

Republic of Congo National HIV/AIDS Programme in 2018: a cross-study analysis

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ABSTRACT

Introduction: Republic of Congo is not a model for the fight against HIV/AIDS. For many years, the number of new infections in the Country is not mastered. The Republic of Congo is undergoing a serious and generalized HIV/AIDS epidemic. This review aimed to provide more detailed analysis on the monitoring of data at the national level in order to identify areas where performance can be improved.

Methods: **Data reporting:** No statistical methods were used to predetermine sample size and the indicator score was calculated by considering the ratio between the annual targets and the targets achieved.

Setting and health data: All data used came from the focal points of the National Program for the fight against HIV/Aids.

Statement of the problem: Republic of Congo was one of the places coined as epicenter of the HIV spread, but in-country follow up and monitoring is poor.

Data collection: Data on HIV were collected from several health facilities dedicated to HIV-1 care and management.

Ethical considerations: Ethical considerations could not be addressed, as this appeared too challenging for administrative personalities giving the ongoing conflict in the country.

Statistical analysis: Not applicable

Findings and Discussion: The proportion of male condoms distributed was 39.74%, while that of female condoms was 1.2%, so very little knowledge and usage of female condom. The total number of people received at the Counseling-Mobile-Screening was 0.4%, those who agreed to take the HIV test was 94.57%. The total number of HIV positive pregnant women received during 2017 was 0.35%. The total number of children born to HIV-positive mothers who received ARVs was 56.43%. The total number of children born to HIV-positive mothers who received antiretrovirals was 37%.

The Republic of Congo should sustainably scale-up on antiretroviral therapy.

Concerning effectiveness of the response to HIV/AIDS, although the denial phase took a long time, in the Congo, we had moved to the recognition phase and very quickly from the recognition phase to the mobilization phase. No data on HIV-related deaths has been reported and is available. The country does not know their level of achievement as the 90-90-90 goal is concerned. The political commitment of Congolese leaders is an important and unavoidable element for the establishment of an effective program to combat HIV/AIDS.

Conclusion: Using this national longitudinal database, this review shows that efforts must be deployed in promoting health and controlling HIV infection. The 90-90-90 strategy is far from achievable for 2020, unless drastic measures are taken to improve HIV care. Health indicators do not meet the WHO performance thresholds for HIV control. Today, the HIV/AIDS still remains the most serious problem in the Republic of Congo.

Key words: Republic of Congo, HIV epidemic control, political commitment

I. INTRODUCTION

HIV/AIDS is a leading cause of morbidity and mortality [1,2] particularly in the Republic of Congo. The HIV/AIDS pandemic marks a severe development crisis in our Country. Free HIV testing and antiretroviral therapy have been provided since 2008. Unfortunately, the first- and second-line regimens and the reagents for the laboratory tests are frequently out of stock. Antiretroviral treatment (HAART) programs cannot be scaled-up, for lack of continuous supply of antiretrovirals, but also for the lack of drugs for opportunistic infections. Patients are often unable to get treatment for a full month. Unplanned interruptions in antiretroviral therapy have negative impacts on HIV treatment outcomes, including increased morbidity and mortality, as well as the development of drug resistance.

Despite the rapid increase in the use of antiretroviral therapy since the mid-2000s and the decline in mortality in many countries around the world and in Africa [3–5], the number of people living with HIV who do not continuously receive treatment is still increasing significantly in the Republic of Congo (**Personal Communication, 2019**). The burden of the national HIV epidemic is disproportionately concentrated in some parts of the country. Pointe-Noire is a port city and an oil industry platform located in the Republic of Congo with an estimated population of 1,158,331 in 2017. The Lékoumou and Bouenza are two of the departments of the Republic of Congo, located in the west and the south of the country with 100 061 and 320 835 respectively, according to the 2009 national population census. Ten years later, no other census has been done to date to update the demographics of these communities. Here you should add the prevalence of HIV in these departments or cities, not just the number of inhabitants.

Republic of Congo is not a model in the fight against HIV virus and AIDS. For many years, the number of new infections in the Country is not mastered. The number of people who died of AIDS is also unknown. Effective responses to the epidemic require a multisectoral approach, including the involvement of the presidency of the Republic, the government through the Prime Minister, the Ministry of Public Health, and HIV associations. In the absence of local information on HIV incidence, knowledge of variation in HIV prevalence can be used to better target prevention efforts in areas of greatest need. The HIV-related mortality rate is unknown and not studied.

This review aimed to provide more detailed analysis on the monitoring of data at the national level in order to identify areas where performance can be improved.

Status of the HIV/AIDS Epidemic in Republic of Congo

The Republic of Congo counts about 5,125,821 inhabitants, in 2016 (<http://countriesid.com/AFrepublic-of-congo.html>). In 2009, HIV prevalence was 3.2% and no other studies were conducted to estimate national prevalence since then [6]. These numbers are far from reflective of reality, as very little national epidemiological study is done to update HIV statistics.

In 2016, the national prevalence rate was estimated at 5% with disparities from one city to another: Brazzaville (3.3%), Pointe-Noire (9.9%), Ouessou (5.0%), Dolisie (11.3%), according to studies conducted by the National Council against AIDS in Congo. The number of people affected by the infection is between 90,000 and 150,000, with a tendency towards feminization [7,8].

UNAIDS estimates that at the end of 2017, there were 91 000 adults aged 15 and over living with

HIV. Children aged 0 to 14 living with HIV were 9100. Women aged 15 and over living with HIV represent the most affected population, 61 000, twice as many as men aged 15 and over living with HIV (30 000) [9].

Although having overall adult prevalence rates (3.1%) lower than in the others Central Africa Countries, the Republic of Congo is undergoing a serious and generalized HIV/AIDS epidemic. Among the countries in the region, the Democratic Republic of Congo, Chad, and Equatorial Guinea show adult HIV prevalence rates under 5 percent. Republic of Congo has been in economic chaos and social saw-tooth development for so long that it is difficult to know exactly what is transpiring with the epidemic there. However, economic growth is projected to slowly recover at 1.9%, on average, over the period 2018 to 2020 (<https://www.banquemondiale.org/fr/country/congo/overview>).

In the Republic of Congo, a life expectancy at birth is estimated at 59.8 years in the general population, the male 58.6 years and female 61.1 years. AIDS is one the leading cause of death in our Country. AIDS-related deaths (all ages) were 4900 in 2017.

Prevention efforts need to be intensified for the epidemic of HIV/AIDS to echo for several generations. In others African countries, prevention, treatment and care programs evolve at a more accelerated pace. However, in our country, prevention, treatment and care programs evolve at a more modest pace. In the absence of local information on HIV incidence, knowledge of variation in HIV prevalence can be used to improve target prevention efforts in areas of greatest need. Table 1 below summarizes the prevalence in different localities in the Republic of Congo in 2009.

Since the seroprevalence and AIDS Indicators Survey conducted in 2009 by the National Center for Statistics and Economic Studies, no other survey has been conducted to date to describe the new HIV situation [6].

National-level indicators are important because they allow the country to assess the progress towards the stated Sustainable Development Goals (SDGs), particularly important in the area of HIV/AIDS [10].

This review has to allow more detailed analysis of monitoring data at the national level in order to identify areas where performance can be improved. The HIV data obtained concerns the management of sexually transmitted infections, the mobile HIV testing counseling, the HIV testing counseling or at the initiative of the provider, the HIV testing advice for women during pregnancy, the guidelines of care for HIV pregnant women and the newborn, the care of the HIV-positive adult, the care of the HIV-positive child and the therapeutic care of people living with HIV. The number of newly HIV-positive diagnosed persons reduces the number of people who are unaware of their infection and

allows HIV-positive people to access antiretroviral therapy for both individual and collective benefits. All the data used for national-level indicators are generated at the local level and communicated to the

national program. However, not all the indicators that are needed or useful at the local level are relevant at the national level.

Table 1 : HIV prevalence in the different localities of the Republic of Congo in 2009.

Bouenza	Brazzaville	Cuvette	Cuvette Ouest	Kouilou	Lékoumou	Likouala	Niari	Plateaux	Pointe-Noire	Pool	Sangha
3,9%	2,4%	1,7%	1,5%	3,9%	4,8%	1,9%	4,4%	3,3%	4,6%	1,7%	4,0%

II. METHODOLOGY

Area of collected data

The health data used in this publication concerns the health department of Brazzaville, which is hierarchical as follows: Departmental Directorate Socio-sanitary - Focal Point - Health Centers. Brazzaville is the capital of the Republic of Congo, a country located in Central Africa. The city is on the Congo River, opposite Kinshasa, capital of the Democratic Republic of Congo. The area is 263.9 km² with a population of about 1,838,348 inhabitants in 2017.

This publication is based solely on HIV health data collected in health centers in Brazzaville.

Data Collection Tools

National HIV/AIDS programs collect different types of HIV data. These include:

- HIV outcomes data about HIV diagnoses, prevalence, incidence, viral load and mother to child transmission rate; medication adherence; and disease progression, which could be obtained from health facilities.
- Health services data to understand how people living with HIV/AIDS are accessing and utilizing support services
- Health facilities data to measure whether patients are remaining in care and attending scheduled appointments
- Law enforcement data, which may include information about the use of male and female condoms
- Program data about HIV/AIDS prevention activities

Data reporting

The reporting is done by the focal point. All health data are usually reported in health record books. The data transmission at the departmental level is done by means of forms, provided by the general direction of the health and that allows collection of all health data from a health center, including HIV related data.

The number of health centers that sent their data to the focal point was 94, representing all health centers in Brazzaville. The health data of the other cities are recorded by the same procedure and sent to the departmental directorates of the cities.

Two objective criteria to evaluate the effectiveness of responses were reviewed: HIV prevalence rates and the level of resources devoted to the epidemic in the country.

No statistical methods were used to predetermine sample size. All Health facilities enrolled in data collection transmitted their data at the level of the departmental directorate of Brazzaville where focal point compiles the data and transmit them to the Ministry of Health and Population. The indicator score was calculated by considering the ratio between the annual target (target expected or planned) and the target achieved. The indicator scores were broken down to: poor- (0 to 29%); mediocre- (30 to 49%); good- (50 to 79%); excellent- (80 to 100%).

Setting and health data

The focal point of the National Program for the Fight against tuberculosis is a service located in each Departmental Directorate of Health, appointed by the Decree n°10212/MSP/CAB of 19 October 2004, on the allocation and institution of the National Program for the Fight against HIV/AIDS in its Article 13. It is composed of a coordinator, a monitoring officer, an evaluation officer and a secretary, according to the note n° 515/MSP/CAB/DDS-BZV of 03 April 2018. All data collected from health centers are sent to the focal point, which is the main coordinator of HIV. The focal point compiles HIV data and send them at the national HIV program level. This program is placed under the political supervision of the Presidency of the Republic and under the technical supervision of the Ministry of Health and population.

Statement of the problem

WHO found that Republic of Congo was one of the places acting as the epicenter of the HIV spread together with the Democratic Republic of Congo. The most alarming finding in this respect was the increase of infection rate, which since 2012 has been significantly increased. A comprehensive study of ARV adherence and possible factors facilitating or constraining adherence to ARV in Republic of Congo has not yet been attempted.

Significance of the study

This review is important to all parties, national and international engaged in the fight against HIV.

Ethical considerations

Ethical considerations were not addressed, as this appeared too challenging for administrative personalities given the ongoing conflict. The health centers transmit health data, to the focal point responsible for HIV, which compiles health information and sends it to the departmental health and social ministry of Brazzaville, for further analyses to guide decisions taking.

Statistical analysis

Not applicable

III. FINDINGS AND DISCUSSION

Prevalence data and evolution

The departments of Lekoumou and Kouilou have the highest rate, 4.8 and 4.6% respectively, while the department of the Bowl has the lowest rate in the world with 1.5% (Table 1). HIV prevalence rate has increased since the 1990's.

The conditions for an effective response and successful policy actions are needed to combat the HIV epidemic. These conditions are based on the crucial role of the authorities to make effective political commitments. HIV-AIDS infection remains in an "implosion phase". HIV prevalence data are variable according to the sources of information, indicating inconsistency in the management of the disease.

Factors that influence success are many and varied, ranging from the individual to the collective. Much of the success of the fight against HIV infection is due to strong political leadership and a high level of social cohesion, as is the case in Senegal [11]. The relative economic chaos recorded over the last 10 years continues, social development is barely perceptible, which is a drag on lowering the level of HIV prevalence.

Pillars of the fight against HIV / AIDS

- **Quantity of condoms distributed**

The proportion of male condoms distributed was 158 400/398 504, or 39.74%, while that of female condoms was 4 800/ 368 504 or 1.2%; so very little knowledge and usage of female condom. The indicator score ranged from poor to very poor with respect to the number of condoms distributed in the Republic of Congo. In the first two quarters of 2018, no condom was distributed. In the fight against HIV/AIDS, condoms are a critical component in a comprehensive and sustainable approach to the prevention of HIV and other sexually transmitted infections (STIs).

- **Management of the sexually transmitted infection and adult living with HIV/AIDS**

The total number of health facilities that integrate the management of STIs as well as the number of providers trained for this remained at 50%. Also, the annual number of people received for complaints or several STI syndromes was only 803/1 992 521 or 0.04%.

Between 7000 and 8000 people infected with HIV in the Republic of Congo need antiretroviral therapy in order to survive but at the end of 2017, only 389/7703 or 5.05% had access to treatment. This represents a national health alarm to which health authorities should commit themselves to work harder in providing treatment to all who are in need.

High priority should be given to the monitoring and evaluation of the reasons behind this profound scale-down of antiretrovirals. It will be interesting for our country to hold a meeting to evaluate the progress towards the set goals and objectives, on how local levels (districts, department and health facilities) should better monitor progress and identify problems.

The total number of HIV treatment centers planned was 18, but by the end of 2017, only 13 sites were implemented. New patients expected to be enrolled in the cohort were estimated at 7703, but at the end of the year there were only 573/7703 registered (7.44%).

Despite the rapid increase in the use of antiretroviral therapy since the mid-2000s in the world and in Africa, in the Republic of Congo the supply of ARVs remains a major problem to be solved for the Ministry of Health and Population. Sustainable Development Goal 3 (Ensuring Healthy Lives and Promoting the Well-Being of All and All Ages) explicitly calls for an end to the epidemic by 2030. What is needed to achieve this is more efforts to develop and implement new strategies for effective action in the fight against HIV in our country.

Local data on current HIV prevalence is a tool to provide effective targeted resources and interventions. One seroprevalence survey was conducted in 2003. The other survey conducted in 2009 gave an HIV prevalence of 4.2% in the adult population aged 15 to 49, with significant disparities between different departments (range: 1.5 to 4.8%), between urban and rural areas and between southern and northern areas. At the national level, the disparity of HIV prevalence in the departments implies greater efforts to control HIV infection and therapeutic management.

The HIV national prevalence obtained so far is part of the projections generated by the software called spectrum [12]. Local estimates of HIV prevalence are useful for estimating the need for HIV services. Local estimates of the number of people living with HIV make it possible to estimate the need for antiretroviral treatment. These data permit to estimate the number of

people tested HIV positive, areas with high HIV prevalence and low coverage of antiretroviral therapy.

• **HIV Counselling -Testing**

Voluntary counselling and testing are defined as when a person chooses to undergo HIV/AIDS counselling so that they can make an informed decision about whether to be tested for HIV. The government should encourage population to come forward to be tested for HIV. Many do not accept to be tested, even though they are sick. Improvement could be achieved if the government actively educates the population through various means: national campaign, television, radio, pamphlet. Rapid voluntary counselling and testing approaches linked to treatment programs optimize uptake of treatment for high-risk populations.

Rapid voluntary counselling and testing is a complex intervention aimed to increase the participation of marginalized populations in HIV testing and treatment programs. Rapid voluntary counselling and testing consists of three components: (1) voluntary enrolment, (2) rapid testing (results within 24 h) and (3) counselling and delivery of results and treatment options. The 2013 WHO HIV guidelines recommend HIV testing be done in conjunction with treatment after counselling.

In order to effectively scale up HIV testing, treatment and viral load suppression specific strategies are needed to guide interventions for people at high risk for HIV exposure.

The total number of people received at the Counseling-Mobile-Screening was 166/398504 or 0.4%, those who agreed to take the HIV test was 157/166 (94.57%), and 4/157 (2.55%) accounted for the total number of people tested HIV-positive through the mobile voluntary counselling and testing. The total number of people presented at the voluntary counselling and testing was 1213/797008 (0.15%), those who agreed to take the HIV test was 522/1213 representing 43.03%, 126/522 or 24.1% represented the total number of people tested HIV-positive through the voluntary counselling and testing. Give the scores as defined poor- (0 to 29%); mediocre- (30 to 49%); good- (50 to 79%); excellent- (80 to 100%). In 2016, WHO estimated a number of people newly infected with HIV to 7600 in our Country [12].

HIV Mother-to-child transmission

The insufficient antiretroviral treatment provision is tied to the chaotic economic situation of the country. The poor economic status of the Republic of Congo hindered the expansion of HIV services. This year 2018, the total number of pregnant women received at the voluntary counselling and testing/PMTCT was 1354 out of 398 504 expected pregnant women so a percentage of 0.33.

All pregnant women presenting at health facilities had received pre-test counseling, only 76.51%

(1036/1354) agreed to take the HIV test, the proportion of HIV positive was 2.2% (23/1036). The total number of HIV positive pregnant women received during 2017 was 56 out of 15 940 expected (0.35%). The total number of children born to HIV-positive mothers who received HAART was 206 out of 365 expected or 56.43%.

In 2016, WHO estimated a percentage of pregnant women living with HIV who received antiretrovirals for PMTCT to 16%. Final mother-to-child transmission rate including breastfeeding period was 25.6%, there were estimated HAART coverage (children, 0-14) to 25% and a percentage of infants born to women living with HIV receiving a virological test within two months of birth 3%.

The number of prescribing doctors trained in the care and management of people living with HIV/AIDS was 14 out of 36 expected or 38.88%. These data on HIV are the only existing and available at the level of the Departmental Directorate of Brazzaville. And these HIV health data give an idea of the exact situation and the reality of HIV infection in the Congolese population.

The small number of women received demonstrates the weaknesses of the prevention of mother-to-child transmission program applicable to the entire country. The number of new HIV positive pregnant women put on antiretrovirals was 80.35% (45/56). No new pregnant women were put on ARVs in dual therapy (Trovada (TDF + FTC 300/200 mg or Duovir (AZT+3TC 300/150 mg or Abacavir (ABC/3TC 60/30 mg) during 2018, the expected annual target was 45 women in therapeutic care.

• **Management of people living with HIV/AIDS (PLHIV) according to the national guidelines**

The total number of children born to HIV-positive mothers who received antiretrovirals was 37, of which only 12 were administered antiretrovirals within 72 hours. Only one out of 50 doctors trained was involved in the care of HIV-positive pregnant women. And only 2/50 or 4% midwives and paramedics were trained in the care of HIV positive pregnant women. The number of prescribing doctors trained in the care and management of people living with HIV/AIDS was 14/36 or 38.88%. The total number of seropositive patients at the end of 2017 was 5250 against 6017 in 2018. The total number of new patients registered in the cohort was 573 (7.44%). The percentage of adult patients on first-line was (4893/7703) or 63.52%, second-line (325/7703) or 4.22% and only 8/7703 adult patients were put on third-line (0.08%). The total number of antiretrovirals patients followed up was 5215/7703 or 68%. The total number of new patients put on antiretrovirals was 389/7703 or 5.05%.

In the WHO documents, the reported data show that PLHIV diagnosed were 29%, those receiving

HAART were 23% and those who virally suppressed are not known, as viral loads are almost not carried out in this country, where reagent breaks become legendary and who depend on the subsidy of the global fund.

- **Medical care for people living with HIV/AIDS according to the national guidelines**

Data shows the exact situation and the reality of HIV infection in the Congolese population. In the Republic of Congo, little progress has been achieved, and more must be done. We see progress in reducing new infections among adults by providing preventive medication and providing oral self-testing for HIV.

There were 40% more people on antiretroviral treatment in 2017 than there were four years ago. Antiretroviral treatment prevents the virus from multiplying and prolongs the life of HIV positive people. It also lowers the risk of transmission from HIV positive to HIV negative people.

The Republic of Congo should scale-up on a sustainable manner antiretroviral therapy. The HIV/AIDS funding from international institutions is declining for the past few years in the Republic of Congo. To achieve and sustain universal access to HIV services, evidence-based planning is essential. In 2017, the Republic of Congo had a concentrated HIV epidemic with estimated HIV prevalence in the general population (age, 15–49 years) at 3.1%. Women aged 15 to 49 HIV prevalence rate was 4.4 and men HIV prevalence rate was 1.9. On the other hand, the prevalence in pregnant women was at 13.4% in 2017.

An estimated 248500 people were living with HIV in 2011 and 60924 adults and children were receiving antiretroviral therapy at the end of 2011. However, antiretroviral coverage compared to estimated needs was still limited to 54%, and further scale-up is critical.

Effectiveness of the response to HIV/AIDS

It is difficult to avoid the consequences of HIV. Although the denial phase took a long time, in the Congo, we had moved to the recognition phase and very quickly from the recognition phase to the mobilization phase. But so far, all efforts at this level are not yet deployed. Two countries in Africa have succeeded in this mobilization phase: Senegal and Uganda [11].

The assessment of the effectiveness of the response is done using objective criteria. These criteria provide elements, key points for assessing the effectiveness of the response in the Republic of Congo. These criteria include trends in HIV prevalence rates, mortality rates, life expectancy and levels of social displacement (for example, the number of orphans). Unfortunately, all these data are not available, the health data collected in 2018 were mainly based on HIV prevalence rates. This implies that since then, political

efforts to improve the control of the epidemic have been ineffective and did not lead to a proper response.

Number of deaths related to HIV / AIDS

In Congo, child data are rare. In 2016, UNAIDS estimated that 6000 children were living with HIV, 1100 were newly infected, and HIV infection is one of the main causes of death in children with nearly 1000 deaths [13,14]. No data on HIV-related deaths has been identified and is available since then. Death-related HIV data is a missing element in data collection registers in all health centers and hospitals in the country. In 2016, WHO estimated number of deaths due to HIV was 3800 [12].

Lack of resources

The infrastructure needed to cope with the increasing number of people living with HIV is often lacking. The human resources needed to manage HIV infection are not sufficient to meet the current need of the epidemic. The material and human resources needed to improve education, social protection and the health of the general population are largely lacking. This lack of resources is closely linked to the country's unstable economic development, which directly associated to a reduction in health budget invested in HIV infection.

Budget allocated in the fight against HIV

The political commitment of Congolese leaders is an important and unavoidable element for the establishment of an effective program to combat HIV/AIDS. Unfortunately, in our country, the political will is without concrete commitment, the good intentions and the action plans are not accompanied by devoted actions. It is just a lack of priority.

Very little financial resources are allocated to health in general and HIV/AIDS in particular, to combat the consequences of the epidemic and prevent other infections such as hepatitis or tuberculosis. Congolese government spending on HIV is extremely low.

In 2016, for the set of investments planned for the year 2016, the initial budget allocated to each investment was Francs CFA 79 billion, then the budget "readjusted" during the year for each was 101 billion Francs CFA. As a result, data vary from one document to another, which may make it more difficult to monitor health projects, particularly HIV projects, which are virtually funded by the global fund [15,16].

Literally Low- and Middle-income Countries governments of such as Republic of Congo had the capacity to spend an additional \$12.1 billion (8.4–17.5), a 125.7% (121.3–133.0) increase, on the fight against HIV/AIDS (including for the care and treatment of people living with HIV/AIDS), assuming that their existing government health budgets are fixed [17]. The portion of the budget that the Congo is allocating

specifically to the management of HIV is not known. The political commitment of Congolese leaders is a must for an effective program to eliminate HIV/AIDS in 2030.

IV. CONCLUSION

This study provides the very first evidence based, nationwide data on HIV management in the Republic of Congo. Using this national longitudinal database, this review shows that efforts must be made in promoting health and preventing HIV infection. Health indicators do not meet the WHO performance thresholds for HIV control. Today, the HIV/AIDS remain a most serious problem in the Republic of Congo. This review reinforces the evidence that national efforts are imperative to change HIV infection trend from the death penalty to chronic disease. As people living with HIV live longer because of ARV treatment, many clinicians and midwives should be trained and several prescribers trained in HIV care and management in order to curb the trend of epidemics in the Republic of Congo.

The 90-90-90 strategy is an attempt to get the HIV epidemic under control by adopting a 'test and treat' approach. Unfortunately, these objectives are to increase the number of people living with HIV, who know their HIV status, the number of people infected with HIV who are screened, who receive sustainable antiretroviral therapy, and finally the number of people receiving antiretroviral therapy who have a sustainably suppressed viral load will not be achievable for 2020 unless drastic measures are taken to improve HIV care.

Competing interests

The authors declare no conflict of interest.

Authors' contribution

GLLS conceived and designed, wrote the article, and critically edited it for important intellectual content. OA analyzed and interpreted the data. CNN gave final approval to the version to be published.

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