

*Full Length Research Paper*

# Human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) clinical trial activity on the African Continent: An analysis of HIV/AIDS trials registered on the Pan African Clinical Trials Registry

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The human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) pandemic is a major public health problem which poses a significant threat to livelihoods and social security in resource-poor countries due to the rapid spread of the infection amongst individuals at the prime of their productive age. Sub-Saharan Africa is the region most affected by HIV/AIDS with an estimated 24.7 million people living with HIV in 2014, and accounts for almost 70% of new infections globally. It is necessary for researchers, health workers, policy-makers and consumers to have information on planned and ongoing clinical trials. This will enable them to effectively assess interventions for the prevention and treatment of HIV/AIDS and its related conditions, as well planning appropriate future research. The aim of this study was to describe the current status of ongoing HIV clinical trials on the Pan African Clinical Trials Registry (PACTR) to inform African stakeholders of gaps in research, and potential areas of duplication. A cross-sectional analysis of trials currently registered on PACTR was conducted and excluded all trials that did not research HIV/AIDS interventions. Currently, there are 66 trials investigating HIV interventions registered with 28 looking at treatment. Co-morbid conditions are investigated in 20 trials. Forty-one of the trials are single-centered and being conducted across 14 countries. The remaining 52 trials are multicentered with sites in 14 African countries. At present, there is a growing number of planned or ongoing HIV/AIDS trials currently registered on [www.pactr.org](http://www.pactr.org). This is encouraging as previous studies of published trials noted that not many were conducted in Africa. There has also been an increase in the number of African principal investigators, an indicator of regional capacity to conduct research.

**Key words:** Human immunodeficiency virus/Acquired immune deficiency syndrome (HIV/AIDS) treatment, clinical trials, trial registration.

## INTRODUCTION

The human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) pandemic is a major

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public health problem which poses a significant threat to livelihoods and social security in resource-poor countries due to the rapid spread of the infection amongst individuals at the prime of their productive age (World Health Organization, 2014). In 2013, 1.5 million people died from HIV and HIV-related causes globally. According to the World Health Organization (WHO), sub-Saharan Africa is the region most affected by HIV/AIDS with an estimated 24.7 million people living with HIV in 2014, and accounts for almost 70% of new infections globally (WHO, 2014).

Combating HIV/AIDS relies on preventing new infections and providing effective therapy to those already infected. With the greatest burden of disease in Africa, it is critical that research is carefully conducted and responds to the health priorities of the continent. Clinical trials are the best research method for determining what works or does not work. Well-conducted African clinical trials will inform the evidence-base for what interventions are efficacious and safe for this high-burden context. It is necessary for researchers, health workers, policy-makers and consumers to have information on planned and ongoing clinical trials. This will enable them to effectively assess interventions for the prevention and treatment of HIV/AIDS and its related conditions, as well as planning appropriate future research.

The Pan African Clinical Trials Registry ([www.pactr.org](http://www.pactr.org), PACTR) developed out of the AIDS, Tuberculosis and Malaria (ATM) Registry based at the South African Cochrane Centre. The PACTR aims to increase regional clinical trial registration by developing awareness of the need to register trials, providing a venue to register, and supporting trialists during registration. As the only (WHO)-endorsed primary registry in Africa, PACTR contributes to WHO initiatives to strengthen the regulatory and research frameworks in Africa. Transparency was ensured in processing and accessing free information related to clinical trial research. Two previous studies provided insight into the regional landscape of published trials in HIV/AIDS research (Pienaar et al., 2013; Siegfried et al., 2005). The aim of this study was to describe the current status of ongoing HIV clinical trials on PACTR.

## METHODOLOGY

This study was conducted using a cross-sectional analysis of completed, planned and ongoing trials currently registered on PACTR. All trials that evaluated an intervention for preventing and managing HIV/AIDS were included. Data from the PACTR database was available in an MSExcel spreadsheet. Extracted data included the number of trials, trial location, intervention description, location of the principal investigator, participant age range, trial population and funder. Where data was not clear, this was checked against the original record in PACTR. The descriptive analysis was run in MS Excel™.

## RESULTS

Since its inception, PACTR has received 500 trial

applications (Table 1). As of 13 October 2014, 353 studies have been registered on PACTR. Eighty one trials applications are incomplete, that is, not all information has been provided and thus registration cannot be completed. The remaining 59 trials were not eligible for registration as they either fall outside the register remit or geographic area; to be eligible, a trial must be a randomized controlled or controlled clinical trial and have at least one recruiting site in Africa. All trials are reported, including planned and not yet recruiting as well as those that have completed recruitment and data analysis.

Four trials were reported as terminated, but no reason for the termination was provided. Table 2 shows status details of the trials.

## HIV/AIDS trials

Of the registered trials, 66 (18%) report on planned or ongoing research on HIV/AIDS interventions. Twenty-eight (28/66) registered trials evaluate different treatment interventions. Fourteen registered trials evaluate prevention strategies; of these, eight investigate vaccines and four behavioural prevention interventions, and one investigates early infant circumcision. Two trials aim to evaluate approaches to diagnosis. Sample sizes range from 15 participants to 80,000 participants. Twelve trials include children, one trial includes participants aged one month to 13 years and one enrolls participants aged three months to 13 years. Of the HIV/AIDS vaccine trials, two trials include participants younger than 18 years.

## Trials investigating HIV/AIDS and other comorbid conditions

Twenty of the 66 registered trials evaluated HIV with another disease or health-related topic. Twelve trials include both HIV and tuberculosis (TB). Of these, eight evaluate treatment and two trials investigate the diagnosis of TB in HIV positive patients. One trial is investigating the prevention of tuberculosis in HIV-infected participants. One trial evaluates co-treatment of HIV and tuberculosis. Three trials evaluate malaria treatment in HIV positive individuals and one trial evaluates the pharmacodynamics of malaria treatment together with antiretroviral treatment.

## Trial locations and Investigators

Forty-one trials are single-centered and being conducted across 14 countries. The remaining 52 trials are multicentered with sites in 14 African countries. Trials are concentrated in South Africa and Uganda. The multicenter trials have recruitment sites in South Africa, Ethiopia, Tanzania, Guinea Bissau, Gabon, Benin,

**Table 1.** Main Results summarized.

| Variable   | Number of trials   |
|--|--|
| Applications received to www.pactr.org                                 | 500  |
| Total number of trials registered                                      | 353  |
| Incomplete applications  | 81   |
| HIV/AIDS trials registered   | 66   |
| Treatment  | 28   |
| Prevention   | 14   |
| Vaccines   | 10   |
| Behavioral interventions   | 4  |
| Early childhood circumcision   | 1  |
| Diagnosis  | 2  |
| Co-morbid conditions   | 20   |
| Malaria  | 3  |
| Tuberculosis   | 12   |
| Single-center studies  | 41 in 14 countries   |
| Multi-center studies   | 52 in 14 countries   |
| Principle investigators  | 48 based in Africa<br>18 from Europe, UK and U.S.A.  |
| Funding: Majority of trials received funding from more than one source | 18 EDCTP<br>38 non-governmental organizations (Including EDCTP )<br>4 universities<br>3 pharmaceutical companies<br>18 government<br>1 self-funded by the principal investigator |

**Table 2.** HIV/AIDS registered trial status.

| Trial status                                      | Number |
|---|--------|
| Not yet recruiting                                | 19     |
| Open to recruitment: actively recruiting          | 19     |
| Closed to recruitment: follow up continuing       | 6      |
| Closed to recruitment: follow up completed        | 10     |
| Completed recruitment and data analysis complete  | 8      |
| Terminated (Reasons for termination not provided) | 4      |

Kenya, Mozambique, Nigeria, Zambia, Uganda, Senegal, Zimbabwe, Cote D'Ivoire, and Cameroon. Figure 1 shows the locations of all registered HIV/AIDS trials.

Forty eight principal investigators are from African countries, the remaining 18 are from Europe, the United Kingdom and U.S.A. The large number of multi-center trials show that researchers are collaborating to answer questions for this region.

### Funding and ethics

Eighteen (27%) of the trials are funded either partially or

entirely by the European and Developing Countries Clinical Trials Partnership (EDCTP). Non-governmental organisations funded 38 trials (including EDCTP's 18), four are university funded, eight are funded by research councils and three by pharmaceutical companies. Eighteen trials receive funding from governments. Eleven of the trials received funding from Africa based non-governmental organizations. One trial is self-funded by the principal investigator. The majority of trials received funding from more than one source.

All trials registered in www.pactr.org have received ethics approval from an approving authority. Approvals are from both local African and non-African institutions.



**Figure 1.** Trial Sites of Registered HIV/AIDS Trials currently in PACTR.

## DISCUSSION

At present, there is a growing number of planned or ongoing HIV/AIDS trials currently registered on PACTR. Almost half of the registered studies (28/66) address treatment of HIV indicating a focus on treatment in the region; this aligns with the region's burden of disease. Many studies address the issue of co-morbid HIV and another illness (20/66). HIV prevention trials are evaluated in 14/66 trials. Twelve (12/66) trials include children as participants. In terms of HIV investigation with comorbid conditions, tuberculosis is the key focus of the trials reported on PACTR, with only a few trials reflecting HIV and malaria co-infection.

## Trial locations and funding

Drawing on historical analysis of this kind from the PACTR database (Pienaar et al., 2013; Abrams et al., 2010b), it is clear that trial locations are more widely distributed across the continent than in previous years, and that there is an increase in African-based principal investigators. This is perhaps a reflection of concerted efforts to increase awareness for the need to register trials. It is equally possible that the increased spread of trial activity is a result of efforts to build human capacity and laboratory infrastructure on the continent. This is linked to the large number of multi-center trials with sites in the Africa region that are collaborating to

answer questions for this region.

This is encouraging as previous studies of published trials noted that not many trials were being conducted in Africa (Siegfried et al., 2005; Zani et al., 2011). The increase in the number of African principal investigators is equally encouraging as it is an indicator of regional capacity to conduct research.

Researching the funding patterns of clinical trials registered on PACTR can provide insight into understanding the clinical trial landscape on the continent. PACTR reflects predominantly non-commercial funding. Registered clinical trial research on PACTR is largely funded by non-governmental funders based outside of Africa with EDCTP contributing to more projects than any other single funding body. The number of trials receiving governmental funding is low indicating a need for government buy-in.

PACTR's regional remit means that individual countries have a venue through which to register trials in line with ICMJE and WHO standards. At the same time, there is no harmonization or legislation across the continent requiring registration (aside from journal publication mandates) although some individual nations have such legislation. Thus, in order for registration to occur across the continent individual nations need to put in place harmonized legislation requiring trial registration in order to ensure that data across the continent is captured and made publicly available in PACTR. While some national regulatory bodies mandate registration formally in PACTR or in other developing national registries (Abrams and Siegfried, 2010 a,b, 2011) the lack of standardized legislation across the continent highlights a potential limitation of the PACTR's dataset; not all trials conducted on the continent are necessarily reported.

Trialists are often required to register in the country of the funders' origin, and thus, while trials conducted in Africa are encouraged to register in PACTR, they are not required to, unless the country in which the study is being conducted mandates this.

## Conclusion

As registrations to PACTR increase, it is becoming a comprehensive tool for regulatory and funding bodies to monitor the changing HIV/AIDS trial landscape in Africa. As a partner registry to the WHO, PACTR provides information on African trials to the global repository, thus ongoing African HIV/AIDS research is reflected in searches of the WHO's International Clinical Trials Registry Platform.

Through continued developments, PACTR is a well-placed resource for decision makers, researchers, funders, healthcare professionals and patients.

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## Conflict of interest

The authors declare no conflict of interest.

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