



Treatment and insecticide resistance

L'INITIATIVE

L'Initiative is a project implemented by Expertise France, which complements the work of the Global Fund to Fight AIDS, Tuberculosis and Malaria. It provides technical assistance and support for innovation to Global Fund recipient countries to improve the effectiveness of grants and strengthen the health impact of programs funded. L'Initiative's recent work has demonstrated its catalytic effect, through building the capacity of health and civil society actors, improving institutional, political and social frameworks, and supporting innovative approaches to respond to pandemics.

4
projects evaluated

13
countries reached
by the projects

12
implementing
partners

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Cross-cutting evaluation of long-term projects

L'Initiative has three calls for proposals a year as part of its Projects Channel mechanism, from which around twenty projects are selected. All projects funded by L'Initiative undergo a final evaluation carried out by independent specialists. In order to make the most of this comprehensive exercise, L'Initiative has put in place a thematic cross-cutting evaluation mechanism for projects. This enables reporting on the use of Ministry of Europe and Foreign Affairs funds to highlight L'Initiative's interventions and draw out learning to improve interventions to respond to the three pandemics and to inform future activities.

KEY DATA

from the "Treatment and insecticide resistance" evaluation

Total project budget:

4,458,809 Euros

PANDEMICS COVERED:

HIV: **2** projects

Malaria: **2** projects

4

projects evaluated

13

countries reached by the projects

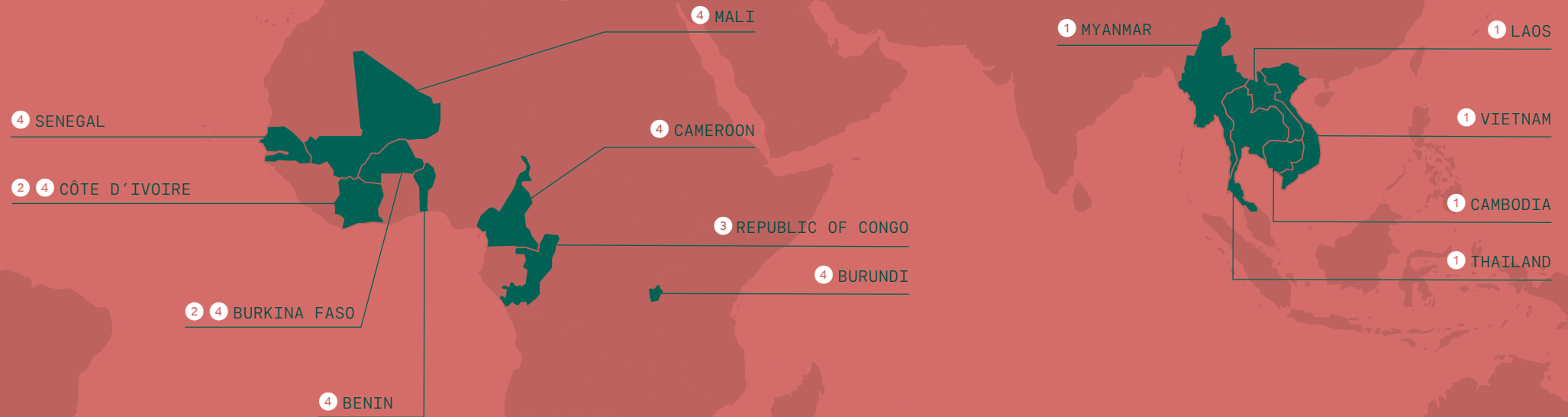
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implementing partners

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Evaluated projects



1 THAILAND, LAOS, CAMBODIA, MYANMAR, VIETNAM (2016-2019)

Molecular and in vitro surveillance of artemisinin-based combination therapy efficacy in the Greater Mekong Subregion (MIVS-ACT)

LEAD

MAHIDOL-OXFORD TROPICAL MEDICINE RESEARCH UNIT (MORU) - MAHIDOL UNIVERSITY

PARTNER

INSTITUT PASTEUR CAMBODIA; WORLDWIDE ANTIMALARIAL RESISTANCE NETWORK, UNIVERSITY OF OXFORD

2 BURKINA FASO, CÔTE D'IVOIRE (2016-2019)

Insecticide resistance management in Burkina Faso and Côte d'Ivoire: Research on vector control strategies (REACT)

LEAD

IRD UMR MIVEGEC

PARTNER

CÔTE D'IVOIRE: UNIVERSITY AO BOUAKÉ, UNIVERSITY FHB ABIDJAN, NMCP; BURKINA FASO: NMCP, CIRDES BOBO-DIOULASSO

3 REPUBLIC OF CONGO (2017-2019)

Study of HIV 1 genotypic resistance and risk factors for development in Congo-Brazzaville

LEAD

CROIX ROUGE FRANÇAISE

PARTNER

NATIONAL PUBLIC HEALTH LABORATORY OF CONGO; DIRECTORATE OF COMMUNICABLE DISEASES AND HIV AND AIDS / STIS OF CONGO; NANTES UNIVERSITY HOSPITAL

4 SENEGAL, BURKINA FASO, MALI, BENIN, CAMEROON, BURUNDI, CÔTE D'IVOIRE (2016-2020)

Prevention of antiretroviral resistance in children: a three-year multi-thematic program of the African international pediatric network "EVA"

LEAD

CRCF - THE REGIONAL CENTER FOR RESEARCH AND TRAINING ON CLINICAL MANAGEMENT

PARTNER

PARTNERS: RÉSEAU ENFANTS ET VIH EN AFRIQUE (EVA), DAKAR; NECKER CHILDREN'S HOSPITAL (HEMATOLOGY, IMMUNOLOGY AND CLINICAL RESEARCH UNIT/INVESTIGATION CENTER)

Introduction

This overview document presents results from the cross-cutting evaluation of four operational research (OR) projects funded by L'Initiative on the theme "resistance", which were implemented in thirteen countries in Africa and South-East Asia.

Health systems in countries across the world affected by HIV, tuberculosis and malaria are weakened by the emergence of resistance, whether it is resistance to treatment or, in the case of malaria vector control, resistance to insecticides. This major public health problem is jeopardizing the scale-up of access to prevention, screening, diagnosis and treatment of the three pandemics and has serious consequences: reduced efficiency of prevention approaches to combat malaria vectors, treatment failure for patients with one or more of these diseases, increased health expenditure related to the use of more expensive second-line treatments, the spread of resistant strains and the need to develop new treatment solutions. In response to the challenges and issues caused by resistance, L'Initiative launched a call for projects in 2015 with the aim of selecting projects focused on:

- Strengthening surveillance of treatment or insecticide resistance.
- Researching factors contributing to the development of these resistances.
- Preventing the emergence of these resistances.
- Strengthening resistance diagnosis and management capacity.

Glossary

- **Drug resistance** is the decrease in the effectiveness of an antibacterial, antiviral, antiparasitic or antifungal drug, developed to treat a disease or reduce its symptoms in patients.
- **Insecticide resistance**, in the context of malaria vector control, is an inherited decrease in mosquito susceptibility to an insecticide, caused by a natural selection process.
- **Operational research (OR) projects** are projects that provide decision-makers with information and knowledge to improve the performance of their programs.¹

1. WHO and Global Fund (n/d), *Guide to operational research in programs supported by the Global Fund*.



METHODOLOGY

This evaluation was carried out by COTA between April 2019 and May 2021. It was led by a team of three specialists in public health, health systems strengthening and project evaluation.

The evaluation involved:

- An individual evaluation of each project in line with L'Initiative's accountability objectives.
- A cross-cutting analysis of the results, making it possible to draw lessons from the combined experience and to promote the best practices in relation to resistance, with the aim of learning and improving the quality of projects funded by L'Initiative.

AREA 1

Strengthening the response to resistance through applying knowledge from research

“To translate research results into action, evidence needs to be contextualized, with messages tailored to the target audience, delivered at the right time and responding to the specific needs of the target group.”

Generating new knowledge

The evaluation concluded that the four OR projects had produced new knowledge that contributed to improving the response to malaria- and HIV-related resistance. The Croix Rouge française (CRF) project in Congo has determined the effectiveness of first-line antiretroviral therapy (ART) and has made it possible to introduce techniques for diagnosing resistance at the national reference laboratory. This made it possible to separate cases of treatment failure caused by resistance to ART from those caused by poor treatment adherence. Thanks to the MIVS-ACT project in South-East Asia, more is known about resistance of malaria parasites to antimalarial treatments in implementing countries and technology transfer for drug susceptibility testing has taken place in Cambodia. In the REACT project, interim data suggest the existence of the additional efficacy of a combination of the four vector control tools, in addition to insecticidal nets, and has made it possible to estimate the additional differential efficacy of each tool. The project also increased knowledge around the adaptation behaviors of the malaria vector (i.e. mosquitos) to entomological response techniques and necessary adjustments in terms of insecticides and preventive measures. Finally, the EVA project showed that the long-term renal toxicity of Tenofovir Disoproxil Fumarate (TDF), an antiretroviral used to treat people living with HIV (PLHIV), is low but progressive and needs to be assessed regularly.

Some projects also generated unanticipated knowledge. For example, the REACT project mapped and accurately characterized breeding grounds at study sites and provided information on the efficacy of a new larvicide. However, when the evaluation took place, several projects had not yet produced all the anticipated results.

Strengthening the response to resistance through applying knowledge from research

Strengthening health systems through mechanisms established by operational research



From communicating research results to knowledge translation

New knowledge produced by research is only useful if it is translated into actions to improve the response to resistance and, ultimately, the health of populations. In order to achieve this, it is necessary to communicate this information to knowledge users; meaning any individuals, organizations or institutions that can change the health system and that will use these results to improve the health of populations. Two projects (REACT and MIVS-ACT) had communications plans that primarily consisted of a list of planned publications and/or a list of conferences the team wanted to attend. No project had developed a knowledge translation (KT) plan. This would have enabled them to identify potential users of the research and plan the best way to reach them to share the information they need in an appropriate and timely way.

In practice, most of the knowledge produced by the four projects has been shared in the «traditional» way (i.e. through scientific communications), with the exception of the MIVS-ACT project. The evaluation highlighted that simply sharing results with policymakers rarely works if scientific data is not also adapted to the skills and appetites of target audiences. As a result, the results of the research projects were not shared in an accessible way with decision makers and other potential users of the results, which impacted on knowledge transfer and translation.

The CRF project (see Good practice p. 11) has had more positive results in terms of knowledge translation. Although the project did not have a communications plan or a KT plan, the team empirically followed a KT model that advocated for the research team to work closely with knowledge users. The EVA project team also applied this empirical approach.

From knowledge translation to health impact

The evaluation highlighted that the CRF and EVA projects were the only ones that had a direct, sustainable and tangible impact on the health of populations. In Congo-Brazzaville, the Ministry of Health has amended PLHIV management recommendations to apply WHO recommendations and information provided by the CRF project. The patient management and treatment literacy guides developed for the EVA project have been adopted by the health authorities and implemented at a national level. Specialists from the project have also been integrated into the national training framework teams in Benin and Cameroon. The patient pathway has been restructured. Finally, urine test strips for monitoring the renal toxicity of TDF have been introduced across the board and made available to health facilities by the National AIDS Committee in Benin.

Enabling factors

The evaluation found that the following factors contributed to knowledge transfer and translation:

- Research teams working closely with health decision-makers, and aligning their respective agendas, as well as having a climate of trust and transparency. This facilitated mutual understanding, communication and helped to limit censorship or information being withheld.
- The relevance of the research, in terms of the fit of the research objectives and the needs of policymakers and other knowledge users. Relevance alone, however, is not sufficient to ensure public health impact.
- The research project lead's positioning around developing an intervention. Research carried out must have a public health agenda, in order to have a tangible impact on the health of populations.

GOOD PRACTICE

SUCCESSFUL KNOWLEDGE TRANSFER

In Congo-Brazzaville, the project manager of the CRF project was also part of the National AIDS Control Program (NACP) team, as head of the research department. Having someone wearing both hats meant that both parties (CRF and NACP) had a strong understanding of each other's agendas, and they were able to align them. Knowledge generated by the project was used by the NACP for the revision of the national guidelines. This close working relationship also created a climate of trust, which enabled decision-makers to understand the constraints of the research team, the strengths and limitations of their data and therefore to be able to use them effectively.



Recommendations

- More effective communication, dissemination and promotion of research results:
 - Reach out to decision-makers and diversify target audiences beyond simply the readership of scientific articles.
 - Tailor scientific messages to target audiences using accessible language, appropriate materials and practical recommendations.
- Foster a close working relationship between research teams and health decision-makers:
 - Set up a formal mechanism for monitoring research by the party in power and partners, integrated into an existing Ministry of Health, relevant program or technical and financial partner (TFP) platform.
 - Prioritize gaining an understanding of the needs of health decision-makers and anticipate their requests.
 - Align the agendas of the research team and decision-makers.
- Involve members of the public in the project who are affected by the research subject, including patient organizations, in order to create the necessary climate of trust to improve the transfer of knowledge and to make it possible to better align with what users of the research want.



AREA 2

Strengthening health systems through mechanisms established by operational research

“The effectiveness of practices used in the research and the quality of knowledge generated have convinced decision-makers to take these findings into account in their countries’ pandemic responses”

Impact on health systems

The evaluation concludes that all four OR projects had an impact on the health systems of the countries in question, either directly through the transfer of technical skills or through equipment support, or indirectly through technical advice to national partner institutions. It was observed that projects had the following impact on health systems of implementing countries:

→ **Strengthened governance of health programs**, albeit minimal, in terms of planning or defining national level strategies. For example, in Cameroon, the EVA project has put pediatric HIV back as a central health system priority (see box). In Congo-Brazzaville, the CRF project’s quantification research into ARV treatment resistance has enabled the health authorities to better plan their supply of second- and third-line treatments.

→ **Strengthening human resources for health**, including capacity building of laboratory technicians (MIVS-ACT, CRF, REACT), clinical teams and project management staff (Resistance, EVA). Generally speaking, research quality requirements mean that care and laboratory protocols have to be standardized and ensure that all personnel involved are trained and able to comply with these protocols. Including master’s and doctoral students in the REACT project has ensured that training interventions are sustainable.

→ **Strengthening health services**, particularly laboratories, through introducing new techniques and in some cases creating new services. In the EVA project, the number of children on ART has increased thanks to a combination of good clinical practice and treatment literacy education.

→ **Strengthening the quality of health information systems** for target diseases, by generating evidence. Some projects have addressed significant information gaps. For example, around 90% of the information published on the WWARN website² comes from MIVS-ACT project analysis. This significantly contributes to how resistance is discussed in the sub-region.

Strengthening the response to resistance through applying knowledge from research

Strengthening health systems through mechanisms established by operational research





GOOD PRACTICE

Pediatricians involved in the EVA project led by CRCF, were part of the health system as they were also health providers in public health facilities in each of the implementing countries. This enabled them to carry out activities developed in the context of the project and to make linkages. In addition, the project's country focal points were often university professors or technical advisers from the NACP and/or the Ministry of Health. These focal points were often co-opted into national training programs to transfer project knowledge and successful practices. As a result, in the seven project countries, the EVA project has enabled the development of National Strategic Plans, national guidelines or guidance, and training and practical tools for the management and treatment of pediatric HIV.

Success factors and constraints

The **following have facilitated** the contribution of projects to health systems strengthening:

- How closely project teams and health authorities worked together (see Area 1).
- Partnerships developed by project teams with end beneficiaries of projects, such as patient organizations in Congo (CRF).
- The effectiveness of practices used during the research and the quality of the knowledge generated by the projects. For the REACT and EVA projects in particular, these factors have convinced policymakers to take research findings into account in the national, or even sub-regional, malaria or HIV responses.
- Sufficient organizational capacity in strengthened structures to foster ownership and sustain project achievements over time.

Constraints identified by the evaluation include:

- Weak drug supply chain systems in some countries and lack of availability of certain commodities. Projects have addressed this by sourcing key commodities directly.
- Challenges strengthening a health system by focusing solely on a vertical program within that system. In the EVA project, for example, the integration of pediatric HIV into the health system package of services would have made sense.
- Lack of human resources in health systems. The projects trained new staff but the issue of the sustainability of these roles has not been resolved.

Strengthening local partners

The evaluation stated that the projects have, in their own way, fostered the involvement of research partners and strengthened their capacity in various areas. Patient organizations, who were involved at different stages of the CRF project in Congo, were able to give tangible arguments when advocating for better PLHIV management, through the option of changing the line of treatment using resistance genotyping and treatment literacy education for patients. The REACT project has strengthened the capacity of national partner institutions and of students trained under master's and doctoral programs in medical entomology, epidemiology or geomatics. The EVA project formed a consortium and mobilized UN agencies, hospitals and laboratories to ensure the transfer of knowledge and know-how to the seven partner countries in Africa. This multidisciplinary between medical and behavioral professions has made it possible to improve the management of pediatric HIV and treatment adherence.

In addition, the evaluation highlighted the fact that projects involving university research laboratories have been successful. Under the MIVS-ACT project, only university research laboratories had the necessary skills and quality requirements to achieve and maintain high quality standards in order to implement molecular surveillance of artemisinin resistance. These academic laboratories, once strengthened, can provide work placements for national staff and training to public health partners, therefore contributing to strengthening the health system.

Recommendations

- Consult with governments and TFPs to ensure optimal participation and to ensure that good project practices are translated into national decisions, plans and/or practices.
- Factor in the lack of human resources in some countries:
 - Support national human resource training around combatting resistance.
 - Anticipate strengthening the skills of professionals in communication and behavioral sciences to ensure comprehensive prevention of resistance that includes behavior change.
- Ensure participation and ownership by partners and other stakeholders at all levels of the project's interventions:
 - Carry out an inclusive stakeholder mapping.
 - Define the role of partners and the involvement of stakeholders in advance, from national to community level, in the different phases of the project.
- Ensure good communication with partners and other stakeholders around the research process and timeline, in order to foster realistic expectations.



Conclusion

The Global Fund does not often fund research activities in target countries, and the evaluated projects responded to a lack of information on HIV and malaria resistance. The evaluation concludes that, overall, the projects have increased the effectiveness, efficiency and/or quality of certain Global Fund financed interventions.

The complementarity of the projects funded by L'Initiative is based primarily on these areas:

- Generation of knowledge on resistance issues.
- Development of good laboratory or patient service practices.
- That improve capacity to provide innovative services and care, focusing on target audiences that are not sufficiently taken into account by the Global Fund, such as vulnerable groups of children (EVA project).
- Improved quality and availability of health information.

However, this complementarity between the Global Fund's interventions and those of L'Initiative could be further strengthened by ensuring genuine synergy and increasing information sharing. In some ways, this compartmentalization has limited the ability of projects to influence the development of country funding requests to the GF. Conversely, the projects evaluated were not able to capitalize on the learning around available operational solutions in relation to funding requests. However, this was discussed with Global Fund staff who confirmed that the potential of these OR projects to generate evidence to inform public health decisions and improve program impact are both critical and welcome.



REFLECTIONS

Since 2018, L'Initiative has launched a dedicated call to support operational research projects that enable changes in health practices and/or policies, with a view to later scale up through Global Fund granting. This call for projects was informed by lessons learned from this cross-cutting evaluation.

Two of the projects evaluated also received follow-on funding from L'Initiative (REACT and EVA projects), to increase their impact on the fight against pandemics.

ACRONYMS AND ABBREVIATIONS

ART	Antiretroviral Therapy
CRCF	The regional center for research and training on clinical management
CRF	Croix Rouge française
GF	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human Immunodeficiency Virus
KT	Knowledge Translation
MEAE	French Ministry of Europe and Foreign Affairs
NACP	National AIDS Control Program
OR	Operational Research
PLHIV	Person Living with HIV
TDF	Tenofovir Disoproxil Fumarate
TFPs	Technical and Financial Partners:
WHO	World Health Organization

This publication is part of a collection presenting the results from cross-cutting evaluations produced by L'Initiative. The following issues have already been published and are available on our website, in the "document resources" section, in both French and English:



This cross-cutting evaluation was carried out by Sophie Goyet, Tiburce Nyiama and Stéphane Vancutsem, from COTA, between April 2019 and May 2021.

It was coordinated at Expertise France by Elsa Goujon, Monitoring and Evaluation Officer in the Health Department.

The analysis and conclusions presented in this document are the responsibility of the authors. They do not necessarily reflect the official point of view of Expertise France or of the organizations and projects evaluated.

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