

Developing an international network for clinical research: the European and Developing Countries Clinical Trials Partnership experience

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The European and Developing Countries Clinical Trials Partnership (EDCTP) supports international networks for clinical research through partnerships. This initiative aims to accelerate the development of new or improved interventions to fight HIV/AIDS, malaria and tuberculosis. The EDCTP experience in fostering international networks through integrated projects and regional networks of excellence with particular focus opportunities and challenges are discussed. The need to develop local scientific leadership and ownership, in addition to African countries taking the lead in both setting their own research agendas and prioritizing financing of these research activities, is emphasized. The need to promote collaboration with industry and public–private partnerships is also highlighted. Moreover, the critical role of monitoring and evaluation of research networks, linking their outputs to the financial investments is underpinned.

Keywords: clinical trial • EDCTP • European and Developing Countries Clinical Trials Partnership • integrated project • networks of excellence • partnership

Improving health through global partnerships

The European and Developing Countries Clinical Trials Partnership (EDCTP) supports international networks for clinical research through partnerships [1–4]. It was established in 2003 as a European response to the global health crisis caused by the three main poverty-related diseases of HIV/AIDS, tuberculosis (TB) and malaria. The primary goal of the initiative is to accelerate the development of new or improved interventions to fight HIV/AIDS, malaria and TB through the coordination and cooperation of European national research programs on poverty-related diseases to work in a balanced partnership with their African counterparts [1] in collaboration with industry and like-minded organizations. This partnership concentrates on the local and international needs of the sub-Saharan African countries, who are involved in the identification of their needs; setting of priorities; and establishing a strategy for a joint research agenda. The international networks supported are mostly established around multicenter–multinational research initiatives that integrate clinical trials, capacity building and networking. Through partnerships, EDCTP facilitates and supports the creation of an enabling environment for clinical research [2] by fostering good clinical and laboratory practice, and strengthening regulatory and ethics capacity in Africa.

The EDCTP approach in fostering international networks & its effects

■ Integrated project approach

In order to appropriately address the current health and clinical research capacity needs of the African region, EDCTP has aligned its support to focus on multinational, multicenter projects that combine clinical trials, capacity development

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and networking. The rationale for integrating these three activities is to ensure that the developed capacity is optimally used to effectively and successfully conduct clinical trials, and the capacity developed is utilized, retained and proliferated, thus enhancing sustainability. In this framework, EDCTP encourages collaborative research and promotes learning by doing [5].

A prototype of these collaborative research initiatives using this approach is the Pan-African Consortium for Evaluation of Antituberculosis Antibiotics (PanACEA), an African–European research collaboration. This network was formed in response to the global emergency of TB burden and the urgent public health need for new or improved TB drug regimens to shorten and simplify therapy. The initial process involved engaging stakeholders through a stakeholder meeting. With the goal of shortening and simplifying treatment of drug-sensitive tuberculosis, EDCTP stakeholders recommended a brokered programmatic strategy to conduct clinical trials for new drugs. This resulted in a call for expression of interest that was released in August 2007 to which several applicants representing a collaboration of several institutions responded. The applicants pooled their ideas together in a brokering meeting that led to the formation of the consortium with the goal of conducting regulatory standard Phase IIa, IIb and III clinical trials for antituberculosis drugs regimens containing moxifloxacin, high-dose rifamycins and SQ109 (a new TB drug) using a shared governance,

administration and capacity development strategy. As well as the institutions listed in [Box 1](#), this network has also brought together cofounding from other partners, including the Global TB Alliance, Bill and Melinda Gates Foundation, Sequella and the South African Medical Research Council.

If this collaborative research produces positive results in changing current tuberculosis treatment, it is anticipated that a significant beneficial public health impact will be achieved. For example, considerable cost improvements to health services delivering TB treatment will allow more patients to be treated and the provision of higher quality services. Importantly, this will reduce patients' visits to health facilities as well as health workers' visits to patients' homes, which often impose a significant financial burden on a population that is least likely to be able to bear the costs. High treatment completion rates will significantly reduce the risk of emerging drug-resistant strains, which is a growing threat in several parts of Africa. The studies and capacity development component will help ensure Africa's ability to successfully evaluate and register future improvements in TB treatments of public health importance through the conduction of high-quality clinical trials. This network directly addresses concerns about the quality required in African TB clinical trial sites to enable them to become world leaders in performing regulatory quality trials. The capacity and tools established through the PanACEA activities will establish an enduring framework for more effective and efficient development of new TB drugs as they progress through the development pipeline. Thus, the success of PanACEA will not only contribute to shorter and simpler regimens, but also build the infrastructure required for drug development.

Box 1. The Pan-African Consortium for Evaluation of Antituberculosis Antibiotics.

- Aurum Institute for Health Research (South Africa)
- Ifakara Health Research and Development Centre (Tanzania)
- Kenya Medical Research Institute (KEMRI; Kenya)
- Kilimanjaro Christian Medical Centre (KCMC; Tanzania)
- Klinikum der Universität München, Institute for Medical Bioinformatics (Germany)
- Leiden University (The Netherlands)
- Makerere University (Uganda)
- Mbeya Medical Research Programme (Tanzania)
- Medical Research Council South Africa
- Medical Research Council (UK)
- National Institute for Public Health and the Environment (RIVM; The Netherlands)
- Radboud University Nijmegen (The Netherlands), Sequella (USA)
- Stellenbosch University (South Africa)
- Swiss Tropical Institute (Switzerland)
- University College London (UK)
- University of Cape Town Lung Institute (South Africa)
- University of the Witwatersrand (South Africa)
- University of Tübingen (Germany)
- University of Zambia (Zambia)

■ Regional networks of excellence

Sub-Saharan Africa is faced with a lack of adequate research infrastructure and established researchers capable of initiating and maintaining competitive research outputs, with many of them working in isolation and engaging in parochial research as a natural consequence. There is a need to espouse south–south collaboration and sharing of facilities and expertise in resource-limited settings in order to enhance synergy. To mitigate this and promote collaborative research, through a consultative process, EDCTP established regional networks for conducting clinical trials and promoting clinical research in sub-Saharan Africa [6]. These networks unite at a regional level on the basis of their individual strengths in different clinical trials capacity and competencies, such as good clinical and laboratory practices, data management, actual clinical trial implementation and management as

well as laboratory support. In this approach the more established institutions explore synergy and complementarities while providing support to the upcoming institutions within the region. Through collaboration they learn and develop, and by doing so they raise the quality of clinical research and practice in sub-Saharan Africa. These networks have brought together different research centers from eastern, western, southern and central Africa to improve clinical trial capacity, readiness for conduct of clinical trials, fostering south–south mentorship and proliferation of knowledge and capacity in respective regions. The networks [7] include the Central African Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM), the East Africa Consortium for Clinical Research (EACCR), the Trials of Excellence for Southern Africa (TESA) and the West Africa Network of Excellence for TB, AIDS and Malaria (WANETAM).

Opportunities & challenges of clinical research networks: the EDCTP experience

There is no single strategy for successful research partnerships. However, adherence to the basic principles of mutual respect and trust is the bedrock of good research partnerships. EDCTP is playing an illustrious role in encouraging the proliferation of partnership-centered networks that transcend the traditional north–south ties and the opening up of new joint ventures. In addition, the program encourages cross collaborations between investigators working on HIV/AIDS, TB and malaria. This bridges the inter-disease knowledge gap on overlapping issues such as coinfections and facilitates optimal utilization of capacity developed with the changing disease epidemiology. Among these include networks formed in different research areas that demonstrate strengthening of existing and formation of new collaborations among northern and southern institutions and scientists:

- The HIV treatment research projects such as the Eastern and Southern Africa Research Network for Evaluation of Second Line Therapy in HIV infection, referred to as EARNEST. This network is investigating boosted protease inhibitor (bPI) containing second-line regimens in patients failing first-line therapy in Africa. This research aims at establishing whether bPI plus raltegravir results in superior long-term clinical and immunological outcomes compared with standard of care bPI plus two nucleoside reverse transcriptase inhibitors and whether the latter regimen results in equivalent clinical and immunological parameters as bPI monotherapy. This network involves partners from Malawi, South Africa, Uganda and Zimbabwe.
 - The HIV prevention of mother-to-child transmission research networks involve Burkina Faso, South Africa, Uganda, Tanzania and Zambia. These embrace various studies including a back-up with zidovudine/lamivudine or single-dose emtricitabine/tenofovir in order to avoid non-nucleoside reverse transcriptase inhibitor resistance after single-dose nevirapine for prevention of mother-to-child transmission, improving the balance between efficacy and development of resistance in women receiving single-dose nevirapine, assessment of the impact of highly active antiretroviral therapy during pregnancy and breastfeeding on mother-to-child transmission and mothers health, and a trial investigating the efficacy and safety of infant peri-exposure prophylaxis with lamivudine to prevent HIV-1 transmission by breastfeeding.
 - The HIV vaccine research networks involve site capacity development in Burkina Faso, Gambia, Kenya, Uganda, Malawi and Tanzania, and studies exploring optimal DNA priming and modified vaccinia virus Ankara (MVA) boosting strategies involving Tanzania and Mozambique.
 - Microbicides research networks involve research capacity strengthening in East Africa in Kenya, Tanzania, Rwanda and Uganda, and characterization of novel microbicides safety biomarkers in both East and South Africa.
 - HIV and TB coinfection studies on prevention of early mortality by presumptive TB treatment in HIV-infected patients initiating antiretroviral therapy (PROMPT) and nutritional support for Africans starting antiretroviral therapy (NUSTART) involving Ethiopia, Gabon, Mozambique, Tanzania, South Africa, Uganda and Zambia.
 - Malaria vaccine research networks include two consortia. These are the Malaria Vectored Vaccine Consortium (MVVC) with partners from Austria, Burkina Faso, Germany, Kenya, Gambia, Italy, Senegal and the UK; and the GMZ2 malaria vaccine network with partners from Burkina Faso, Denmark, Gabon, the Gambia, Germany, Tanzania, Uganda and the UK. The former is working on the assessment of the safety and immunogenicity of the candidate malaria vaccines, MVA METRAP and AdCh63 METRAP, in healthy African adults and children, and the latter is conducting a Phase IIb efficacy and safety clinical trial of GMZ2 (GLURP plus MSP3 hybrid) malaria vaccine candidate.
- Other research networks are involved in malaria drug treatment studies and activities linking with the Malaria in Pregnancy Consortium.

Although the EDCTP program has resulted in the establishment of a strong and innovative partnership between Africa and European institutions and researchers, with over 60% of the projects led by African institutions, there are still some challenges to be surmounted. African countries must take the lead in both setting their own research agendas and prioritizing financing of these research activities. There are still very limited contributions from African governments towards health research and development [8]. This creates heavy reliance on funding from the northern partners, which produces an imbalance in the partnership. This inevitably negatively impacts on African ownership of the research in collaborations. Historically, the northern collaborative partners have been perceived as the legitimate scientific leaders and therefore reversal of this role, although progressively happening, remains a challenge. In a few African countries, because of the unfavorable political and social conditions, it is difficult to transfer research funds to and between institutions.

There is dearth of established researchers to develop and maintain competitive research outputs in most African countries and, therefore, the development of local scientific leadership still remains a big challenge. Nonetheless, a number of initiatives, including EDCTP, have made significant investment in human capacity development in the south. There is also need, however, to ensure that these human resources are optimally utilized and remain in Africa through creation of an enabling research environment for them, ensuring that they are networked, and facilitating them to be more competitive in order to attract sufficient research funding.

Although some African countries have well established north–south collaborations, there is still very limited networking between southern scientists and institutions. This is reflected in the limited south–south collaborative research outputs from the majority of the southern institutions. Unfortunately some institutions with favorable epidemiological disease data but limited research capacity are often left out because of inappropriate pace of development to avoid delays in research implementation. The establishment of networks of excellence and making networking mandatory in all EDCTP supported projects are attempts to mitigate these limitations. In health research and service delivery, south–south partnerships have the benefits of encouraging scientists and institutions to work together on shared problems while broadening the opportunities for researchers working in developing countries. In addition, collaborating countries help each other develop their indigenous capacity to generate, manage and use science and technology to address

their needs and encourages a more cost-effective way of using resources including co-sharing of facilities and training.

There is need to reinforce collaboration with industry and public–private partnerships. These are key partners that need to be engaged in equitable partnerships for research and innovation. This is especially important as scientific knowledge about genetic diversity increases and the need for global clinical trials that involve the developing countries also increases.

Monitoring and evaluation of research networks becomes more complex as the number of partners, goals and operational activities increase. It is critical that the networks address priority research questions appropriate to the local settings, function efficiently and effectively using best practices, and that these performance outputs are measurable and linked to the level of funding invested. Different groups are involved in developing networks' evaluation systems [9–11], but this remains a challenge.

Research and development that promotes balanced partnerships and development of local capacity must be prioritized by developing countries' governments and funding agencies. Fostering local ownership is critical and this hinges on the development of local scientific leadership. Moreover, this should be aligned with the local institutional and national research capacity development strategic plans and priorities in order to be effective and sustainable in resource-limited settings.

Future perspective

Building on the achievements to date, the plan is to gradually extend and expand the current EDCTP platform to involve other neglected tropical diseases and health services research [12], as well as extend collaboration with other developing countries beyond sub-Saharan Africa. It is envisaged the second phase of EDCTP will run for a 10-year period, divided into three terms, to allow a measured and gradual expansion while maintaining the current focus of working on HIV/AIDS, malaria and tuberculosis in partnerships. This especially, will be more important when it comes to the more expensive Phase III pivotal clinical trials.

Financial & competing interests disclosure

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Executive summary

- The European and Developing Countries Clinical Trials Partnership (EDCTP) has aligned its support to focus mainly on establishing multicenter–multinational research initiatives that integrate clinical trials, capacity building and networking. In this framework, EDCTP encourages collaborative research and learning by doing.
- This partnership addresses the local and international needs of the sub-Saharan African countries, who are involved in the identification of their needs, setting of priorities and establishing a strategy for a joint research agenda.
- EDCTP has encouraged proliferation of partnership-centered networks that transcend the traditional north–south ties and the opening up of new joint ventures. Practical examples of these collaborative research initiatives are given.
- Challenges associated with establishment of international networks and some solutions are discussed from the EDCTP's perspective.

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