Challenges facing HIV treatment in Guinea-Bissau: the benefits of international research collaborations

Sanne Jespersen, a Bo Langhoff Hønge, a Inês Oliveira, a Candida Medina, b David da Silva Tê, b Faustino Gomes Correia, b Zacarias José da Silva, c Christian Erikstrup, d Lars Østergaard, e Alex Lund Laursen, e & Christian Wejse f on behalf of the Bissau HIV cohort study group

Introduction

In sub-Saharan Africa, the introduction of antiretroviral therapy (ART) for patients with human immunodeficiency virus (HIV) infections has improved the lives of millions of people and decreased mortality.1 However, despite support from the Global Fund to Fight AIDS, Tuberculosis and Malaria and other donor organizations, the infrastructure for delivering ART in low-resource settings is still affected by substantial problems.2 Earlier diagnosis and more aggressive treatment of opportunistic disease could decrease mortality beyond that achieved by ART alone.3 Moreover, as the use of ART has increased, there have been reports of drug stocks running out because of insufficient human resources or poor infrastructure. In addition, frequently the means of monitoring the effects and side-effects of ART are not available.

The aim of this article was to reflect on the challenges faced in the field at an HIV clinic in Guinea-Bissau. Principally, we wanted to describe how an international research partnership helped identify clinical problems and find solutions while, at the same time, building the capacity of the health-care system.

Local setting

Guinea-Bissau is located in Western Africa and is one of the poorest countries on the continent.4 It gained independence from Portugal in 1974 after a war of liberation that caused tremendous damage to the country’s economic infrastructure. Since then, it has experienced considerable political and military upheaval. Unlike most countries in the subregion, Guinea-Bissau has experienced an increase in the spread of HIV-1 infection in recent years. In 1989, the country had the highest prevalence of HIV-2 infection ever reported whereas HIV-1 infection was nonexistent. However, the prevalence of HIV-2 infection is now decreasing, while that of HIV-1 infection is on the rise.5,6

In 2005, a national HIV programme was implemented in Guinea-Bissau by the Ministry of Health. However, it was only during 2007 that the programme led to an increase in the number of patients being treated. The Bissau HIV cohort study group was established in 2007 by the Bandim Health Project in Guinea-Bissau and Aarhus University Hospital in Denmark in collaboration with nurses and physicians from the Hospital Nacional Simão Mendes, which is Guinea-Bissau’s main hospital and is located in the capital Bissau. The Bandim Health Project is a member of INDEPTH, which is a network of 42 demographic surveillance system field sites in 20 countries in Africa and Asia.7 Since 1978, a demographic surveillance system established in Bissau by the Bandim Health Project has generated population and health data at the household level as part of a collaboration between the Ministry of Health in Guinea-Bissau and the Statens Serum Institut in Denmark. All patients with HIV infections who attended the HIV clinic

Problem

The introduction of antiretroviral therapy (ART) for HIV infection in sub-Saharan Africa has improved the quality of life of millions of people and reduced mortality. However, substantial problems with the infrastructure for ART delivery remain.

Approach

Clinicians and researchers at an HIV clinic in Guinea-Bissau identified problems with the delivery of ART by establishing a clinical database and by collaborating with international researchers.

Local setting

The Bissau HIV cohort study group was established in 2007 as a collaboration between local HIV physicians and international HIV researchers. Patients were recruited from the HIV clinic at the country’s main hospital in the capital Bissau.

Relevant changes

Between 2005 and 2013, 5514 HIV-positive patients were treated at the clinic. Working together, local health-care workers and international researchers identified the main problems affecting ART delivery: inadequate drug supply; loss of patients to follow-up; and inadequate laboratory services. Solutions to these problems were devised. The collaborations encouraged local physicians to start their own research projects to find possible solutions to problems at the clinic.

Lessons learnt

The HIV clinic in Bissau faced numerous obstacles in delivering ART at a sufficiently high quality and patients’ lives were put in jeopardy. The effectiveness of ART could be enhanced by delivering it as part of an international research collaboration since such collaborations can help identify problems, find solutions and increase the capacity of the health-care system.

Abstracts in العربية, 中文, Français, Русский and Español at the end of each article.

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6 Projecto de Saúde de Bandim, INDEPTH Network, Apertado 861, 1004 Bissau Codex, Guinea-Bissau.
7 National HIV Programme, Ministry of Health, Bissau, Guinea-Bissau.
8 National Public Health Laboratory, Bissau, Guinea-Bissau.
9 Department of Clinical Immunology, Aarhus University Hospital, Denmark.
10 Department of Infectious Diseases, Aarhus University Hospital, Aarhus, Denmark.
11 GloHAU, Center for Global Health, Aarhus University, Denmark.
Correspondence to Sanne Jespersen (email: sanne.jespersen@clin.au.dk).
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at Hospital Nacional Simão Mendes were eligible for inclusion in the Bissau HIV cohort. The cohort study group created a database for all patients in the cohort and set up a biobank where blood samples from these patients were stored for use in research. The purpose of the database and the biobank was to help study how clinical, virological and immunological parameters influence the effectiveness of therapy.

Following the establishment of the Bissau HIV cohort study group, two doctoral students and 10 master’s students from Denmark, Iceland and Spain have worked at the HIV clinic for one to two years each and senior Danish researchers have visited on a regular basis. The close collaboration at the clinic between local HIV physicians and international researchers provided a unique opportunity for sharing experiences and knowledge with ART in similar clinics and blood samples were stored in the associated biobank.

The delivery of ART involved a multitude of challenges at the clinic; these were identified during daily clinical work and routine data entry into the database as well as during ongoing research projects. These problems, their effects and proposed solutions are presented in Table 2. Local staff had heavy workloads and many of these problems would not have been identified in the absence of collaborative research with organizations in other countries.

Subsequently, awareness of these problems led to additional collaborative research projects between local HIV physicians and international researchers that aimed to explore possible solutions. In addition, the collaborations have encouraged local physicians to start their own research projects to find possible solutions to problems at the clinic. As a result, courses on good clinical practice, good laboratory practice and data management have been implemented and staff have taken part in English language lessons. Throughout, it was important to ensure that training for local staff was individualized. Furthermore, the synergies inherent in the rich spectrum of parties involved in research meant that knowledge and insights were multiplied.

### Discussion

The largest HIV clinic in Guinea-Bissau faced numerous obstacles in delivering ART at a sufficiently high quality and, as a result, patients’ lives were put in jeopardy. These difficulties may have been exacerbated by the frequent recurrence of political instability in the country. If similar issues are faced by the many ART facilities in Africa that report few data, it is likely that the implementation of ART in affected areas will be impaired. Moreover, there will also be a risk of publication bias since the clinics discussed in scientific publications may not be representative of the real situation in many areas. Previous studies have shown that there is little collaboration between researchers within developing areas and that most research on HIV is carried out in the developed world. Consequently, it is increasingly recognized that international collaborative research is important for tackling global public health problems. In particular, international partnerships, especially those between developed and developing nations, are necessary in the fight against diseases that are endemic in, or disproportionately affect, the developing world. As summarized in Box 1: (i) we identified a range of persistent problems affecting ART delivery in Guinea-Bissau that involved drug supply, patient retention and inadequate laboratory facilities; (ii) we believe that underreporting of experience with ART in similar clinics in Africa may lead to publication bias; and (iii) we observed that international collaboration is important for identifying health-care problems and devising solutions.

### Relevant changes

Between June 2005 and June 2013, 5514 patients older than 15 years were diagnosed with HIV infections and were offered care at the HIV clinic at the Hospital Nacional Simão Mendes (Table 1). All medical consultations, laboratory investigations and treatment were free of charge. Information on these patients was stored in the clinical database created by the Bissau HIV cohort study group and blood samples were stored in the associated biobank.

The largest HIV clinic in Guinea-Bissau
Transboundary Research Partnerships Countries has developed Research Partnerships with Developing tries. Also, Guinea-Bissau has taken partnerships with developing coun-
tries to aid the establishment of academic networks. The Swiss Commission for the coordination of such partnerships have increased recently. The Swiss Commission for Research Partnerships with Developing Countries has developed A Guide for Transboundary Research Partnerships as an aid to the establishment of academic partnerships with developing countries. Also, Guinea-Bissau has taken part in international collaborations for many years through the INDEPTH network.

Our experience demonstrates that collaboration between physicians in high- and low-resource settings and between clinicians and researchers can help solve everyday clinical problems and enhance the capacity of the healthcare system. Consequently, we believe that international research collaboration can help improve the effectiveness of ART in low-income countries and can benefit both partners. One unique facet of the collaboration in Guinea-Bissau was that researchers from developed countries lived in Guinea-Bissau and, as a result, developed a clear understanding of the problems faced in daily practice. In addition, the fact that we were able to follow up the large number of subjects in our HIV cohort for seven years despite difficult working conditions indicates that collaboration can be sustainable. An increasing number of scientific publications have resulted and it is hoped that additional funding for the cohort study group will further improve the capacity of the health-care system.

In conclusion, the management of people with HIV infection in vulnerable countries is still very challenging. However, international research collaboration can help identify problems and solutions, as well as enhance the capacity of the health-care system. Future research by the Bissau HIV cohort study group will demonstrate whether our identification of problems with the delivery of ART has led to measurable benefits, such as fewer patients being lost to follow-up, lower mortality, bet-

| Problem | Effect | Solution |
|---------|--------|----------|
| Inadequate drug supply | Patients with a high CD4+ T-lymphocyte count experienced Stevens–Johnson syndrome on switching from efavirenz to nevirapine after stocks of efavirenz ran out; development of drug resistance due to treatment interruptions | Improve stock management, increase investment in health-care infrastructure and capacity |
| Clinic relocation | Patients lost to follow-up | Increase the focus on HIV infection at the hospital to give the disease a higher priority among policy-makers |
| Widespread loss to follow-up | Patients not adequately treated | Identify risk factors for patients being lost to follow-up so that effort can be focused on the most vulnerable; introduce educational activities for patients to improve health literacy; telephone patients who are late for appointments; visit patients lost to follow-up at home |
| Poor treatment adherence | Treatment failure and drug resistance | Identify risk factors for poor adherence; improve health literacy |

Table 2. Problems with ART delivery at an HIV clinic, Guinea-Bissau, 2005–2013

| Problem                                      | Effect                                  | Solution                                                                 |
|----------------------------------------------|-----------------------------------------|--------------------------------------------------------------------------|
| Laboratory inadequacies                     |                                         |                                                                          |
| Inadequate validation of HIV rapid tests     | Errors in discriminating between infection with HIV-1, HIV-2 and both HIV-1 and HIV-2 occurred with the SD Bioline HIV 1/2 3.5 rapid test (Standard Diagnostics Inc., Yongin, Republic of Korea); ineffective treatment for HIV-2 infection using non-nucleotide reverse transcriptase inhibitors; expensive treatment for HIV-1 infection using protease inhibitors | Use other rapid HIV diagnostic tests                                        |
| Temporary unavailability of biochemical tests and CD4+ T-cell count measurements | Delayed initiation of ART; late diagnosis of treatment failure; adverse events not diagnosed | Increase awareness of possible treatment failure |
| No HIV-RNA monitoring                        | Late diagnosis of treatment failure; development of drug resistance | Increase the ability of the laboratory to perform HIV-RNA measurements |
| Insufficient tuberculosis screening          | Tuberculosis not diagnosed, leading to no tuberculosis treatment and increased mortality; no detection of drug-resistant tuberculosis | Introduce a simple clinical tuberculosis score together with a rapid urine test for the disease; introduce tuberculosis culture and drug-resistance tests |
| Insufficient hepatitis screening             | No hepatitis treatment due to low sensitivity of rapid tests for hepatitis B and C viruses | Increase awareness of the limitations of rapid tests |

Box 1. Summary of main lessons learnt
- In Guinea-Bissau, there were substantial, persistent problems with the delivery of ART, due to inadequate drug supplies, loss of patients to follow-up and inadequate laboratory services.
- The occurrence of similar problems at the many ART facilities in Africa that report few data could impede the implementation of ART and result in publication bias.
- International research collaborations between high- and low-resource settings can help identify problems, find solutions and enhance the capacity of health-care systems to manage HIV infection.

ART: antiretroviral therapy; CD4: cluster of differentiation 4; HIV: human immunodeficiency virus; RNA: ribonucleic acid.
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The challenges that we face with the treatment of HIV in Bissau—Bissau: Issues to address in the provision of care.

The healthcare setting did not implement ART for 5,514 HIV-positive patients. Local health care workers and international researchers worked together to identify the major issues that affect ART provision: inadequate drug supplies, patient loss to follow-up, and limited laboratory services. Solutions were designed to address these issues. Collaboration encouraged local doctors to begin their own research projects to find possible solutions to clinic problems.

Lessons learnt that we can improve ART provision in Bissau—Bissau: The importance of field experience.

The clinic at the Hospital Nacional Simão Mendes faced multiple challenges in providing ART due to the infrastructure required to support the treatment of HIV in Guinea-Bissau. Patient adherence to ART was a major issue.

The team at the clinic worked with international researchers to improve ART provision. They identified the main issues that affect ART implementation: inadequate drug supplies, patient loss to follow-up, and limited laboratory services. Solutions were designed to address these issues.

The experiences in Bissau—Bissau with ART provision can be improved through international research collaboration. This collaboration helps to identify and address the main issues that affect ART provision in the clinic.
treating HIV and other international researchers treating HIV. The patients have been recruited to the clinic HIV situated in the hospital principal du pays à Bissau, la capitale.

**Changements significatifs** Entre 2005 et 2013, 5514 patients séropositifs ont été traités à la clinique. En travaillant ensemble, les personnels de santé locaux et les chercheurs internationaux ont identifié les problèmes principaux qui affectaient la distribution de la TAR un approvisionnement inapproprié des médicaments; des patients perdus de vue et des services de laboratoire inadéquats. Des solutions visant à résoudre ces problèmes ont été envisagées. Les collaborations ont encouragé les médecins locaux à lancer leurs propres projets de recherche afin de trouver des solutions possibles aux problèmes rencontrés à la clinique.

**Leçons tirées** La clinique viH de Bissau a dû faire face à de nombreux obstacles pour distribuer une TAR d’une qualité suffisamment élevée, et les vies des patients ont été mises en péril. L’efficacité de la TAR pourrait être augmentée en la distribuant dans le cadre de collaborations de recherche internationale, puisque ces collaborations peuvent aider à identifier les problèmes, à trouver des solutions et à augmenter la capacité du système de santé.

**Resumen**

**Principales problemas** La introducción de la terapia antirretroviral (TAR) para tratar la infección del VIH en el África subsahariana ha mejorado la calidad de vida de millones de personas y ha reducido la mortalidad. No obstante, siguen existiendo problemas considerables relacionados con la infraestructura para el suministro de la terapia antirretroviral.

**Enfoque** En una clínica del VIH de Guinea-Bissau, los médicos y los investigadores detectaron problemas en el suministro de la terapia antirretroviral mediante la creación de una base de datos y la colaboración con investigadores internacionales.

**Marco regional** El grupo del estudio de cohorte para el VIH de Bissau se creó en 2007, fruto de la colaboración entre los médicos del VIH locales y los investigadores del VIH internacionales. Se seleccionó a los pacientes de la clínica de VIH en el hospital principal del país de la capital Bissau.

**Cambios importantes** Entre 2005 y 2013, se trató a 5514 pacientes séropositivos para el VIH en la clínica. Trabajando en equipo, el personal sanitario local y los investigadores internacionales identificaron los problemas principales que repercuten en el suministro de la terapia antirretroviral: el suministro inadecuado de medicamentos, la pérdida de pacientes durante el seguimiento y los servicios de laboratorio inadecuados. Se diseñaron soluciones en estos problemas. Las colaboraciones animaron a los médicos locales a emprender sus propios proyectos de investigación a fin de hallar soluciones a los problemas en la clínica.

**Lecciones aprendidas** La clínica del VIH de Bissau afrontó diversos obstáculos en el suministro de una TAR de calidad suficientemente alta y se pusieron en riesgo las vidas de los pacientes. Es posible aumentar la eficacia de la terapia antirretroviral si esta se suministra como parte de la colaboración de una investigación internacional, ya que este tipo de colaboraciones pueden ayudar a identificar los problemas, hallar soluciones y aumentar la capacidad del sistema sanitario.
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