidemic Preparedness Innovations (CEPI) is funding Enable, the largest-ever study of Lassa fever, an endemic hemorrhagic fever in West Africa, in which Epicentre is participating. The initial aim is to estimate the incidence of the disease, the location of infected cases and how the virus spreads in Benin, Guinea, Liberia, Sierra Leone and Nigeria. The knowledge generated will then serve as the basis for the implementation of a vaccine trial against this disease by the international consortium LEAP4WA (Lassa Fever Vaccine Efficacy and Prevention for West Africa), of which Epicentre is a member. Enable's data will be used to define high-incidence areas to be targeted in the trial, as well as possible sub-groups of populations at greater risk.

Tuberculosis: the challenge of diagnosis

At the end of June 2022, the Mbarara Research Center organized a conference to present several studies on tuberculosis to local partners and stakeholders, and to identify the challenges ahead in the fight against this infectious disease in Uganda and beyond.

FujiLAM: an easy-to-use, affordable point-of-care diagnostic test

Epicentre and MSF, with the support of ANRS, have evaluated the performance of the FujiLAM test, which looks for a urinary biomarker to diagnose tuberculosis in people living with HIV. The results, presented at the Mbarara TB conference and published in The *Lancet Infectious disease* (2), showed FujiLAM to be 60% more sensitive than the microbiological reference test, compared with 40% for AlereLAM, the only test currently on the market and recommended by the World Health Organization (WHO). In addition, 94% of healthcare professionals found the FujiLAM test overall easy to perform, and urine sampling is well accepted and often preferred to sputum sampling by patients (3). However, following analysis, FIND, who supplied the tests, and the FujiLAM manufacturer reported disparities in diagnostic performance between test batches, delaying new recommendations and the widespread use of the test.

Mbarara center involved in several tuberculosis projects

Contact study, conducted by the Institut de Recherche pour le Développement (IRD), compares the effectiveness of a community-based approach to screening and initiation of treatment (TPT) in children in Uganda - at the Mbarara center - and in Cameroon. Preliminary results presented during the Mbarara TB conference seem to show a contribution of community-based interventions with screening of contact children, initiation and follow-up of TPT at home by a trained community health worker.

The Mbarara center is also heavily involved in the TB-Speed consortium led by IRD and the University of Bordeaux on the management of pediatric tuberculosis and the improvement of early detection. In particular, research presented at the Mbarara TB conference demonstrated the feasibility of detecting tuberculosis in children hospitalized for severe pneumonia, the good performance of a simplified stool sample preparation method for the molecular diagnosis of tuberculosis, the evaluation of diagnostic algorithms to guide rapid treatment decisions in vulnerable children living with HIV or suffering from severe acute malnutrition, and the feasibility of decentralizing care to the community level. In particular, the results of the TB-Speed study argue in favor of more systematic use of the Xpert Ultra rapid test in these children, especially those suffering from severe acute malnutrition.

The Mbarara TB conference was an opportunity to reiterate the need to improve diagnosis, particularly in children, to reduce treatment times and to pursue the decentralization of care in order to improve its acceptability and feasibility in communities, all of which will form the basis for future studies, some of which will be launched in 2023.



Simplifying diagnosis through imaging

Countries with a high prevalence of tuberculosis often have a shortage of X-ray equipment, due to cost and need for personnel trained in its use and image interpretation, which further limits access to tuberculosis diagnosis. In Papua New Guinea, an affordable portable ultrasound machine has the potential to help the diagnosis of pulmonary tuberculosis. Epicentre is conducting a prospective study comparing ultrasound to chest X-ray in people aged 15 and over referred for diagnosis to the MSF clinic at Gerehu General Hospital. In Manila, Philippines, Epicentre is assessing whether the implementation and use of chest radiography assisted by an artificial intelligence algorithm to interpret images is feasible and acceptable.

Continuing efforts to combat malnutrition

Malnutrition has been on the increase in several countries in recent years. In Koutiala, Mali, an Epicentre survey identified the district as being on alert for global acute malnutrition (GAM), with a prevalence of 11.45%, and on emergency alert for severe acute malnutrition (SAM), with a prevalence of 2.57%, according to the WHO classification. Epicentre's teams advised strengthening nutritional management activities. In the Guérada district (Wadi Fira province, Chad), GAM prevalence was estimated at 5.1% and SAM at 0.9% in the 4 zones surveyed. While the estimated levels of GAM do not reveal an alarming situation, vigilance is still required to avoid a deterioration in the situation of children suffering from moderate acute malnutrition (MAM) without continued nutritional support.

Decentralized care

Despite improvements in the management of SAM in children, coverage of treatment programs remains low. The remoteness of outpatient care centers, and the investment associated with weekly visits to provide clinical monitoring and distribution of ready-to-use therapeutic food rations (RUTFs), is one of the major obstacles to accessing treatment. A clinical trial conducted in Nigeria by Epicentre revealed that, although weekly monitoring of

children in care is preferable, monthly monitoring may be considered in settings where more frequent monitoring is unfeasible (4).

StimNut: adapting and developing psychosocial stimulation in Mali

Malnutrition in young children can have long-term and potentially irreversible consequences, particularly on the cognitive level. Epicentre has therefore adapted to the Malian context a five-session psychosocial stimulation protocol for children suffering from SAM, initially implemented by Action Contre la Faim (ACF) in Nepal. By the end of 2022, this approach had been rolled out to 36 families. Weekly sessions between parents or carers of severely malnourished children and psychosocial agents trained to support families are held in two health centers and the pediatric ward of MSF's Koutiala hospital. This approach is now being evaluated for feasibility and acceptability, and if results are positive as expected, can be scaled up to benefit more families affected by severe malnutrition.

Malaria: Reducing mortality among children under 5 years of age

Since 2012 in the Moïssala district of Chad, MSF-OCP, in collaboration with the Ministry of Public Health and the National Malaria Control Program, has been implementing seasonal malaria chemoprevention (SMC), which involves administering antimalarial treatment during the high-transmission season. Different strategies have been proposed over the years, and in 2021 the door-to-door strategy has been chosen, with a 5th visit (instead of the previous 4) to better cover the period of high transmission. Coverage of children aged between 3 and 59 months, the subject of a report in 2022, fell steadily between the 1st and 5th rounds. The main reason for this seems to be the absence of the child or parents at the time of the visit, as the proportion of children who did not participate due to parental refusal is marginal. On the other hand, there is a discrepancy in coverage between the verbal declarations and the data on the cards which leads to uncertainty in SMC coverage in the area. Epicentre has therefore recommended in future years, to consider other strategies for information feedback and access to children or parents who are absent at the time of the distributor's visit.

Integrating new tools for better understanding

In the Ituri region of the DRC, MSF-OCG is carrying out mass distributions of antimalarials (MDAs) in part of the Angumu health zone, where there are many displaced people. A survey carried out in 2021 revealed distribution coverage of over 90% in the villages and 96% in the IDP camps, illustrating good acceptance by the population. But what the survey highlighted above all was a spectacular reduction in malaria mortality among children under 5 after the MDA (5). The results of a 2nd survey carried out 1 year later, in April 2022, were much less straightforward. In two of the four health areas where MDA had taken place, mortality was still lower than in areas without MDA. In the other two, however, mortality was higher. Even more surprising: malaria was still the main cause of death according to the heads of household. This excess mortality, visible from the start of 2021, seemed to affect certain villages and IDP camps in particular, leading Epicentre's epidemiologists to put forward

several hypotheses, including whether the cause of death was really malaria. A new investigation was therefore launched at the end of 2022, using a verbal autopsy to find out more.

Evolving and fitting into its environment

In 2022, Epicentre continued to evolve and change to best meet MSF's needs, while maintaining its model at the crossroads of humanitarian action and world-class research. At the beginning of the year, the Mbarara Research Center laboratory was accredited GCLP (Good Clinical Laboratory Practice). "This is an important milestone for our laboratory," explains Juliet Mwanga-Amumpaire, Director of the Centre. "This accreditation demonstrates the quality and reliability of the clinical trial data we generate, and our compliance with standards that guarantee the rights and safety of participants and safeguard their confidentiality." GCLP accreditation will enhance the Centre's visibility, enabling it to strengthen its partnerships and roll out new clinical trials.

In April 2022, Niger, with Epicentre as project leader, officially joined the Organization for Women in Science for the Developing World (OWSD). This organization, which brings together women scientists from around the world, aims to increase the participation of women from developing countries in scientific and technological research, teaching and leadership, and to promote recognition of the scientific and technological achievements of women scientists and technologists in developing countries. This recognition is a springboard for developing the role of women doctors and scientists within the center and beyond.

In October, the Research Department obtained Research Fairness Initiative (RFI) certification from COHRED (Council on Health Research for Development) and became a member of the Initiative. The Initiative offers organizations a learning tool designed to help them assess their current partnerships and develop strategies to become fairer partners over time. Epicentre forges partnerships to develop ambitious research projects in line with MSF's mission.

Towards less carbon-intensive research and care

The year 2022 was also marked by the election of Dr Maryline Bonnet, Director of Research at IRD, as Chairman of the Epicentre Board of Directors. She succeeds Prof. Pierre Lombrail. Trained as a lung specialist, Maryline Bonnet will draw on her long experience as a humanitarian doctor and conducting research projects in complex and unstable environments to support Epicentre in pursuing its commitments, which since the end of 2021 have included reducing its carbon footprint by 50% by 2030. To achieve its objectives, Epicentre, like the other MSF sections involved in this approach, is supported by the non-governmental organization (NGO) Climate Action Accelerator. The year 2022 was devoted to calculating the carbon footprint. Epicentre's total greenhouse gas emissions in 2019, the year chosen as a reference, amounted to 3,891 tons of CO2 equivalent emissions. They are concentrated in three categories of emissions: transportation (particularly long-distance



travel), energy and purchases of goods and services. Workshops were held throughout the year to identify the decarbonization solutions best suited to Epicentre, culminating the establishment of a roadmap in mid-2023. At the same time, Epicentre has embarked on a process of reflection on how to integrate the reduction of greenhouse gas emissions into the construction of its research and study projects: what linkages should be made with other quality imperatives, what commitments should be made to the populations rescued and to technological developments? Over and above the essential need to reduce our footprint, this approach also raises the question of the adaptation and resilience healthcare services and research activities. to the challenges of global warming.

Facilitating implementation, access and innovation

To promote access to healthcare, we must provide practical solutions for the populations concerned. The development of social sciences within Epicentre will allow us to better consider the beneficiary's role in the design and implementation of our projects, by developing research questions together, results are more in line with beneficiary needs.

At the same time, Epicentre must step up its efforts to promote its work, increase its impact and access to its new medical practices, and ultimately influence healthcare policies. The two

Research Centers play a central role in this mission, through their involvement in multi-centric, multi-country studies and their links with local and international authorities and partners. The work of the data science team, which has been strengthened in 2022, is another area of development and strategic partnership. Its output enables the planning of larger-scale studies and contributes to the analysis of epidemics. It is a gas pedal of innovation.

The fact that Epicentre is rooted in both research and operational activities makes it a unique place to answer the questions that MSF teams are asking, to provide key information for defining the priorities of MSF programs, and ultimately to provide solutions aimed at improving access to quality healthcare.



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Epicentre in figures

- Number of full-time equivalent employees: 360, 59% of whom are scientific staff and 41% support staff (almost half of whom are domestic support staff).
- 63% men and 37% women
- 39 nationalities.
- 179 MSF trainees took part in one of the 8 training courses (Response to Epidemics, Populations in Precarious Situations, etc.) organized by Epicentre.
- 50 publications in peer-reviewed journals (find all Epicentre publications <u>HERE</u>)
 - o 50% of publications with 1st or last Epicentre author
 - o 25% of articles with Impact factor greater than 10
- Budget 2022: €17.8 M of which 31% external funding

*https://www.who.int/fr/news-room/feature-stories/detail/world-malaria-report-2019#:~:text=Cas%20de%20paludisme&text=Six%20pays%2C%20%C3%A0%20eux%20seuls,Niger%20(4%25%20chacun).

- (1) <u>Differential symptomology of possible and confirmed Ebola virus disease infection in the Democratic Republic of the Congo: a retrospective cohort study.</u> Nsio J, et al. *The Lancet. Infectious diseases* 2022 Nov 09; doi: 10.1016/S1473-3099(22)00584-9.
- (2) Novel FujiLAMassay to detect tuberculosis in HIV-positive ambulatory patients in four African countries: a diagnostic accuracy study. Huerga H et al. *The Lancet. Global health* 2023 Jan; 11(1). doi: 10.1016/S2214-109X (22)00463-6.
- (3) Feasibility and acceptability of using the novel urine-based FujiLAM test to detect tuberculosis: A multi-country mixed-methods study. Chenai Mathabire Rücker S et al. *Journal of clinical tuberculosis and other mycobacterial diseases 2022* May; 27. doi: 10.1016/j.jctube.2022.100316.
- (4) Effectiveness of a monthly schedule of follow-up for the treatment of uncomplicated severe acute malnutrition in Sokoto, Nigeria: A cluster randomized crossover trial. Hitchings MDT et al. *PLoS medicine* 2022 Mar; 19(3); e1003923. doi: 10.1371/journal.pmed.1003923.
- (5) Effect of large-scale mass drug administration for malaria on mortality and morbidity in Angumu health zone, Ituri, Democratic Republic of Congo. Grout L et al. *Malaria journal* 2023 Feb 06; 22(1). doi: 10.1186/s12936-023-04469-7.



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