Trials

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Implementing a pragmatic randomised controlled trial in a humanitarian setting: lessons learned from the TISA trial

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Abstract

Introduction High-quality evidence is crucial for guiding effective humanitarian responses, yet conducting rigorous research, particularly randomised controlled trials, in humanitarian crises remains challenging. The TISA ("traitement intégré de la sous-nutrition aiguë") trial aimed to evaluate the impact of a Water, Sanitation and Hygiene (WASH) intervention on the standard national treatment of uncomplicated Severe Acute Malnutrition (SAM) in children aged 6–59 months. Implemented in two northern Senegalese regions from December 22, 2021, to February 20, 2023, the trial faced numerous challenges, which this paper explores along with the lessons learned.

Methods The study utilised trial documentation, including field reports, meeting minutes, training plans, operational monitoring data and funding proposals, to retrace the trial timeline, identify challenges and outline implemented solutions. Contributions from all TISA key staff—current and former, field-based and headquarters—were essential for collecting and interpreting information. Challenges were categorised as internal (within the TISA consortium) or external (broader contextual issues).

Results The TISA trial, executed by a consortium of academic, operational, and community stakeholders, enrolled over 2000 children with uncomplicated SAM across 86 treatment posts in a 28,000 km^2 area. The control group received standard outpatient SAM care, while the intervention group also received a WASH kit and hygiene promotion. Initially planned to start in April 2019 for 12 months, the trial faced a 30-month delay and was extended to 27 months due to challenges like the COVID-19 pandemic, national strikes, health system integration issues and weather-related disruptions. Internal challenges included logistics, staffing, data management, funding and aligning diverse stakeholder priorities.

Discussion and conclusion Despite these obstacles, the trial concluded successfully, underscoring the importance of tailored monitoring, open communication, transparency and community involvement. Producing high-quality evidence in humanitarian contexts demands extensive preparation and strong coordination among local and international researchers, practitioners, communities, decision-makers and funders from the study's inception.

Trial registration Clinicaltrials.gov NCT04667767.

Keywords Pragmatic trial implementation, Humanitarian setting, Severe acute malnutrition, WASH, Operational research, Capitalization

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Background

The need for more evidence-based humanitarian responses has been identified as a priority repeatedly over the last two decades by both operational and research communities [1, 2]. The pursuit of more effective strategies and greater accountability in the humanitarian sector led to the Sphere project and the development of the widely used Sphere Handbook which includes a Humanitarian Charter and Minimum Standards in Humanitarian Response (first edition in 1998; latest edition 2018) [3, 4]. Policy-making institutions have since made high-level commitments towards more evidence-based interventions [5] and humanitarian donor agencies are increasingly under pressure to demonstrate effectiveness and account for impact [6]. More recently, the COVID-19 crisis has highlighted the importance of updating global evidence-based guidance to meet "context-specific and evolving needs in fragile settings" [7].

A *Lancet* Series on improving evidence for health in humanitarian crises [8] concluded that evidence on public health interventions in humanitarian crises (defined as event or series of events that represents a critical threat to the health, safety, security, or well-being of a community or other large group of people, usually over a wide area) is limited and, where it does exist, study quality was low, making it difficult to determine causation or attribution of interventions. This review called for investment in research in humanitarian settings as lack of evidence limited the effectiveness of strategies to address the needs of populations in crises [9].

Evidence-based decision-making requires not just scientific evidence but expertise and communities' culture and values to be taken into account [10]. The lack of evidence in support of many humanitarian interventions can be attributed not only to the challenges associated with the conduct of research in insecure settings but also to the use of inappropriate methodologies and unsuitable study designs [6, 9, 11]. Challenges faced include insecurity, insufficient resources and skills for data collection and analysis, equity and ethical issues and absence of validated methods [12, 13]. Conducting operational research in these contexts is complex and challenging, especially so for experimental designs such as randomised controlled trials. While randomised trials are not the only scientifically "valid" option, they are often perceived as the "gold standard" when it comes to generating causal evidence, even if they are often said to be unfeasible or unethical in humanitarian emergency settings [10]. Literature on trial implementation in humanitarian settings is scarce and only a few publications discuss the inevitable challenges faced in implementing such studies and the lessons learned [11, 14, 15].

The *Traitement Intégré de la Sous-nutrition Aiguë*[1] (TISA) trial was designed as a pragmatic cluster-randomised trial in two northern Senegalese regions covering four districts: Dahra, Linguère, Pété, and Podor. The objective was to assess the impact of a Water, Sanitation, and Hygiene (WASH) intervention as part of the standard national treatment of uncomplicated Severe Acute Malnutrition (SAM) in children aged 6–59 months. The WASH intervention included a simplified "WASH kit" (safe water storage container, chlorination tablets, and three bars of soap) as well as water treatment instructions and hand hygiene promotion (ref: clinicaltrials.gov, NCT04667767). The study population was admitted to one of 86 treatment centres for outpatient treatment programmes (OTP) for SAM with no medical complications. The aim of the trial was to assess the effectiveness, acceptability, and cost-effectiveness of including the WASH kit in the Senegalese OTP for uncomplicated SAM cases.

The study was implemented by Action Contre la Faim (ACF) Senegal in collaboration with the London School of Hygiene and Tropical Medicine (LSHTM), the Research Laboratory on Economic and Social Transformations (LARTES-IFAN) from the Cheikh Anta Diop University, and ACF-France and Spain, and in partnership with the Ministry of Health (MoH) of Senegal and UNICEF. The participant enrolment phase was active from December 22, 2021, to February 20, 2023. The study experienced significant challenges due to several external and internal factors which we describe here.

Although these challenges were ultimately overcome, and the trial was completed successfully, we believe that sharing these challenges—along with the mitigation strategies developed and lessons learned—may be useful for other teams embarking on similar initiatives. The aim of this article is to document our experience, share learnings with a wider audience and contribute to the ongoing discussion on how evidence relevant to the health needs of populations in crisis can be strengthened.

Study setting

The TISA trial was implemented in the Saint-Louis and Louga regions with a population of approximately 600,000 residing across a 28,000km^2 area (see Fig. 1). The study setting was selected on the basis of political stability, ACF's longstanding relationship with health system actors, high SAM prevalence rates (comparable to conflict-affected settings), and the MoH and UNICEF's support of the WASH and nutrition-integrated approach [16].

[1] Translated to English as "Integrated Treatment of Acute Malnutrition".

Fig. 1 TISA study setting. Adapted from "Les subdivisions administratives du Sénégal (régions et départements)", page" Subdivisions du Sénégal". Last updated on April 28, 2022, Wikipedia)

Management of SAM in Senegal follows the national protocol for the *Prise en Charge Communautaire de la Malnutrition Aiguë*[2] (PECMAS) [17] based on the internationally established Community-based Management of Acute Malnutrition (CMAM) approach [18]. SAM children without medical complications are treated at home with Ready-to-Use Therapeutic Food (RUTF) and followed up weekly at health posts for a period of 8 weeks [17].

Of the 97 health posts providing SAM treatment existing in both districts, 11 were excluded from the study due to very low SAM admission rates of under five patients per year. The remaining 86 health posts were included in the trial and randomly allocated on a one-to-one basis to either a control arm where patients received the standard SAM treatment (by local health workers) only or to an intervention arm where patients received the WASH intervention integrated in the standard SAM treatment.

Methods

Between June 26, 2022 to April 28, 2023, trial documentation was used to retrace the trial timeline, challenges encountered and solutions implemented. Trial documents included field reports, meeting and workshop minutes, standard operating procedure (SOP) training plans, operational monitoring and funding proposals. This was completed with correspondence between the TISA consortium and with a range of stakeholders (e.g. ACF management, donors, communities, authorities). Interviews were also held with key staff on specific topics regarding the trial implementation. All TISA key staff (field and headquarters) contributed to the collection and interpretation of information. Challenges encountered during the trial were classified as internal (emerging from within the TISA consortium) or external (caused by border contextual factors impacting the trial implementation). Lessons were drawn from these events and were regrouped under key themes.

Results

The study faced challenges that impacted the trial timeline and enrolment rate as presented in Fig. 2. Table 1 summarises the challenges encountered during the implementation, solutions and lessons learned. External challenges, shown in blue, included COVID-19 pandemic, repeated national strike actions, collaboration with the existing health care system and weather-related issues. Internal challenges, shown in green, included logistics, staffing, data management, funding as well as difficulties reconciling the priorities and approaches of the numerous stakeholders involved. The following section describes the actions taken to address these challenges and corresponding lessons learned.

[2] This is the French translation of "Community-based Management of Acute Malnutrition" therefore equivalent to CMAM.

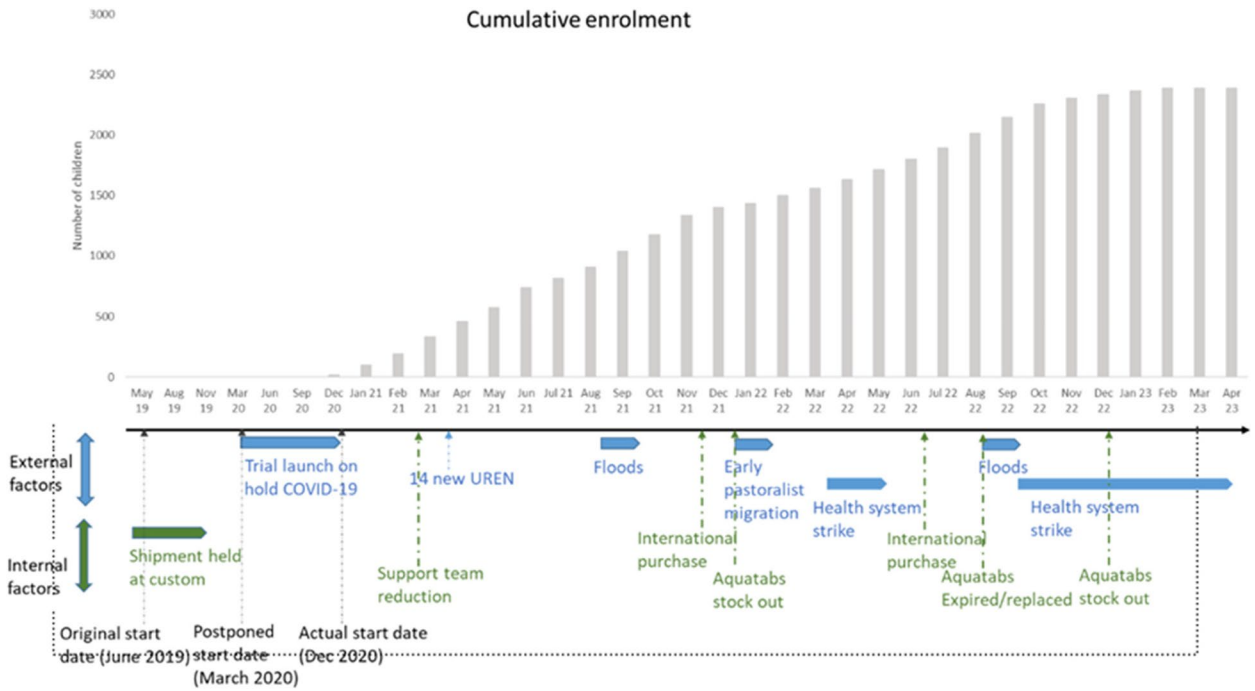

Fig. 2 TISA trial timeline showing challenges due to external and internal factors and their impact on enrolment

External challenges and identified mitigation strategies

COVID-19 pandemic

Following the first confirmed case of COVID-19 in Senegal on March 2, 2020, the Senegalese government declared the state of emergency, restricting movements between regions and banning gatherings of over 10 people. As a precaution, and in line with the MoH guidance and ACF Senegal's own internal strategy, the trial launch was postponed. The advent of the pandemic caused three main problems for the trial. Firstly, the COVID-19 pandemic raised safety concerns among the research staff and among counterparts within the health system. Second, the pandemic was associated with a reduction in general health-seeking behaviour and a marked reduction in the admissions of SAM children at health posts. The actual enrolment rate was therefore lower than the expected enrolment rate, which had been estimated based on the admission rate for the preceding 3 years. Third, the COVID-19 pandemic led to movement restrictions that had an impact on the study at the local level, as visits to health posts and homes were restricted; at the national level, as travel by study staff between Dakar and study sites was restricted; and at an international level, as international travel was prohibited or subject to mandatory quarantine and shipments of laboratory supplies were delayed.

Our response to these challenges was as follows:

- A risk analysis was conducted in July 2020 based on field information and the WHO COVID-19 incidence rate in Senegal. It showed that the risk of infection could be safely managed, and that operational staff had the capacity to perform the trial activities while applying the recommended COVID-19 prevention measures without affecting the integrity of participants. After communicating this to donors and health authorities, the trial was launched in December 2020 (see Fig. 2).
- LSHTM adapted the trial SOPs to include barrier gestures, protective measures and additional personal protective equipment (PPE). New training sessions were organised and delivered remotely. The MoH authorization to proceed with the trial relied on the implementation of PECMAS adaptations to COVID-19 and ACF therefore ensured health workers attended biannual safety trainings.
- Awareness-raising and communication through posters and leaflets were carried out in communities to highlight the implementation of safety measures at health posts and to encourage attendance.
- Increase digitalisation of the trial monitoring. Remote monitoring was improved with the use of WhatsApp groups for field staff. Refresher trainings on protocol adherence and environmental sample collection were conducted remotely, and pre-recorded videos were shared with the team.

Lessons learned from implementing the TISA trial during the COVID-19 pandemic highlighted the importance

Table 1 Challenges, mitigation strategies and lessons learned during the TISA trial

Challenges	Mitigation strategies	Lessons learned
External factors		
COVID-19 pandemic		
Suspension of activities due to COVID	Postponement of the trial launch A risk analysis showed that risks of infection could be safely managed A request for a cost extension was asked from BHA to complete the trial After communicating with all stakeholders, the trial was launched in December 2020	Close operational follow-up by the entire consortium, frequent communication with stakeholders as well as dialogue, sensitization of donors and transparency are key
Staff and patient safety concerns regarding COVID	The LSHTM adapted the trial SOPs to include barrier gestures, protective measures and the use of additional personal protective equipment New training sessions were organised and delivered remotely	The development of a contingency plan (including budget requirements) is necessary to face unexpected events
Low inclusion rate due to COVID	Communication and sensitization sessions organised within communities	Close monitoring, frequent communication with the stakeholders and communities is essential
COVID movement restrictions	Better planning of the visits and remote monitoring (at the national and international level)	Remote monitoring options should be anticipated
WASH kit and study supplies use for the pandemic response		
WASH Kit component used at health post level	Additional sensitisation of the nurses in charge to underline the importance of having complete stocks for the trial continuation	In context such as the COVID pandemic, it is necessary to sensitise all parties on research and emergency aid requirements to ensure staff safety and trial continuation
Trial protective equipment used by health personnel as emergency supplies	Additional supplies were procured and positioned Re-training of staff and sensitisation at community level	
National strikes		
Health worker strikes	Dialogue with the parties responsible for the strikes explaining the risks to the trial and jointly identifying strategies to ensure participant safety and not compromise the integrity of the trial Communication with the MoH, health staff and population to ensure that the minimum service could be delivered	Open dialogue is necessary to maintain research prerequisites during disruptive events Building strong relationships with communities and authorities before the study enables to rapidly put in place mitigation strategies to protect it
Data retention	Several meetings with health staff to sensitise them on the importance of the study completion Extension of the enrolment period	A close and trusting relationship with all the stakeholders is essential to understand the implications of local events on the trial and propose adapted strategies
Late rainy season and floods		
Nomadic pastoralism and early migrations leading to low enrolment and high dropout rates	Sensitization on the enrolment pre-requisites (8 weeks follow-up at the same health post) Adjustment of the enrolment phase and estimation of the financial consequences Anticipation of the return of the population migrating and prepositioning of the WASH kits	Delays in the rainy season and seasonal disruptions are increasingly likely to occur and should be budgeted and accounted for in the project timeline Good knowledge and understanding of the study population (livelihoods, population movements, etc.) is essential to build relevant coping strategies and limit drop-out
Study interruptions due to floods	A cost extension was requested as nothing could be done to compensate for the delays in enrolment and disruption in follow-up	Extreme weather events are increasingly likely to disrupt research activities and should be budgeted and accounted for in the timeline
National health system roles and responsibilities		
Task shifting from nurse to CHW and midwives	Documentation of the task shifting and inclusion of CHWs and midwives in the training	Local HR specificities of the health system should be documented and taken into account Training of contingency HR resources should be included from the beginning and budgeted
Stock out of supplies (e.g. ready-to-use therapeutic food for the SAM treatment)	Use of ACF internal stock from other projects	Provision of buffer stocks of key items should be maintained Co-financing and mutualisation from other operational projects can be used for research purposes when implemented by an NGO

Table 1 (continued)

Challenges	Mitigation strategies	Lessons learned
Transfer of nurses in charge to non-TISA area	Extra training sessions with new nurses	When planning a study, consider possible contextual changes and corresponding contingency plans and mitigation strategies (such as resources for extra training sessions) Such projects can only be carried out successfully by institutions that have created long-standing relationships with the community and the relevant authorities
SAM treatment decentralised at the community level leading to lower enrolment	It was deemed important that the study protocol remained unchanged to ensure the external validity of the results Communication with health authorities to obtain a derogation allowing for the SAM treatment guidelines to not be changed in the TISA area Clear justification, communication and sensitisation were given at health posts level to ensure protocol adherence	
Change in the admission criteria for outpatient SAM treatment at national level		
Opening of new health posts leading to a decrease in enrolment rates	A 12-month extension was requested and approved by partners and donors	Frequent communication with local health authorities to stay informed about health system changes that could affect the trial
Internal factors		
Human resources: trial team and partnership		
Incorporating research in an operational setting	Extensive sensitization from research staff and field visits by researchers for capacity building are necessary to ensure a good understanding of the differences between aid and research activities and the conditions required to implement a large-scale trial	Although differences between a research study and an operational project are clear, reconciling both can lead to difficulties Close collaboration and communication are essential from the start of the project and throughout its implementation
Key staff turnover	Recruitment and training of new staff	Effective protective and retention measures are needed for a trial with a multiannual enrolment phase
Sharing information with health system staff at the national, regional and district level was not enough to ensure buy-in	Establishing local follow-up committees with relevant community stakeholders Promote the participation of key health authorities (like the District Medical Chief) in the local monitoring committee meetings and joint supervision missions Share frequent reports on the status of the project	Actively involve health system staff in trial activities Joint supervision of missions with the relevant local health authorities is a good way to strengthen involvement Accountability to these constituencies in feeding results back trial progress and results should be a standard practice
Geography		
Difficult localisation of participants	Collection of additional information from the participants (name of nearby villages or landmarks, the mother and father's name, etc.)	Close monitoring and strong logistical support are essential Extra budget should be included for unplanned resources requirements
Large area to cover and poor transport infrastructures complicating health post and home visits	Improved activity planning, close monitoring and real-time tracking of the missed visits	
Monitoring costs and logistical capacity to cover such a large and remote area had been underestimated	Additional funding requested for additional staff hiring, vehicles and fuel	
Logistical challenges		
Delay in the delivery of supplies and detention at customs	Negotiation with customs officers	Extensive context analyses and a long development phase are required to anticipate such delays
Expiration of prepositioned chlorine tablets due to various delays	Purchase of extra chlorine tablets and donation of tablet by the Louga regional health district	When possible, procure supplies locally, especially for supplies with an expiration date
Data management		
Data quality	Data checks and analysis of the weekly and monthly evolutions Implementation of automatic data checks in data collection tools (e.g. birth date not accepted if out of range, identification number entered twice, etc.) Biannual trainings on data quality, research standards and how to maintain protocol adherence	Daily and weekly data checks are crucial to spot errors. It is essential to have a robust data management plan that involves a local partner who communicates with field data collectors
Need for closer data management, planning and logistical support	Development of a real-time dashboard to summarise progress for each trial activity. It was disaggregated by health district to enable the deployment of additional support where needed in terms of monitoring, training and logistics Request of additional fund to strengthen logistical support	Good monitoring tools allow for greater ownership of the project by all stakeholders. It enables transparency in progress sharing which allows for a greater push towards the same goal A "buffer" budget must be set aside to ensure the continuation of intervention delivery

Table 1 (continued)

Challenges	Mitigation strategies	Lessons learned
Funding gaps		
Delays and extra cost encountered throughout the trial and lack of funds for the uptake strategy	Regular communication and justification of the various delays with the different funders were given throughout the project Cost and no-cost extensions were requested New funding opportunities were explored throughout the study	Frequent and transparent communication with donors is crucial A contingency plan including extra budget for the unexpected should be developed in the planning phase of a research study Flexible mechanisms for research funds (multi-annual, carry-over from 1 year to the next, etc.) should be discussed with donors It is important to give visibility to the uptake process and its cost to ensure that research leads to change and not only to generating evidence

BHA USAID's Bureau for Humanitarian Assistance, *WASH* Water, Sanitation and Hygiene, *CHW* community health worker, *RUTF* ready-to-use therapeutic food, *HR* human resources, *MoH* Ministry of Health, *NGO* non-governmental organization, *SAM* severe acute malnutrition, *SOP* standard operating procedure

of adaptive management, rapid and transparent communication with partners, the MoH and funders to enable trial continuation without affecting patient or staff integrity.

WASH kit and study supplies used for the pandemic response

WASH kits and sample collection supplies were positioned in health posts just before the beginning of the COVID-19 pandemic in preparation for the planned start date of April 2020. With the advent of the pandemic and the postponement of the trial start, in line with MoH guidance issued in March 2020, many of these materials were used by health post staff. WASH kit components, such as soap and buckets, as well as PPE intended for clinical sample collection (e.g. such as gloves), were used by health personnel as emergency supplies to protect staff.

These issues were quickly identified, and the following measures were taken:

- Additional training for head nurses to emphasise the importance of having a full stock of supplies required for the trial. Additional supplies were purchased and distributed.
- Staff were re-trained and awareness-raising to the community health workers and community volunteers involved in the trial was carried out.

Even in a committed team, different points of view could mean that the interest of research and emergency aid may collide. In our case, it was important to sensitise all parties on the overall aim of the project and their respective responsibilities. Emphasis was put on the need to collectively focus on the safety of the affected population without hindering the research. To this end, repeated reminders on the prerequisites for successfully carrying out a research project of this scale was needed.

National strikes

Two national healthcare workers' strikes took place during the enrolment phase, for 2 months from March to May 2022 and then 7 months between September 2022 and April 2023. Even though patient care was still ensured some days of the week, the strikes did impact the trial. Some patients stopped attending health posts for fear of finding the facilities closed after long and costly journeys, leading to lower enrolment rates during these periods (see Fig. 2). Furthermore, national healthcare staff actively withheld patient data as a basis for negotiation with their employer's action such that some data (e.g. patient information from registries) could not be accessed during the strikes.

To overcome these challenges, the following response was given:

- The research team maintained dialogue with the parties organising the strike actions, jointly identifying strategies to ensure participant safety and not compromising the integrity of the trial.
- The TISA field team conducted several individual interviews with health workers to determine their working days and share this with the population through community radio broadcasts and other relays, thereby encouraging health post visits and making sure patients were still enrolled, treated and followed.
- The TISA team extended the enrolment phase and visited health posts to collect data from the strike periods until mid-June 2023.

The impact of both strikes is hard to estimate but certainly contributed to delays and additional costs. These events highlight the importance of building a close and trusting relationship with communities and local authorities before the start of enrolment to promptly put in place mitigation measures enabling the continuation of the trial.

Late rainy season and floods

The TISA study is set in a pastoralist livelihood zone and admissions at health posts are very seasonal. Although a dip in enrolment due to pastoralists migration was expected, it happened particularly early in 2022 due to an unusual lack of rain leading to a reduction in crop production and earlier migration out of the study area (migration usually starts in April but it started as early as December the year before). An inclusion criterion for the trial was that patients planned to remain in treatment for the full term—up to 8 weeks—so any patients who stated at enrolment that they intended to migrate during treatment were not enrolled in the trial, although they did receive the standard treatment.

Furthermore, between August and September 2021 and 2022, activities were halted in six health posts due to unexpected flooding (see Fig. 2). This prevented participants and health workers from accessing health posts and hindered agents from re-stocking supplies. In addition, participant household visits could not take place in affected areas. Activities resumed as soon as the flooding resided.

The following actions were taken to address those challenges:

- Health workers were re-sensitised on the importance of enrolling participants that were able to follow a complete 8-week treatment, both for treatment efficacy and to reduce dropouts in the study (i.e. dropping out of weekly follow-up visits before the end of treatment or because moving to another region).
- The duration of the enrolment phase was adjusted, and the financial consequences were estimated. The TISA team pre-positioned WASH kits in health posts that were expecting a return of the migrating population.
- Since delays in enrolment were due to outside contextual reasons that could not be compensated, a no-cost extension was requested to allow more time to reach the target sample size. These challenges revealed the importance of seasonal risk management strategies that should be defined early on and specifically adapted to the study area and population. Furthermore, weather phenomena anticipated during the planning of the study could enable a more rapid response.

National health system roles and responsibilities

The trial was implemented within the national health system, in partnership with the MoH and with the active involvement of nurses responsible for the outpatient treatment of SAM at the health posts. Coordination systems, primarily through weekly health post visits by trial field staff, were in place to monitor activities and ensure the intervention was implemented as per protocol. However, the trial pragmatic design embedded in the national health system led to some difficulties.

Firstly, even if SAM treatment consultations and trial enrolment were completed by head nurses at the health post level, other commitments meant that tasks were sometimes assigned to community health workers (CHWs) or midwives, such as the delivery and explanation of the WASH kit. Secondly, health posts faced regular stockouts (which is common in this region and was not related to the trial) of crucial supplies (such as RUTF) and transfer of nurses in charge of the SAM treatment to non-TISA areas. Thirdly, the SAM treatment was decentralised at community level in late 2020 which led to a lower enrolment rate at health post level. National admission criteria for SAM treatment also changed during the study (notably, mid-upper arm circumference was recommended as the sole admission criterion, rather than mid-upper arm circumference or weight-for-height *z*-score as recommended by WHO) which led to difficulties, although the TISA protocol remained unchanged.

Finally, in March 2021, after 3 months of enrolment, the MoH opened 14 new health posts in the study area. As a result, enrolment in some of the 86 TISA health posts, specifically in proximity to newly opened health posts, reduced notably (see Fig. 2). It became clear that this reduction in enrolment coupled with the decrease in enrolment due to other factors mentioned above made it unfeasible to meet enrolment objectives in time.

To respond to those difficulties, the following solutions were adopted:

- CHWs and midwives were included in trainings so that the quality of treatment would not be affected.
- RUTF stocks from other ACF projects were used to lessen the impact on TISA.
- Extra-training sessions were organised with new nurses in charge of SAM treatment
- Communication with health authorities led to a derogation granted by the MoH allowing for the SAM treatment protocol to remain unchanged in the TISA study area. Extensive awareness-raising was carried out by the team to ensure protocol adherence.
- A 12-month extension of the enrolment period (until December 2022) was requested and approved by partners and donors.

Although opting to deliver the intervention through the national health system ensures real-world applicability of the results, pragmatic trials should include a diagnostic

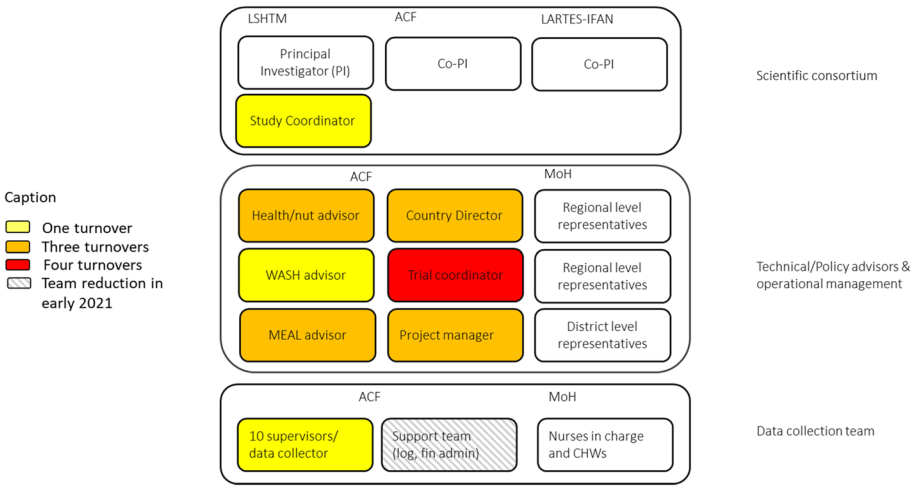

Fig. 3 TISA study organigram. LSHTM London School of Hygiene and Tropical Medicine, ACF Action Contre la Faim, MoH Ministry of Health, LARTES-IFAN Research Laboratory on Economic and Social Transformations, MEAL monitoring, evaluation, accountability, and learning, CHW community health workers

of strengths and limitations of the study ecosystem in which they will be implemented. This will enable effective contingency plans to be drawn up.

Internal challenges and mitigation strategies

The external challenges detailed above contributed and/or exacerbated internal challenges presented below.

Human resource: trial team and partnership

The study consortium was deliberately diverse in composition with the aim of bringing research, operational and policy experience and expertise together to design and implement a study that would generate high-quality evidence relevant to actors in the humanitarian health sector. The consortium was led by an operational non-governmental organisation (ACF France, Spain and Senegal) which also houses a research department. It also included two academic actors, The London School of Hygiene and Tropical Medicine (LSHTM) and LARTES-IFAN from the Cheikh Anta Diop University, as well as the MoH, other stakeholders (UNICEF, as a potential future implementer of the intervention in the West and Central African region in countries with high burden of SAM) and donors (including the Bureau of Humanitarian Assistance (BHA) of the United States Agency for International Development (USAID)) (see organigram Fig. 3). To effectively implement the trial, this study consortium partnered with the national health system (notably at the district level), local key actors and the affected communities.

To reconcile the different perspectives across the stakeholders, close collaboration and communication were essential. For example, as an operational structure, ACF Senegal's operational activities had to be aligned with the research objectives of the study requiring extensive training and awareness-raising.

Furthermore, the consortium also suffered from significant staff turnover within ACF which contributed to delays in the initiation of the project and required frequent recruitments and training of newly recruited staff. Key staff, including the ACF country directors, research and monitoring, evaluation, accountability, and learning (MEAL) focal points, TISA project managers, the study coordinator as well as the country office Health and Nutrition advisor changed multiple times (up to four times) during the trial. Moreover, as the study was carried out within ACF's operations, some support was shared with other ACF projects, which terminated in 2021. This led to substantial logistical, financial and reduction in the team (see Fig. 3).

In response to these difficulties, the following actions were taken:

- Specific communication streams were set up between (1) local and international researchers to ensure protocol adherence, (2) community members and the local project team, (3) operational staff and researchers on research requirements and feasibility, (4) managers of each component to ensure synergy and efficiency, (5) the project team and the existing health system to enable a robust implementation, and (6) the project team and the funders to promptly communicate the impact of unexpected events.
- Extensive training for TISA operational staff was carried out prior to the trial by academic members

of the study consortium and continued periodically throughout the trial. Training covered research methods, highlighting differences between aid and research activities. All staff involved in implementing the intervention were trained (nurses, the trial field officers, community health workers and volunteers) on good clinical practices, behaviour changes, clinical sample collection and storage. Training followed a pre-established plan that was delivered by national or international staff with several refreshers throughout the operational phase of the trial.

- New trial and health system staff recruited in the course of the project were trained on the TISA protocol.
- Training of CHWs by the nurses was carried out at health posts to develop skills, improve protocol adherence, build awareness and community trust.
- Local follow-up committees were established by ACF Senegal and in the four health districts of Linguère, Dahra, Podor and Pété. Constituted via purposive sampling, these committees integrated members of organizations such as district's health and administrative authorities, district management teams, hygiene sub-brigades, the district's local development department, social action services, and the Unit for the fight against Malnutrition (Cellule de Lutte Contre la Malnutrition) and other relevant local partners. The main goal was to ensure community involvement and consultation on the project. More specifically, the local follow-up committee's responsibilities were as follows:

  - Provide advice on operational matters, as needed and as requested by the TISA team;
  - Provide feedback from the local stakeholders to the TISA team;
  - Keep the community informed on study progress;
  - Explain the study and its goals to the community;
  - Contribute to result dissemination locally.

- Workshops were also held in Podor and Linguère prior to the launch of the study with all stakeholders including administrative authorities of each district, district management teams, hygiene sub-brigades, local development service of the district, social action services, local partners and national and international researchers to answer concerns about the trial. Two community dissemination meetings of the results were held at the end of the operational phase to present the preliminary trial results. Furthermore, reports on the status of the trial were shared regularly with relevant stakeholders to maintain their involvement in the study despite delays.

An important lesson was the need to focus on the retention of key staff for a trial with a multiannual enrolment phase and the importance of close working relations between the study team and with the communities. This can be seen as an investment to have a more accepted intervention and a long-lasting, sustainable change in practices and policy.

Geography: a large research area

The TISA trial was conducted in a very large Sahelian area. Due to poor road conditions and variation in enrolment numbers, which affected the time required to reach each health post and the duration of visits, it was often challenging for TISA staff to visit each health post on a weekly basis, as planned. It was also difficult for CHW to visit each patient at home twice during their treatment because of distances and difficulty in locating households, as many did not have an address nor directions. Monitoring costs were higher than expected and the logistical capacity required had been underestimated.

In response:

- Participants were asked to provide reference points, such as nearby villages or landmarks, as well as both the mother's and father's names, which often helped locate participants.
- Additional funding, better planning and closer management of household visits resolved these challenges. Additional staff were hired and closely supported by the MEAL advisor of ACF Senegal, and additional resources were mobilised for vehicles (also including motorbikes that could reach areas inaccessible by car) and fuel.

These specific issues underlined the need for a buffer in the monitoring budget of a trial implemented in a large and remote area.

Logistical challenges relating to shipping and supplies

The trial suffered significant delays in the delivery of supplies due to internal ACF procurement procedures (see Fig. 2), which were then further exacerbated by the COVID-19 pandemic. Prior to the launch of the trial, an international shipment of materials required for clinical sample collection was held at customs for seven months. This delay, combined with slower than anticipated enrolment, led to the expiry of some supplies (e.g. chlorine tablets).

The following measures were put in place:

- Negotiations with custom officers led to the release of supplies by the end of November 2019.

- Expired supplies were replaced in hundreds of WASH kits that were already dispatched to health posts. New chlorine tablets had to be purchased (late 2021 and late 2022) and the Louga regional health district provided an additional donation of tablets early 2023.

This highlights one of the advantages of procuring supplies locally, especially for supplies with an expiration date.

Data management

In the first months of the project, data entry errors occurred primarily relating to participant IDs, which were adopted from the national health system. The identifiers consisted of a combination of numbers, letters and special characters, making them prone to data entry errors.

To improve data management at the beginning and maintain high-quality data collection throughout the project, the following solutions were implemented:

- Daily to weekly data quality checks, with data reporting issues discussed on a weekly basis.
- Automated data quality checks embedded in questionnaires, such as identifier length or date limits.
- Biannual trainings on data quality, research standards and protocol adherence.
- An online dashboard (see Fig. 4) was developed by LSHTM to summarise progress for each study activity, support planning and monitor missing data. This was disaggregated by agent and districts to provide targeted training and The dashboard (see Fig. 4) saved time and funds for monitoring and provided the international study team with real-time progress.

Funding gaps

The numerous delays and slow enrolment rates due to the COVID-19 pandemic, the national health sector strikes and changes in the national protocol led to an extension in the enrolment phase and had significant financial consequences, which were largely borne by ACF. The original budget was of approximately $1 million and increased to almost $1.7 million by the end of the trial. Funds for the uptake process to translate evidence generated by the trial into practice were lacking.

The following action were taken accordingly:

- Delays were regularly and clearly communicated to funders.
- ACF used its own funds to cover the completion of operational activities (37% of the total final budget).
- A costed extension in July 2020, followed by two no-cost extensions until the end of 2022 and end of 2023.
- New funding opportunities, especially for the uptake strategy of the trial, were explored.

The capacity of the operational actor (ACF) to bear some of the financial consequences of the trial delays was essential to the continuation of the trial.

Furthermore, the funding challenges highlighted the added value of a diverse and reactive consortium. It enabled to give a holistic perspective to the various donors on the technical, scientific and operational implications of the delays and the feasibility of the proposed mitigation strategies.

Flexible mechanisms for the utilisation of research funds (multi-annual, carry-over from 1 year to the next, etc.) should be proposed to the donors before the research launch and plans to finance the uptake strategies should be drawn early on.

Discussion

The TISA trial is an example of an operational and research consortium undertaking ambitious research in a challenging context. Several lessons learned were documented during its implementation, which may be useful to others seeking to undertake similar studies in a humanitarian context. We believe the following elements were essential for a successful trial implementation:

Plan for the unexpected

Unexpected events, especially those related to climate change, are inevitable and likely to occur during long-term research studies This is especially relevant in a humanitarian contexts where such events are can have significant consequences (World Disaster Report, 2021). Due to ongoing climate and environmental crisis, we are experiencing increasingly frequent and intense weather events, including droughts, floodings and tropical storms. These events are expected to intensify over the next 10 to 20 years (IPCC, 2021). Therefore, the impact of such events should be anticipated before launching a trial, with pre-specified contingency plans and additional budget allocation included in the research design to manage unforeseen circumstances.

Sufficient time for planning

Long inception and planning stages with field actors are essential. This phase is necessary to identify potential issues and pathways, prioritise actions and ensure they are effective and acceptable. Specificities and uncertainty of the setting must be considered and the intervention should be designed to be contextually relevant

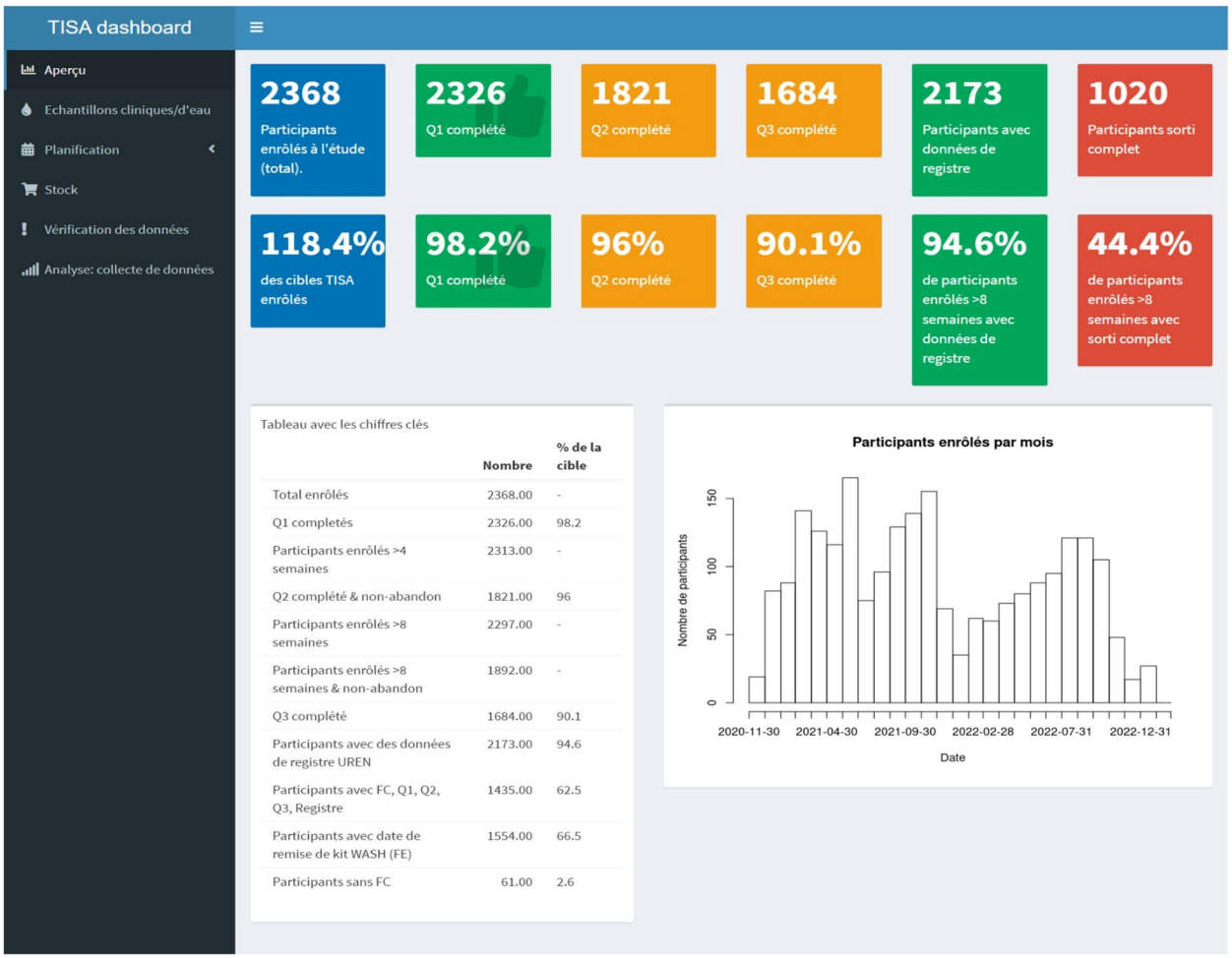

Fig. 4 Online TISA dashboard developed by LSHTM

at each stage of implementation. It is crucial to regularly reassess the context, particularly through close dialogue with communities, local staff and healthcare personnel.

Responsive and adaptive management

A responsive and adaptive management model is essential for early identification and proactive addressing of challenges, transparent sharing with partners and collective decision-making. The challenges encountered during the trial underscored the importance of closely monitoring trial activities in real-time, using tools like the TISA dashboard. Participation from the whole consortium in this close follow-up enables efficient troubleshooting and helps dissemination of information to all stakeholders. It is particularly crucial to actively seek input from the field team, as they are at the front line, delivering the intervention, facilitating the trial and addressing issues. Lastly, implementing active staff retention measures is crucial to maximise the likelihood of human resources staying throughout the study. It is important to ensure that hired staff are committed and motivated to stay until the end of the study.

Close collaboration with the community, health system and relevant stakeholders

Close collaboration with the community, the health system and relevant stakeholders is crucial from the development phase of the trial and throughout. This early collaboration built trust and trial ownership and helped facilitate problem-solving. Furthermore, it enabled joint interpretation of results and development of the dissemination strategy. Accountability to these constituencies in feeding results back on trial progress and results should be a standard practice.

Close monitoring and regular training/refresher sessions are crucial

Close monitoring of data collection is key and remote monitoring options should be explored. Regular training and refresher trainings should be planned and budgeted from the start of the trial to ensure protocol adherence and high-quality data. Furthermore, streamlining recruitment and training, for example by synchronising new training with refreshers for existing staff, could save cost and time.

Working in close partnership with donors

Regular communication with the donor maintains a good understanding of the progress and challenges faced in the field and allows donors to be part of the solution. This dialogue ensures better understanding and awareness on their side and provides transparency on the side of project implementers regarding the use of funds and operations progress.

Our study has several limitations. First, high staff turnover in the trial may have hampered the dissemination exercise proposed. However, previous staff were consulted to contribute to this initiative. Secondly, although trial challenges and responses over the course of the study have been well documented, the project's development phase began as early as 2017, potentially leading to recall bias. Finally, solutions proposed by the TISA team appear to be suited to our study context but may require adaptation to other settings.

Conclusion

The TISA project illustrates how a pragmatic randomised controlled trial can be implemented in a humanitarian setting with a strong design, good knowledge of the setting, an adaptable and flexible management team, and strong communication with—and inclusion of—communities, the health system and donors. Such research efforts are essential for producing high-quality evidence to enable better-suited and adapted interventions in low-resource and high-disease burden public health settings. While challenges were numerous, open communication, transparency and strong community involvement enabled us to complete the operational phase of this ambitious trial in an uncertain and unfavourable context without affecting participants' integrity. The production of high-quality evidence to face current and future humanitarian emergencies is only possible with strong coordination between local and international researchers, practitioners, communities, decision makers and funders.

Abbreviations

ACF	Action Contre la Faim
BHA	Bureau of Humanitarian Assistance
CHWs	Community health workers
CMAM	Community-based Management of Acute Malnutrition
LARTES-IFAN	Research Laboratory on Economic and Social Transformations
LSHTM	The London School of Hygiene and Tropical Medicine
MoH	Ministry of Health
MEAL	Monitoring, evaluation, accountability, and learning
OTP	Outpatient treatment programmes
PECMAS	Prise en Charge Communautaire de la Malnutrition Aiguë. Translated to English as "Community-based Management of Acute Malnutrition"
RUTF	Ready-to-use therapeutic food
SAM	Severe acute malnutrition
SOP	Standard operating procedures
TISA	Traitement Intégré de la Sous-nutrition Aiguë, Translated to English as "Integrated Treatment of Acute Malnutrition"
WASH	Water, Sanitation and Hygiene

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Authors' contributions

DSND contributed to the conception, design, data acquisition, analysis, and interpretation of the data and has drafted and revised the work substantively. OC and LB contributed to the conception and interpretation of data and drafted and revised the work substantively. SF contributed to the data acquisition, analysis and interpretation of the data and revised the work substantively. MB, EC, FS, AD, CM, MS, ABT, TC, DL and KG contributed to the acquisition of the data and revised the work substantively. MLL contributed to the acquisition of the data and the first draft. SS and AVB contributed to the first draft and revised the work substantively. JL and YG revised the work substantively. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

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Competing interests

The authors declare that they have no competing interests.

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