PhD defence of Florian Vogt

Operational challenges during the scale-up of antiretroviral therapy in Sub-Saharan Africa

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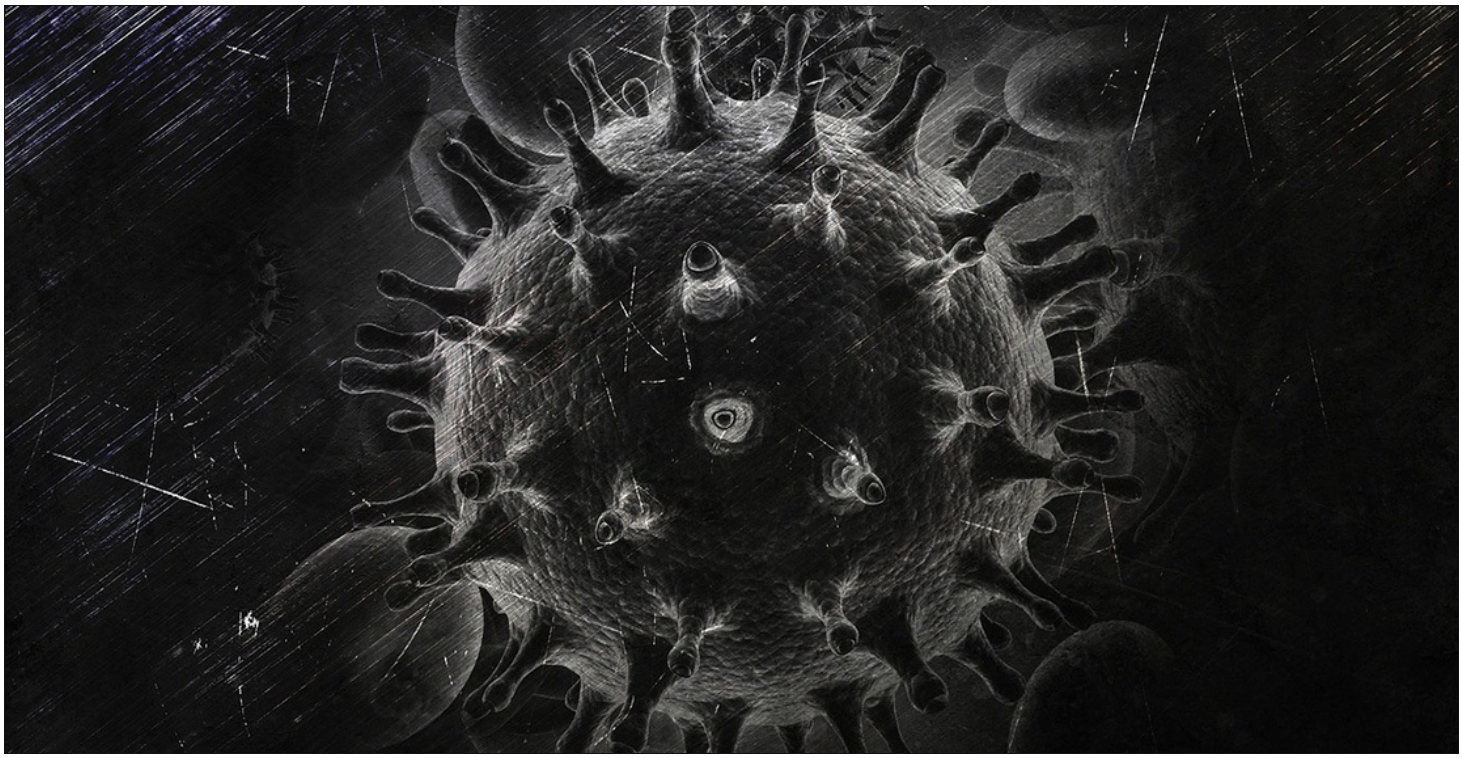
Promotiezaal, Building Q, Campus Drie Eiken, University of Antwerp - Wilrijk
Registration not required



Dit is de omschrijving

Supervisors:

- Prof. dr. Johan Van Griensven (Institute of Tropical Medicine Antwerp)
- Prof. dr. Bob Colebunders (University of Antwerp)

Summary:

Tremendous progress has been made in the scale-up of antiretroviral therapy (ART) in recent years thanks to better and cheaper drugs, increased funding, and a unique political momentum. This prompted enthusiasm in the global human immunodeficiency virus (HIV) community leading to the historic proclamation of the end of the acquired immune deficiency syndrome (AIDS) epidemic by 2030 as the next long-term goal. However, challenges ahead are enormous, in particular in Sub-Saharan Africa (SSA). Despite all efforts, incidence of HIV infections and AIDS-related mortality remain high. Further, funding has started stagnating recently. To match the newly proclaimed goals, treatment eligibility criteria have been broadened progressively over the years, with latest guidelines now recommending starting all HIV-infected persons on ART for life irrespective of clinical or immunological status. Such recommendations are mostly based on efficacy estimates derived from controlled trial settings rather than on what actually works under routine care conditions. The extent to which such ambitions and recommendations match the harsh realities of ART provision in routine care in SSA is often overlooked.

At this point, where the efforts to fight the HIV/AIDS pandemic have reached a crossroad, this thesis takes a critical look at how HIV care is actually being provided in routine care settings in SSA, focussing on core aspects of ART provision in patient populations that have long been the focus of scale-up efforts. This is needed to put recent achievements and thus new goals into perspective, and to have a realistic understanding of the challenges ahead.

This research aims to unveil shortfalls in ART provision under routine care conditions in SSA, and to explore innovative ways to overcome them. The objectives of this research were:

1) to improve laboratory diagnostics for HIV patients in rural areas; specifically to assess discrepancies in immunological testing between rural and urban patients, and to evaluate innovative stabilizing blood collection tubes for improved access to cluster of differentiation type 4 (CD4) cell count measurement.
2) to improve retention among pregnant women; specifically to assess the effect of community health worker-based defaulter tracing on retention in care and on HIV transmission among pregnant mothers and their newborns.
3) to improve long-term drug supply for stable patients; specifically to assess treatment outcomes among clinically stable patients after decentralizing ART supply from centralized care to community-based drug distribution sites.
4) to improve treatment initiation in adolescents; specifically to assess the effect of time to ART initiation on mortality and retention among treatment-eligible adolescents.
Five peer-reviewed journal articles are presented in this thesis. All data used in this thesis originate from routine care settings in HIV projects run or supported by the international humanitarian non-governmental organization Médecins Sans Frontières/ Doctors Without Borders in Zimbabwe and in the Democratic Republic of the Congo (DRC).

Regarding objective 1, we compared differences between rural and urban HIV patients in CD4 testing at recommended time points in Beitbridge district, Southern Zimbabwe, and assessed whether using innovative blood stabilization tubes offers a solution to the need for rapid sample transportation as required by conventional tubes. We found large discrepancies between urban and rural HIV patients in receiving CD4 testing at treatment start and during follow-up. Rural patients were up to nine times more likely to miss CD4 testing when indicated as per guidelines from the World Health Organization (WHO). We were able to attribute the observed differences in CD4 testing between urban and rural patients to deficiencies on the provider side rather than the demand side. Commonly used laboratory diagnostics require quick testing after sample collection, which is difficult in rural and other hard-to-reach populations. In our evaluation study, we found poor agreement of CD4 stabilization tube results compared to the reference testing method beyond the first day after blood drawing. Therefore, these tubes do not offer a solution for sample transportation problems in these settings. Though CD4 testing is being replaced by viral load measurement, it will remain an important test to screen for and treat certain opportunistic infections. Laboratory infrastructure in SSA needs to catch up with rising diagnostic needs in the upcoming test-all-treat-all era.

Regarding objective 2, we examined retention in a prevention of mother to child transmission (PMTCT) programme during pregnancy and the early post-natal period in rural Tsholotsho district, Eastern Zimbabwe, and whether active tracing of defaulting mothers through community health workers reduces attrition from care and vertical HIV infections in newborns. We found good retention during pregnancy but poor retention after delivery. Tracing defaulting women through community health workers increased retention after delivery moderately but failed to substantially reduce overall vertical HIV transmission. This shows how difficult it is to ensure good quality PMTCT services even with extra investments to improve retention. Life-long ART for all HIV-infected pregnant women (PMTCT Option B+) will become the norm in the upcoming treat-all era, which will exacerbate retention issues further. Community involvement does not offer quick fixes to these problems.

Regarding objective 3, we investigated a novel task-shifting model of care in which drug supply for clinically stable long-term patients on ART was provided through community-based drug refill centres in Kinshasa, DRC. We found retention and mortality levels to be superior compared with regular services and similar to those from other community-based models of ART provision. Such drug refill centres are a promising decentralization approach in urban contexts. This will become increasingly important in the upcoming universal treatment era to decongest the conventional health care system.
Regarding objective 4, we investigated the trade-off between decreased post-initiation retention through rapid ART initiation, and increased post-initiation mortality through delayed initiation in HIV infected treatment-eligible adolescents in urban Bulawayo, South-Eastern Zimbabwe. We found high mortality shortly after ART initiation, but no evidence that the length of the time until treatment is started affects post-initiation outcomes. Health care providers and caregivers should adapt the initiation process to the adolescents' individual needs. Such an individualized approach needs to be balanced with efficiency considerations, which will become increasingly important in the upcoming treat-all era.

All presented studies are operational research (OR) studies. Such research is embedded in routine care, mostly using programme data, and aims to improve the implementation of health services under local conditions. At this stage of the epidemic, it is well known what needs to be done, but less so how. Operational obstacles now threaten the success of further ART scale-up more than a lack of financial resources or scientific advancements. ART will remain the main method to fight HIV/AIDS in the decades to come. Its role will become even more important given the recently emerging evidence on its preventive effects. OR will be the only way to find out how different models of care work best for which populations under which circumstances. The new universal treatment approach further increases the relevance of OR as the gains from current interventions need to be maximized.

Much has been achieved in the response to HIV/AIDS since the role-out of ART started more than a decade ago. However, more work still needs to be done. The proclamation of aspirational long-term goals, though important to mobilize and unite political, scientific, and financial efforts, must not lead to wishful thinking and complacency. Patient populations that have been the focus of scale-up efforts for a long time continue with very poor HIV service delivery in very essential aspects of HIV care. Treatment guidelines should consider local constraints better, and should make more use of local knowledge about what works and what does not work in certain settings and populations. More high-quality OR studies are needed to overcome obstacles in the implementation of HIV care, and to better understand how ART is best provided under local circumstances.

If prevailing operational challenges in the scale-up of antiretroviral therapy in Sub-Saharan Africa are not overcome, the goal to eventually end the HIV/AIDS epidemic will remain illusive.