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Carbon emissions of a vaccine trial implemented in Uganda: retrospective assessment to identify actions to enhance researchers' environmental responsibilities

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ABSTRACT

Objectives To estimate the carbon footprint of a vaccine trial conducted in Uganda and to identify opportunities to reduce greenhouse gas emissions in future trials.

Design Retrospective carbon footprint assessment of all trial-related activities conducted in Uganda (ClinicalTrials.gov ID NCT02991495), following the Greenhouse Gas Protocol and the guidance provided by the Low Carbon Clinical Trials Group.

Setting The activities related to the yellow fever vaccine fractional dose trial implemented in Mbarara, with contributions from international collaborators.

Participants The study assessed processes; no participants have been included.

Methods Trial activities were retrospectively quantified and converted into a greenhouse gas estimate using publicly available emission factors. The boundaries of the study were defined to cover the set-up, implementation and close-out phases. Emissions were categorised by source, including personnel, travel, medical supply and laboratory.

Results The vaccine trial produced an estimated 224.66 tonnes of carbon dioxide equivalent (tCO_2e). The largest emission category was related to the research centres, accounting for 78.80 tCO_2e (35.07%), with the Mbarara research centre representing 75.74 tCO_2e (32.38%), including commuting (21.01 tCO_2e), waste disposal (19.31 tCO_2e), goods and services (18.66 tCO_2e) and energy (13.75 tCO_2e). International travel, including air, non-air travel and accommodation accounted for 59.37 tonnes CO_2e (26.43%), with the majority attributed to air travel (53.60 CO_2e). Additional contributors included road travel by trial team and participants' travel to attend trial's visits. The storage of samples at −80°C in ultra-dry freezers was not a significant contributor due to the low volume of samples stored. However, important differences were observed in sample storage emissions between settings that relied more heavily on oil-based electricity and those with greater dependence on hydroelectric power.

Discussion This study highlights multiple opportunities to reduce the carbon emissions of clinical trials. These include already recognised actions such as higher use of solar energy and reduction of international travel. Nevertheless, to improve sustainability of trials, attention should be given to all controllable processes across the trial lifecycle and not solely to the main drivers of emissions. For this, environmental considerations should be present from the initial trial conception phase, involving for instance decisions about the number of trial visits and where these are conducted and taking rational decisions about the long-term storage of samples.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We retrospectively estimated the carbon emissions of a vaccine trial implemented in Uganda.
⇒ The estimate includes most activities needed to implement a vaccine trial, providing a good indication of the total carbon dioxide equivalent emissions.
⇒ The emission factors used are generally not specific to the context where the vaccine trial was implemented, as these are lacking.
⇒ The study did not include other environmental impacts, for instance on local resources.

INTRODUCTION

Human-induced climate change constitutes a global health emergency, with sub-Saharan Africa facing warming above the global average and increased risk of drought, floods and extreme heat.[1] It is estimated that healthcare systems are responsible for 4%–5% of the total worldwide greenhouse gas (GHG) emissions,[2] and clinical trials, as remarkably resource-intensive health activities, are an important contributor to this burden. A recent study estimated that the 350 000 trials registered at ClinicalTrials.gov generate an estimated 27.5 million tonnes of carbon dioxide equivalent (tCO_2e).[3] This represents

over 4 times the emissions generated by Uganda in 2024.[4] This evidence should motivate efforts to put in place measures to reduce the environmental impact of clinical trials.

Improving quality and relevance of clinical research is essential to reduce biomedical research waste and, consequently, the impact of clinical trials on planetary health.[5] In addition, mitigating the environmental harms associated with clinical trials requires consideration of the entire trial life-cycle, including pretrial, in-trial and post-trial activities.[6] This covers core aspects of the study, including trial design, participant recruitment and retention strategies, participant assessments and sample collection, analysis, transport and storage, and dissemination of results. An essential step in informing such mitigation strategies is the quantification of the carbon footprint associated with the trial life-cycle activities, alongside the identification of opportunities to reduce these emissions while maintaining trial quality and scientific integrity.[7 8]

A recent literature review on clinical trials and climate change highlighted the recent interest in this area, with most publications on GHG emissions generated by clinical trials emerging after 2020.[9] However, most publications are from a few high-income countries, and there is little data on how emissions manifest in other contexts. Of the 12 studies quantifying the carbon output of clinical trials, three evaluated large clinical trials that included sites located in sub-Saharan African countries.[10–13] Additionally, two recent studies have focused specifically on trials conducted in South Africa[14] and Mali.[15] The South African study assessed emissions associated with paper usage and printing, local travel between sites and electricity consumption in a randomised controlled trial assessing mental health service delivery interventions.[14] In contrast, the Malian study adopted a broader life-cycle perspective, evaluating the environmental impact of the trial activities, including carbon emissions as well as other environmental impacts, in a phase 2 malaria treatment trial.[15] Despite these advances, to our knowledge, no comprehensive carbon footprint assessment encompassing the full lifecycle of clinical trial activities, including components such as long-term storage of samples, has yet been conducted in a sub-Saharan African setting. Moreover, as emissions can be closely related to trial design and the specific intervention under investigation,[13] further evidence is required across a wider range of research types and study designs to adequately inform effective mitigation strategies.

In 2019 Epicentre, a Médecins Sans Frontières (MSF/Doctors Without Borders) satellite dedicated to epidemiology and research, aligned with MSF goals,[16] committed to reduce GHG emissions by 50% by 2030.[17] Following this commitment, the carbon footprint of selected activities was estimated to determine the main drivers of GHG emissions. Among these, we measured the carbon footprint of the activities implemented in the Epicentre research centre in Mbarara, Uganda, in the context of the YEFE trial (ClinicalTrials.gov ID NCT02991495). This included all stages of the trial, from design to dissemination activities, including sample storage for future use. The aim of this exercise was to determine the aspects and phases of the trial that contributed the highest to the carbon emissions, allowing the consideration of these elements in the design and implementation of future trials.

The YEFE trial was a randomised, blinded, controlled trial that assessed the non-inferiority of fractional doses of yellow fever vaccines. This trial was prompted by major yellow fever outbreaks affecting several countries in sub-Saharan Africa in 2016. As an exceptional response to vaccine shortages during outbreaks, the WHO reviewed available evidence and recommended considering fractional dosing as a dose sparing strategy. At the same time, WHO called for research to generate additional evidence to facilitate flexibility in the use of fractional doses during yellow fever vaccine shortages.[18] Following the call for research from WHO, and in coordination with WHO, a group of experts was convened to agree on the design of a trial that responded to the research gaps. The YEFE trial was sponsored by MSF and implemented in Kilifi, Kenya by the KEMRI Wellcome Trust Research Programme and in Mbarara, Uganda by Epicentre Mbarara research centre. The trial was implemented in two phases, with the evaluation of fractional doses of the 4 WHO-prequalified yellow fever vaccines in an adult population,[19] followed by sub-studies evaluating fractional doses of one WHO-prequalified yellow fever vaccine in HIV+ adults[20] and in children.[21] The trial aimed to provide the evidence needed to broaden and simplify WHO recommendations for yellow fever vaccine fractional dosing during severe vaccine shortages. The YEFE trial-related activities implemented by Epicentre Mbarara (referred to as YEFE-Mbarara) included the recruitment of 480 adults, corresponding to half of the adults recruited in the first phase and implementation of the substudy recruiting 420 children. These activities took place between November 2017 and September 2020. Laboratory analyses to assess the trial's immunological outcome were conducted at the Institut Pasteur Dakar, Senegal. Within this framework, we conducted a carbon footprint assessment to quantify trial-related GHG emissions, expressed in tCO_2e by applying global warming potential factors, and to identify decision-relevant levers for sponsors and investigators to reduce emissions without compromising scientific integrity.

METHODS

This study consisted of a retrospective evaluation of the carbon footprint of the YEFE-Mbarara trial activities. The GHG Protocol was followed to obtain a climate indicator.[22] The scope and boundaries of the study were defined to include all trial-related activities under Epicentre's direct operational control. These included all trial activities conducted by Epicentre Mbarara, responsible for the direct implementation of the trial activities and Epicentre headquarters office, providing support required to implement the trial in Mbarara, Uganda. Shipment of samples

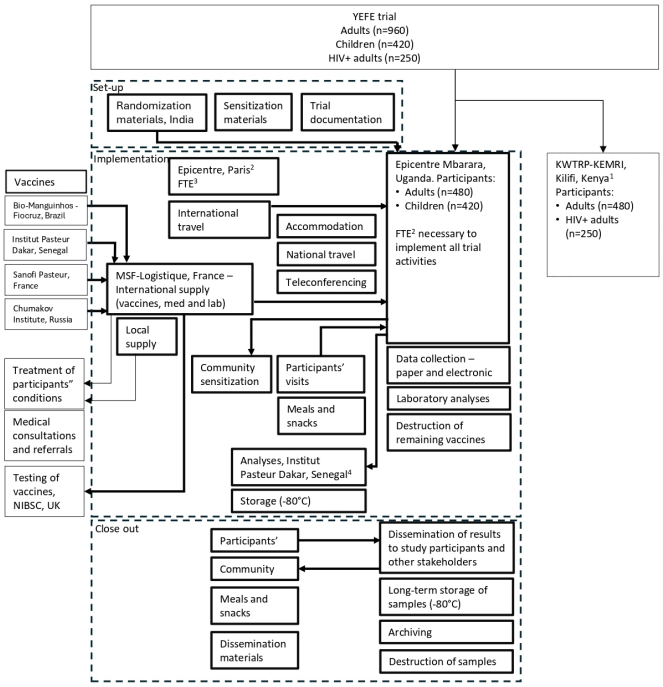

Figure 1 Boundaries of the study. Dark arrows indicated a movement accounted for in the carbon footprinting. [1]KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya. Activities related to the Kilifi site are excluded. [2]Epicentre, Paris provided support to the implementation of the trial in Mbarara, Uganda. Oversight activities related to the sponsorship role conducted at the Kilifi site are excluded. [3]Full-time equivalent (FTE). Energy use, waste disposal, IT and telecom services, IT equipment, office supplies and commuting to work for the total staff FTE dedicated to the trial. [4]Energy required to perform the analyses, considering the laboratory surface used, personnel and time. Exclude materials. MSF, Médecins Sans Frontières.

to the laboratory and energy required to conduct the analysis were also included. The boundaries covered all trial stages, from conception to implementation and closure (figure 1). The identification and mapping of trial activities was conducted between February and June 2023 and subsequently reviewed by the same team in September 2025 using guidance from the Low Carbon Clinical Trials Group.[8] This guidance was used to structure the carbon footprint to reflect the operational conduct of the clinical trial and to allow comparability with other carbon footprint assessments.

Overview of the YEFE trial activities

The YEFE trial was a randomised double-blinded non-inferiority trial assessing fractional doses of the yellow fever vaccines against the standard full dose. Volunteers were recruited from rural communities generally located around 18 km from the study site. Participation involved four study visits, including a vaccination visit followed by three follow-up visits. Blood samples, collected at each study visit, were processed at the study site laboratory. Serum samples were aliquoted into 3 samples and stored at −80°C at the study site, requiring an estimated 30% of an ultra-dry freezer volume. One serum aliquot was shipped to the Institut Pasteur Dakar to assess neutralising antibodies against yellow fever by plaque reduction neutralisation test. Remaining laboratory samples were kept at the trial site laboratory for a period of 5 years after the end of the trial. Trial supplies for the YEFE-Mbarara site including vaccines were largely sourced from MSF-Logistique in Bordeaux, France. Dissemination of results activities, including to trial participants, were conducted at the end of the trial.

Conversion of activity data into carbon footprint

To identify and map trial activities, staff meetings were held to discuss the areas of activities and listing exercises were conducted. Trial activity data were gathered using the site investigator file, trial databases and financial records. To the maximum extent, activities were quantified to represent an amount, such as km of air travel, kWh of energy used, kg of paper, etc. When information about the activity was insufficient to quantify it, expenditure data were used.

Emission factors were applied to convert activity data to carbon dioxide equivalent (CO_2e). GHG estimates combine several GHGs that contribute to global warming, including carbon dioxide (CO_2), methane (CH_4), nitrous oxide (N_2O), hydrofluorocarbons, perfluorocarbons and sulphur hexafluoride, and express them as a mass of CO_2e. We reported emissions across Scopes 1–3: Scope 1 including direct emissions generated from the combustion of fossil fuels and fugitive gas emissions, such as fuel for vehicles and air conditioning; scope 2 or emissions associated with the consumption of purchased electricity; and finally, scope 3 including all other indirect emissions related to travel, purchase of goods and services, freight and general waste.[22] The collected data were converted into CO_2e using publicly available established emission factors, including sources such as the French Base Carbone[23] and the UK Government GHG Conversion Factors for Company Reporting.[24] These factors are standardised values that represent the amount of CO_2e produced per unit of a specific activity or resource. The results were used to determine the total CO_2e produced by the trial activities and to identify those activities that would have the highest impact in cutting GHG emissions. The uncertainty associated with the estimated CO_2e was quantified using an analytical error propagation approach.[25] An uncertainty value, expressed as a relative percentage, was assigned to each emission source based on the quality and source of the underlying activity data and emission factor. For each activity data, an uncertainty range was applied using pre-defined qualitative definitions of the data reliability considering its precision, completeness and data source. Emission factor uncertainties were derived from the sourced databases, reflecting variability in underlying processes and parameter estimation. When no uncertainty value was provided, a default uncertainty level was assigned according to the reliability of the emission factor. The uncertainty of each emission

source was calculated by combining the relative uncertainties of activity data and emission factors using a quadratic sum. Total uncertainty was then estimated by aggregating sources of similar categories using a weighted quadratic approach, in which each category source's contribution to total emissions was used as a weighting factor. This categorisation allowed us to assume independence between categories, but not necessarily within them. Details on the uncertainty values are presented in the online supplemental appendix.

We aimed to include all the pretrial, in-trial and post-trial activities related to the YEFE-Mbarara site. However, due to difficulties obtaining reliable data or the availability of publicly available emission factors, we excluded procurement of medicines and treatment of participants' conditions during study follow-up, and the materials needed to perform the analyses at the Institut Pasteur Dakar laboratory. Email communication was also excluded. The manufacture of the intervention was considered outside the scope of the study. The boundaries of the assessment and the activities included are presented in figure 1 and table 1 and are detailed in the online supplemental appendix.

Quality control procedures were implemented throughout activity data collection and analysis. Activity data were systematically checked for completeness and consistency across sources, with particular attention to alignment between financial records and other available sources such as visit reports and clinical data. Emission factors were selected from widely available and traceable sources and were chosen to best represent the underlying activities and the relevant temporal and geographical context.

Table 1 Description of activities included in the carbon footprint assessment

Category	Activities	Description
Set-up	Materials	Production of sensitisation materials. Production and shipment of randomisation booklets
	Services	Cost of ethics review and regulatory submission. Translation of informed consent documents
	Documentation	Production of ISF documentation
Research centres	Staff Paris	Use of energy and goods and services, commuting to work and disposal of the waste generated by the FTE based in Paris dedicated to the Mbarara site trial activities
	Staff Mbarara	Use of energy and goods and services, commuting to work and disposal of the waste generated by the FTE based in Mbarara dedicated to the Mbarara site trial activities
Meetings and travel	Air travel	Trial staff travel for site visits and meetings
	Accommodation	Hotel or guesthouse stays for site visits and meetings
	Ground travel	Trial staff travel for site visits and meetings (includes travel to/from airports)
	Teleconferencing	Meetings held by teleconferencing
Data collection	Paper	Data collection and documentation (including CRFs, ICFs and other source documents)
	Electronic	Data collected via electronic trial database and trial documentation
Supplies and equipment	Freight	Shipment of equipment, supplies and study vaccines from MSF-Logistique to the trial site
	Supply and equipment	Medical and laboratory consumables purchased from MSF-Logistique* (international supply) and purchased in Uganda (national supply) for vaccination, blood sampling and processing of blood samples. Costs of repairs and calibration of medical equipment.
Intervention	Trial vaccines	Shipment of vaccines from manufacturers to MSF-Logistique. Destruction of remaining vaccines.
	Trial team travel	Travel to the communities for trial sensitisation and follow-up activities
	Participants' visits	Travel to the study site for trial visits. Meals and snacks provided to participants during trial visits
Laboratory	Freight	Shipment of sample at ultra-low temperature from trial site to Institut Pasteur Dakar, Senegal. Shipment of vaccines for potenty testing to the NIBSC, United Kinkdon
	Analyses	Estimated energy required to perform the analyses at the Institut Pasteur Dakar, Senegal. HIV-PCR tests conducted in Mbarara (excludes tests accounted in supply and analyses related to treatment of participants' conditions and unrelated to trial procedures)
	Sample storage	Storage of samples in ultra-dry freezer at the Institut Pasteur Dakar, Senegal

Continued

RESULTS

The carbon footprint for the activities conducted at the YEFE-Mbarara was estimated at 224.66 tCO_2e (table 2). Accounting for uncertainty in activity estimates and emission factors, we estimate a 28.5% uncertainty level.

The largest emission category was related to Epicentre Paris and Epicentre Mbarara centres, which accounted for an estimated 78.80 tCO2e (35.07% of total emissions). Emissions generated by the personnel working at the Mbarara research centre accounted for 72.74 tCO_2e (32.38%), with the main contributors being staff commuting (21.01 tCO_2e), disposal of the waste generated (19.31 tCO_2e), the purchase of goods and services, predominantly related to vehicles and Information Technology equipment (18.66 tCO_2e), and energy use from the local electricity networks and generator (13.75 tCO_2e). Travel associated with trial site visits and meetings was the second-largest source of emissions, accounting for an estimated 59.37 tCO_2e (26.43% of total emissions), with air travel contributing to the majority of these emissions (53.60 tCO_2e). The trial-specific participant intervention accounted for 50.74 tCO_2e (22.58%), with emissions generated by road travel by study team accounting for an

Table 1 Continued

Category	Activities	Description
Close out	Storage	Long-term storage of samples in ultra-dry freezer
	Dissemination	Production of dissemination materials. Activities to disseminate trial results to participants and other stakeholders.
	Archiving	Electronic data and physical documentation
	Destruction	Incineration of remaining biological samples

*MSF-Logistique: MSF distribution centre of medical and non-medical supplies and equipment located in Bordeaux, France.
CRF, case report forms; FTE, full-time equivalent; ICF, informed consent forms; ISF, Investigator Site File; MSF, Médecins Sans Frontières.

estimated 29.33 tCO_2e (13.06%) and participants' travel to attend trial visits accounting for an estimated 16.10 tCO_2e. The laboratory category accounted for 18.01 tCO2e (8.02%) with energy required for laboratory analysis and storage of samples at −80°C in ultra-dry freezers at the Institut Pasteur Dakar, accounting for approximately 8 tCO_2e each due to a high reliance on oil-based electricity. Air freight, related to international supply, including vaccines, and laboratory analyses, contributed overall to 9.37 tCO_2e. The trial set-up phase was the least carbon-intensive accounting for 0.70% of the total emissions. The close-out phase contributed an estimated 2.62% of the total emissions, mostly attributed to dissemination activities. The results are presented in table 2 and are detailed in the online supplemental appendix.

DISCUSSION

To our knowledge, this is the first estimate of the carbon footprint of the entire clinical trial cycle' activities needed to implement a vaccine trial in a sub-Saharan African country. A previous study in South Africa focused on the estimation of the GHG emissions generated by paper use and printing, local travel and electricity consumption, of a clinical trial.[14] A study in Mali covered a wider range of activities but excluded the long-term storage of samples.[15] Studies implemented in different settings have shown that the emissions generated by clinical trials vary widely from less than 20 tonnes produced by studies implemented in a single European country[12 13] to over 1500 tonnes for trials implemented in multiple countries.[12 26] The evaluation of a phase 3 vaccine trial recruiting 1124 participants in 23 sites located in the USA, Belgium, Germany, Spain and Sweden resulted in 359 tCO_2e.[26] Differently, a phase 3 malaria treatment trial following 80 participants, implemented in Mali resulted in 20.5 tCO_2e.[15] Considering that our assessment of the carbon footprint only included activities related to the Mbarara site and did not account for the trial site located in Kenya, the carbon emissions generated by the entire trial could likely double, exceeding 400 tCO_2e. Nevertheless, important differences in the scope of the trial activities included in

Table 2 Results of the carbon footprint

Category	Subcategory	tCO_2e	%
Set-up		1.57	0.70
	Administrative	1.39	0.62
	Documentation	0.09	0.04
	Materials	0.09	0.04
Trial site and headquarters office		78.80	35.07
	Epicentre Paris	6.06	2.70
	Commuting	0.33	0.15
	Energy	1.51	0.67
	Goods and services	3.67	1.63
	Waste	0.56	0.25
	Epicentre Mbarara	72.74	32.38
	Commuting	21.01	9.35
	Energy, generator	8.24	3.67
	Energy, local network	5.51	2.45
	Goods and services	18.66	8.31
	Waste	19.31	8.60
Meetings and travel		59.37	26.43
	Air-travel	53.60	23.86
	Accommodation	1.67	0.74
	Ground travel (related to visits and meetings)	4.11	1.83
	Teleconferencing	0.00	0
Data collection		0.38	0.17
	Paper	0.38	0.17
	Electronic	0.00	0.00
Trial supplies and equipment		9.90	4.41
	Freight international order	5.59	2.49
	Supply and equipment	4.04	1.80
	Repairs and calibration	0.27	0.12
Trial-specific participant interventions		50.74	22.58
	Freight vaccines	1.66	0.74
	Team travel for sensitisation/ participant follow-up	29.33	13.06
	Participant travel for trial visits	16.10	7.17
	Food and drinks	3.65	1.62
	Destruction of remaining vaccines	0.001	0
Laboratory		18.01	8.02
	Freight Mbarara to Institut Pasteur Dakar	2.12	0.94
	Other freight	0.024	0
	Analyses Institut Pasteur Dakar	7.98	3.55
	Storage of samples Institut Pasteur Dakar	7.90	3.51
	Analyses Mbarara, Uganda	0.02	0.1
Trial close out		5.90	2.62
	Road travel for dissemination meetings	1.71	0.76
	Dissemination materials	0.03	0.01
	Drinks and snacks, dissemination meetings	2.36	1.05
	Storage of samples	1.61	0.72
	Archiving of documents	0.16	0.07

Continued

Table 2 Continued

Category	Subcategory	tCO_2e	%
	Electronic data storage	0.01	0
	Incineration of remaining samples	0.02	0.01
Total		224.66 tCO_2e	100%

tCO_2e, tonnes of carbon dioxide equivalent.

the carbon footprint assessment, as well as differences in the trial itself, including differences in the trial population, geographical scope and trial processes measured, and the approach used for carbon quantification, make comparison of different carbon footprint estimations challenging.[9] To improve comparability, we followed the carbon footprinting guidance developed by the Low Carbon Clinical Trials Group.[8] This guidance provided a useful framework for structuring activities across the different stages of the trial. However, to reflect the activities undertaken in our trial, we adapted the categories and excluded those that were not relevant. The main modification concerned emissions related to the clinical trial unit. While the guidance primarily focuses on energy consumption and commuting by trial team, we adopted a broader approach by also including research centre activities necessary for trial implementation, such as IT equipment and services, office supplies, vehicle-related activities and waste disposal. When these additional activities were excluded, emissions associated with the research centres decreased from 5.4 to 1.61 tCO_2e in Paris and from 75.6 to 34.8 tCO 2e in Mbarara.

Although in our trial international travel was limited by the use of virtual meetings, this was still an important contributor highlighting the need to implement alternative management and monitoring methods requiring fewer international movements. Options include web-based training and remote investigator meetings[27] and risk-based monitoring plans that reduce onsite visits.[10] Sponsors should also invest in local capacity to reduce reliance on international support and associated travel.

Unlike treatment trials in which participants' visits might be combined with other medical visits, in vaccine trials, participants' assessments are generally conducted solely for trial purposes. This requires attention to reducing participants' visits to a minimum, considering the purpose of each visit and combining them when possible[28] or conducting visits at facilities closer to the participants.[13] Telephone follow-up could be considered for adverse events assessments. In our trial, the dissemination activities conducted to share results with participants took two different approaches. Adults recruited during the first phase of the study were requested to come to the study site to be given the results. Differently, for children recruited during the second phase of the trial, dissemination activities took place at the community, requiring only the use of motorised transport by trial team. For the dissemination activities conducted in the first phase, 467 adults travelled a mean of 39 km by moto taxi, producing 1.61 tCO_2e. In the second phase, trial team members conducted 12 visits in total to different communities to meet caregivers of 420 participants of nearby villages, producing an estimated 0.1 tCO_2e. This comparison highlights the importance of considering alternative designs to obtain the same objective.

Storage of samples during analysis and for long-term storage produced overall 9.50 tCO_2e (4.23%). Clinical trials routinely store samples for future exploratory research, but it has been recognised that few of these are actually used.[12] Biobanking plans should explicitly justify sample retention duration and intended use. Moreover, storing samples at −70°C instead of at −80°C has been shown to lead to up to 30% reduction in energy consumption.[29] Whether ultra-low freezers can be set to −70°C should be assessed considering the type of samples and the length of storage. Another parameter to consider is the location of storage. Countries produce different GHG emissions depending on energy sources and use of renewable systems. Moreover, there might be differences in the use of generator use in response to electricity outages. For instance, the emissions generated by electricity supply in Uganda are considerably lower than in Senegal, due to the use of hydroelectric systems instead of a higher dependence on oil.[30 31] However, in Mbarara, 8% of the energy used during the storage period was sourced from a generator that ensured the continuity of the electricity supply, increasing considerably the emissions from the use of renewable energy. Storage of samples in Kampala, the capital city, where electricity outages are rare, could have maximised the benefits of storing in a country with a higher proportion of renewable energy sources and low generator use. Since the implementation of this trial, the Mbarara site has installed a solar system that provides energy to the pharmacy and logistics store. This will also be installed at the laboratory. The use of solar energy will considerably reduce the emissions related to energy use by future trials implemented by Epicentre Mbarara.

The results show that many activities generated less than 2% of the total emissions. Consequently, to improve the sustainability of trials, it is important not only to focus on major drivers of emissions but also address controllable processes across the trial lifecycle.[13] For instance, the YEFE trial used a paper-based investigator site file. The use of an electronic system would have reduced the emissions by 0.09 tCO_2e without requiring the use of additional electronic devices. In terms of supply, the study site relied heavily on international supply from MSF-Logistique, which accounted for 5.59 tCO_2e related to freight. The reduction of the amount and frequency of international orders, including an increase in local purchases, anticipation of needs and combining orders, could lead to additional CO_2e savings. Although this was outside the scope of our study, efforts should also be directed towards the reduction of single-use items and the optimisation of procedures that minimises needs and reduces wastage. This emphasis on controllable processes

highlights the critical role that local teams, who are directly responsible for the conduct of research, play in adapting and implementing these processes. While regulatory requirements might dictate certain aspects of trial conduct, local teams are best positioned to ensure that these are also adapted to local conditions and that can be successfully implemented.

An additional point to consider in the assessment of the carbon footprint of clinical trials is the impact that the results would have on the carbon footprint of the health intervention.[5] The YEFE trial provided essential information for the use of 1/5th of yellow fever vaccine dose for outbreak response. Considering that decisions to use fractional dosing will be mainly made to respond to large outbreaks targeting millions of people, the use of $1/5^{th}$ of fractional dose could have substantial savings in terms of vaccine doses, reducing transport, refrigeration capacity and waste. Including carbon footprint analysis as a secondary outcome could support policy-makers and funders in selecting effective interventions with lower environmental burdens.[7]

Limitations

This study quantified GHG emissions but did not assess other environmental impacts, including, for instance, water, soil and air pollution. Previous studies have similarly focused on GHG emissions and excluded broader environmental impact categories. However, the study in Mali adopted a more comprehensive approach and found that electricity in Mali and international travel were the primary contributors to fine particulate matter formation, terrestrial acidification and ozone formation. In contrast, other impact categories, such as water and land use, contributed relatively little to overall environmental damage and were mostly associated with the use of laboratory consumables and soap.[15] Future work should take this comprehensive approach to better identify the consequences of trial-related activities on the environment.

We used all available data to retrospectively quantify the activities to be able to convert these into tCO_2e. Nevertheless, we made assumptions where primary data were unavailable. Furthermore, some activities, such as medical consultation and medications provided for participants' clinical care, were excluded from the assessment due to lack of reliable activity data. The quantification of the activities would have been facilitated by the integration of the carbon footprint exercise into the trial planning and implementation phases, allowing for the design and use of a specific data collection system.

We aimed to use emission factors that reflected local conditions and accounted for differences in energy sources. However, as previously reported,[14] in the context of sub-Saharan Africa, this was complicated by the lack of publicly available country-specific emission factors, resulting in the use of emission factors that largely represent European or global data. The recently launched Lancet MedZero platform,[32] which aims to provide emissions data for a wide range of healthcare-related products globally, may help improve the accuracy of future estimates.

The GHG emissions were expressed in tCO_2e and were not disaggregated by different GHGs. Although such disaggregation may provide further insight to inform targeted mitigation strategies, it is unlikely to substantially alter the identification of dominant emissions sources or the prioritisation of mitigation strategies.

Despite these limitations, the analysis identified key emissions drivers and mitigation opportunities and enables to implement measures to reduce the carbon footprint of clinical trials implemented in sub-Saharan African settings.

CONCLUSIONS

This study estimated the carbon footprint of pretrial, in-trial and post-trial activities of the Ugandan site of the YEFE vaccine trial, providing a comprehensive quantification of emissions across most trial processes and identifying the principal drivers of emissions. MSF and Epicentre are using the footprint calculations to develop decarbonisation road maps and define action plans. The resulting estimates provide a foundation for evidence-based decision-making and support the implementation of mitigation strategies aimed at reducing emissions of future trial activities while maintaining scientific rigour and trial integrity.

To strengthen this approach, clinical trial protocols and registries could consider requiring reporting of estimated tCO_2e and planned mitigation measures, analogous to existing expectations for data sharing and safety reporting. Embedding low-carbon requirements within clinical trial reporting frameworks could drive broader change across the clinical research ecosystem. Future work should also expand environmental assessment beyond GHG emissions to include additional environmental impact metrics, ensuring that the effect on local resources and ecosystems is adequately considered and minimised.

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