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Onchocerciasis in Nigeria 1: History of control efforts

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Abstract

Nigeria is the most endemic country for onchocerciasis in the world and accounts for about 40% of the global cases. With about 50 million persons in over 40,000 communities at risk, it has been recognized as a communicable disease that is not only a social problem but also a major threat to productivity and the economy of the country. It is especially prevalent among the poor rural farmers, ''people at the end of the road'' living around the vector breeding sites who produce the bulk of our food and industrial raw materials. This review brings to focus the historical background of black fly and onchocerciasis control in Nigeria beginning from 1953 when the Oji power station-vector control operation was implemented and subsequently extended to River Niger at Lokoja, Kaduna River and the rivers in the Abuja emirate area. Other areas, which followed were Hawal River Valley and the Kainji Dam site in the 1950s and 1960s. The establishment of the National Onchocerciasis Control Programme (NOCP) in 1982, the introduction of mass ivermectin distribution in 1988 and the involvement of Non-Governmental Development Organizations (NGDOs) and African Programme for Onchocerciasis Control (APOC) were later progressions. This historical era of onchocerciasis control in Nigeria (from the 1950s and 2009) ended when there was evidence that long-term mass ivermectin distribution in endemic communities showed promise in the interruption of disease transmission and elimination. The strategies used and lessons learned during this era are highlighted.

Keywords: Nigeria, Onchocerciasis, Historical Background, Control Efforts

Introduction

Human onchocerciasis, commonly called river blindness is a chronic parasitic disease caused by the filarial worm, *Onchocerca volvulus*. The adult worms live mainly in subcutaneous nodules, where the female worms (during their 9-14 years of sexually active life) give birth to millions of microscopic embryos called microfilariae. Microfilariae are picked up from the skin during a blood meal and transmitted to another person by female black flies of the genus *Simulium* [1].

In Nigeria, onchocerciasis is transmitted by sibling species within the *S. damnosum* complex namely *S. damnosum s.s., S. sirbanum, S. squamosum, S. yahense, S. Sanctipaul* and *S. soubrense*. These flies breed in fast-flowing, well-oxygenated water with nutrients. This habitat preference by these flies limits the vectors mainly to communities around these breeding sites. This preference determines the distribution of onchocerciasis.

An overwhelming majority of the skin-dwelling microfilariae is never ingested by the blackfly; therefore these microfilariae eventually die in the human tissues. The dead microfilariae herald complex immunological manifestations leading to the dreaded clinical complications associated with the disease: onchocercal skin disease (OSD) (onchodermatitis), lymphadenitis (resulting in hanging groin), ocular lesions (impaired vision and blindness) and systemic manifestations

The distribution of onchocerciasis, intensity and endemicity levels are largely determined by the ecology and behaviour of the black fly vector [2]. One such vector's behaviour is that it has an effective flight range which is unlikely to exceed a 15 km radius of breeding sites. By this, the severely affected communities by onchocerciasis are almost invariably located within this area. Blindness and or impaired vision are the most serious and overt clinical manifestations of onchocerciasis which are most prevalent among villagers living around *Simulium* breeding sites. Onchocerciasis is thus believed by the rural endemic communities to be caused by the gods of the rivers; hence, they call it "river blindness". No wonder then many villagers in endemic communities implicate the gods of the river to be the cause of onchocercal manifestations. In desperation for relief from the flies and disease, some of them consult the oracle and appease the gods [1].

Prevalence of Onchocerciasis

Onchocerciasis, by 1987 was endemic in 37 countries (in sub-Saharan Africa, Central and South America and Yemen), with about 20-40 million people infected. It was estimated that 350,000 were blinded by it and, 500,000 were visually impaired. An additional 122.9 million people were at risk, over 6 million suffered different onchocercal skin diseases [3] and about 1.6% of infected individuals suffered lymphatic complications [4].

Nigeria is the most endemic country in the world and accounts for about 40% of the global prevalence [3,5]. About 32 million Nigerians living in 36,000 communities in 413 LGAs of 32 States and FCT was estimated to be at risk of the disease [5]. An estimated 15% of this population was children less than 5 years, while 26.3% were between the ages of 5 and 15 years. By 2002, all States except Lagos, Sokoto, Bayelsa and Rivers were endemic for Onchocerciasis. Katsina State has sporadic hypoendemic communities [6].

Socioeconomic Impact

Onchocerciasis apart from causing social problems is also a major threat to productivity and the economy of the country. Onchocerciasis is chronic and cryptic. It is a "disease at the end of the road" as well as for poor rural farmers who produce the bulk of food and industrial raw materials.

The bite of the vector flies causes an intolerable nuisance and pain; and is usually followed by intense, unbearable pruritis and scratching, rashes, and ulcerative lesions at the site. The psychosocial stigmatization and rejection suffered by persons affected by the troublesome itching and reactive onchodermatitis complications are far-reaching [7]. The impact of stigmatization on affected individuals (with onchodermatitis) is a serious issue. This is because it results in fear, discrimination and low self-esteem [8], as well as psychological distress and limited life chances including occupational opportunities.

Women and most especially young ladies with lesions are usually victims of overt discrimination at social gatherings [9]. Stigmatized persons suffer great social and psychological stress. Onchocercal skin disease in women is considered a curse, robbing the victim of her beauty, self-confidence and self-pride [10] and marriage [11]. Furthermore, the dreadful malformation as a result of lymphatic complications (hanging groin and genital elephantiasis), nearly always reflect in the infected individual's unwillingness, fortified by shyness towards free social interaction within their communities [7, 12, 13]. In affected male patients with pendulous sac, sexual life is greatly affected if not completely hindered [14].

Onchocerciasis has an adverse effect on the effective cultivation of land in Africa by causing desertion of many fertile river valleys in the Savannah zone of West Africa. This has led to the emigration of young from remote lowland areas in search of better health and educational facilities, as well as an increase in the number of disabled people begging for alms in the cities. For example, Bradley [15] observed that in onchocerciasis hyper-endemic villages there is serious population movement out of the endemic areas leading to village abandonment.

The socio-economic effects of onchocerciasis on the effective supply of labour have in the recent past presented a major concern. Evidence has indicated that at least onchocerciasis affects the effective supply of labour in three ways:

(a)As a cause of death, it removes the individual's supply of labour years in the future. It was observed that mortality rates among blind persons over 30 years of age were 3 - 4 times higher than among sighted persons of the same age group [16]. The consequence of this is a decreased mean life expectancy of about 13 years of 30 – 40% of adults in endemic communities [17].

(b) As a cause of permanent disability through blindness and serious visual impairment, onchocerciasis withdraws the affected individual's potential supply of labour years to activities requiring vision [18].

(c) Partial visual impairment and or other non-disabling manifestations may also reduce the efficiency of labour days worked. In Nigeria, blindness is concentrated in the working age groups and reaches very high levels in hyper-endemic areas [1].

Onchocerciasis in endemic areas impedes national and individual development, it renders fertile land inhospitable, impairs intellectual and physical growth and exacts a huge cost in treatment and control." Onchocerciasis robs affected people of their dignity and hope, especially among the poorest "people at the end of the road". This disease therefore should not be taken for granted, hence the need for control.

Onchocerciasis Control Efforts in Nigeria

Initial control efforts

Human onchocerciasis was first reported in Nigeria in 1909 when Parsons observed the occurrence of the disease pathogen, then known as *Filaria volvulus* in four Nigerians seen at Lokoja but migrants coming from Kabba, Onitsha and Tola [19]. Independently, and coincidentally in the same year, E. E. Austen published the first record of black flies, noting its capture in 1906 at Cross River by Dr R. W. Gray of the West African Medical Services[20]. In 1926, Dr S Dyce reported the occurrence of microfilariae of *Onchocerca volvulus* in the skin of 55 out of 100 prisoners at Kaduna [21]. Later in 1937, Dr J. L. Mcletchie wrote a letter to the Director of Medical Services, Lagos informing him that in Adamawa Province, he saw a group of elderly people all of whom had onchocercal nodules and varying degrees of loss of vision up to total blindness [22]. Ridley and Anderson reported the case of a European Administrative Officer, on leave in the United Kingdom from Northern Nigeria suffering from ocular onchocerciasis [23]. The work of Crosskey on the appraisal of current knowledge of *S. damnosum* sl in Nigeria highlighted this stage of the history of onchocerciasis in Nigeria [24].

In a pioneer, comprehensive work, facilitated by the establishment of rural eye clinics, Dr F. H. Budden in the early 1950s confirmed that "endemic onchocerciasis was widespread in Northern Nigeria and constituted an important cause of blindness in many parts of the area [22]." In the Eastern region, the first organized research on work was reported when Nwokolo examined some patients at a hospital in Enugu [25]. During the mid-1950s, vectors were caught biting men at Enugu as well as Ikom, near the Nigerian-Cameroon border [24]. In the Western region, the disease was first noticed in 1964 when serological evidence of the infection was described from cases studied at the University Hospital Ibadan [26]. Since these initial studies, a lot more research has been carried out in different parts of the country. Today, human onchocerciasis and its blackfly vector are considered to be widespread in the country.

Before the Advent of Ivermectin

Pioneer operational research efforts on river blindness sent strong signals to the Federal Government and the International community as far back as the 1950s that the disease and its vectors constituted major public health problems in endemic areas in the country.

To protect the workers constructing the Oji River power station in 1953, the control of *Simulium damnosum* was carried out using DDT [27]. Similarly, Rimi mimi, a tributary of River Niger at Lokoja was also treated with insecticide. Furthermore, the larviciding of the Kaduna River and the river systems in the Abuja Emirate was carried out in the 1960s to protect the inhabitants of Kaduna and Abuja areas [28, 29, 30]. Larviciding at Abuja continued until 1977. Vajime reported that these control operations were resumed in the 1980s to protect workers engaged in the construction of the new Federal Capital city of Abuja [31]. Other onchocerciasis control activities include those carried out in Hawa River Valley and Kainji Dam site in the 1960s [31].

To control the scourge of human onchocerciasis and the debilitating effects of the disease the Federal Ministry of Health and Social Services established the National Onchocerciasis Control Programme (NOCP) in 1982. As a Division of the Department of Primary Health Care and Disease Control, NOCP was made functional in 1986 and charged with the responsibility of coordinating all onchocerciasis control activities (including operational research) in the country.

Given the significance of operational research in onchocerciasis control in the country, NOCP established a research or field base at Kaduna "where various aspects of controlling the disease cost-effectively would be investigated and disease surveillance carried out". Again, NOCP, in 1986 identified and appointed reputable experts mainly from the Universities and research institutes to constitute a technical Advisory Committee (TAC) on technical and operational research. In course of time, the TAC was reconstituted and renamed Steering Committee (SC). The SC provides technical operational research and professional expertise for the programme implementation.

In addition to the Steering Committee, the administrative plan of NOCP provides for National Onchocerciasis Task Force (NOTF), made up of Director, Primary Health Care and Disease Control as chairman, NOCP National Coordinator, NGDOs, members of the Steering Committee, Zonal Managers/Coordinators and State Onchocerciasis Programme Coordinators.

With the establishment of a functional NOCP, and in the realization of the need to have comprehensive prevalence data on the disease for successful planning and implementation of the control programme, NOCP initiated the first extensive and intensive nationwide prevalence survey in 1987/88-1990. This survey was based on the use of the skin-snip method. This gave NOCP and indeed the international community a bird's eye view of the pattern of the disease in the country. However, the actual disease distribution and intensity as well as the socio-cultural and economic impact on the population at that time were still unclear, as many endemic areas were yet unidentified and unstudied.

Mobile Strategy in Ivermectin (Mectizan®) Distribution Programme (IDP)

With the discovery of ivermectin as the drug of choice targeted against the microfilariae, Nigeria commenced a pilot project of Ivermectin Distribution in endemic communities of Kwara (now in Kogi) and Kaduna States in 1988/89 in partnership with Africare and Sight Savers International (through the National Eye Centre) respectively. With the support of UNICEF/Nigeria, Ivermectin Distribution Programme (IDP) commenced in February 1991 in Benue, Oyo, and Bauchi States. With support from other Non-Governmental Development Organization (NGDO) partners such as Lions Clubs International, River Blindness Foundation, German Technical Co-operation Agency (GTZ), International Foundation for and Self Help (IFESH), Christofel Blinden Mission (CBM), International Eye Foundation (IEF), MITOSATH and Helen Keller International, IDP progressively spread to other endemic parts of the country. To harmonize the control programme, NGDO formed a coalition in 1992.

To ascertain the intensity and distribution of the actual disease in the country, UNICEF Nigeria supported the first nation-wide Rapid Epidemiological Mapping of Onchocerciasis (REMO), which was later refined by the African Programme for Onchocerciasis Control (APOC) (Fig 1). This was between 1990 and 1995. By these results, it was estimated that about 50 million persons living in over 40,000 communities were at risk of onchocerciasis [32].

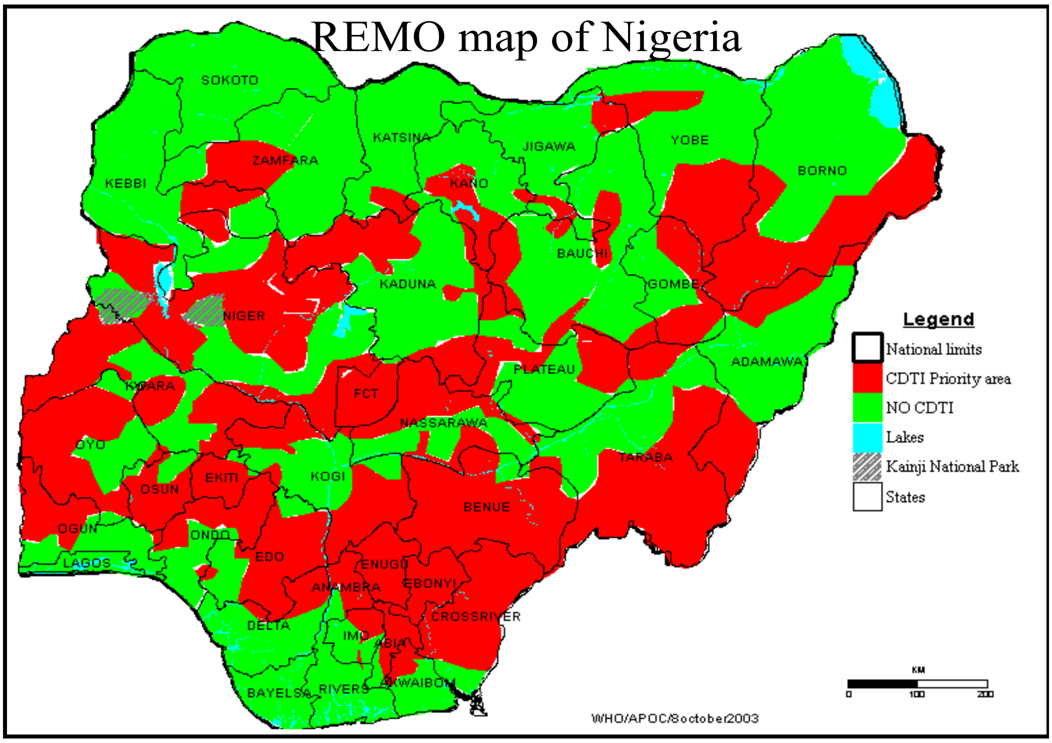

Fig. 1: Pre-intervention onchocerciasis prevalence map based on the Rapid Epidemiological Mapping for Onchocerciasis (REMO) approach (WHO (1998), Guidelines for analysis of REMO data using GIS. TDR/TDF/COMT/98.3, WHO Geneva)

Control under African Programme for Onchocerciasis Programme (APOC)

The initial ivermectin distribution programme (IDP) strategy was Mobile System, where mobile health personnel from State, LGAs and Districts and staff from primary Health clinics were used to distribute ivermectin in endemic communities. This IDP strategy experienced a lot of operational and logistic limitations. WHO therefore launched the African Programme for Onchocerciasis Control (APOC) in 1995. The mandate of APOC was to establish within 12-15 years effective and self-sustaining community-directed treatment with ivermectin (CDTI) through collaborative partnership, within the framework of primary health care activities in the remaining endemic areas in Africa and, if possible, eliminate the vector and hence the disease by using an environmentally safe method in selected foci. APOC partnership involves 19 participating African countries and WHO is the executing agency while World Bank is its fiscal agency.

APOC started its support to Nigeria with assistance to four (4) States viz: Cross River, Kaduna, Kogi and Taraba, for CDTI implementation and to NOCP HQs project, for its coordinating role and oversight functions. The support from APOC was gradually extended to one NOCP HQ project and 27 CDTI projects which cover all 31 States and FCT where onchocerciasis is endemic.

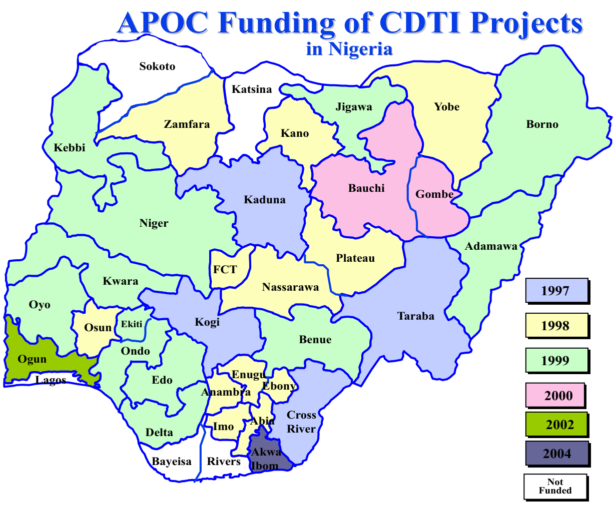

Fig: 2: APOC-supported CDTI projects in Nigeria [6]

Operational achievements in CDTI in Nigeria
Nigeria and most other endemic African countries opted for a CDTI strategy to control the disease. This strategy is because field observations showed that treatment with ivermectin has a significant impact on the microfilaria load of *Onchocerca volvulus*, which suggests that the effect of the drug on the microfilaria production by female parasites is long-lasting [33]. This effect causes the elimination of skin microfilariae thereby making it very difficult for the vector flies, *Simulium*, to pick up skin microfilariae during a blood meal. Hence large-scale ivermectin distributions with increased coverage were observed to reduce transmission of *O. volvulus* by 45% - 75% [34]. It was therefore the strong view that if the ongoing large-scale ivermectin distribution (through Community Directed Treatment with Ivermectin (CDTI) was carried out and high coverage achieved for up to 15 years, it could lead to the interruption of transmission and elimination of infection in flies [33].

The CDTI embodies the philosophy of Primary Health Care in that communities are encouraged to take responsibility for the organization and distribution of the drug (Ivermectin/Mectizan®), which is provided free of charge through the Community Directed Distributors. This assures greater community participation and involvement in programme planning and implementation. Table 1 and Figure 3 below show the distribution and treatment coverage from 1988 to 2009.

S/N	YEAR	TOTAL POPULATION	No TREATED	TREATMENT COVERAGE
1	1988	N/A	6,270	-
2.	1989	N/A	6,149	-
3.	1990	22,918	16,496	71.9%
4.	1991	941,543	217,082	23.0%
5.	1992	1,692,301	612,056	36.2%
6.	1993	2,378,502	1,252,869	52.7%
7.	1994	3,647,268	2,303,917	63.2%
8.	1995	5,030,189	3,824,378	76.0%
9.	1996	7,918,428	5,867,535	74.1%
10.	1997	10,884,133	8,617,602	79.2%
11.	1998	16,815,571	10,456,411	62.2%
12.	1999	22,708,000	13,183,734	58.1%
13.	2000	23,290,312	15,368,967	66.0%
14.	2001	22,936,390	16,880,334	73.6%
15.	2002	25,430,704	19,049,065	74.9%
16.	2003	25,264,077	20,398,504	80.7%
17.	2004	25,588,496	20,072,845	78.4%
18.	2005	27,940,670	21,104,647	75.5%
19.	2006	28,188,595	22,034,624	78.2%
20.	2007	29,327,021	22,782,949	78.0%
21.	2008	29,327,021	23,600,000	80.5%
22.	2009	33,415,549	25,089,3928	75.1%

N/A = Not Available

At the end of 2008, the Federal Ministry of Health (FMoH) reported that a multi-country study to assess the impact of APOC interventions on communities using epidemiological and entomological parameters showed a reduction in skin and eye lesions. There was a significant decrease in the three entomological indicators. The report went further to state that socio-demographic indicators and knowledge of the symptoms of the disease in both phases were overwhelmingly high in the study sites. Later findings from epidemiological studies in Kaduna State where Mectizan was distributed for 16 years with good coverage showed that sustained ivermectin distribution in endemic communities had the potential to interrupt the transmission of onchocerciasis [5].

Evidence of Onchocerciasis Elimination with long term Ivermectin Treatment

Ivermectin kills the microfilariae and a single oral dose of ivermectin (150 micrograms/kg) repeated once a year leads to a marked reduction in skin microfilaria counts and ocular involvement. Ivermectin also temporarily interrupts the production of microfilaria but does not kill the adult worms (Fig. 3). Merck & Co., Inc., the company that manufactures the drug agreed in 1987 to donate Ivermectin free of charge to countries where onchocerciasis is endemic. This resulted in annual treatments for all eligible community members where over 60 million people were treated in 26 African countries in 2008 [35]. However, although this large-scale treatment enabled the control of onchocerciasis in Africa, it was not clear then whether it could also be used to eliminate infection and transmission to the extent that treatment with ivermectin could be safely stopped.

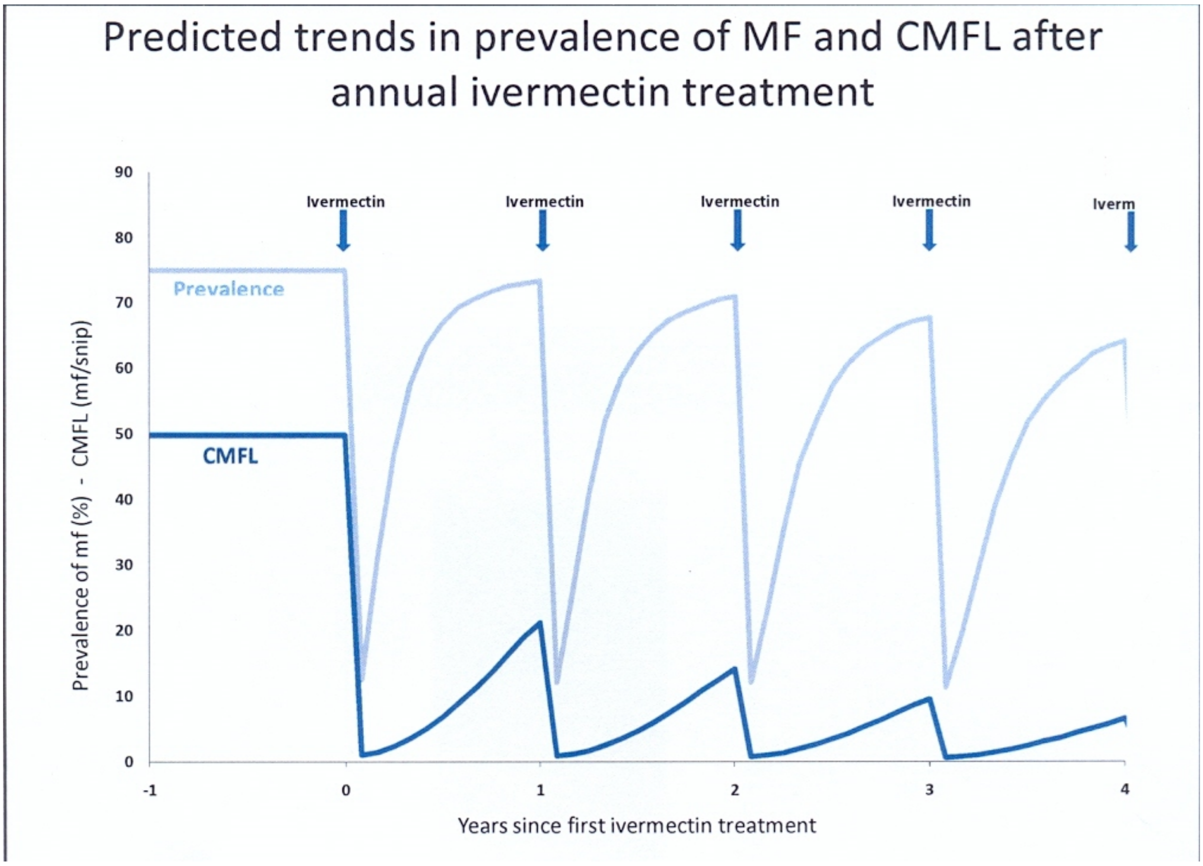

Fig. 3: Predicted trends in the prevalence of microfilaria (MF) and community microfilarial load (CMFL) after annual ivermectin treatment – the basis of mass ivermectin distribution in endemic areas [36]

Follow-up action by APOC to the evidence of onchocerciasis elimination with long-term ivermectin treatment

Conceptual framework of Onchocerciasis Elimination

With the results from foci in Mali and Senegal [37], the principle of onchocerciasis elimination with ivermectin was established and it became urgent for APOC to consider the implications of these findings for onchocerciasis control in the rest of Africa. Giving the emerging findings, and to refine the APOC strategy in moving towards the elimination of onchocerciasis, an Informal Consultative Experts meeting on the Elimination of Onchocerciasis Transmission with Current tools in Africa was organized by APOC, February 25 – 27, 2009 at Ouagadougou, Burkina Faso. The Expert Group provided a definition of onchocerciasis elimination and developed a conceptual framework that was subsequently refined by the Technical Consultative Committee of APOC [38]; developed the technical and operational definition of elimination of onchocerciasis as well as break-point and transmission zone as follows:

(a) Definition of Onchocerciasis Elimination: The reduction of infection and transmission to the extent that intervention can be stopped, but post-intervention is still necessary.

(b) Operational Definition:

(i) Interventions have reduced *Onchocerca volvulus* infection and transmission below the point where the parasite population is believed to be irreversibly moving to its demise/extinction in a defined geographical area.

(ii) Interventions have been stopped

(iii) Post-intervention surveillance for an appropriate period has demonstrated no recrudescence of transmission to a level suggesting recovery of the *Onchocerca volvulus* population; and

(iv) Additional surveillance is still necessary for the timely detection of recurrent infection if a risk of reintroduction of infection from other areas remains. In interpreting the definition of elimination of onchocerciasis, the conceptual framework was graphically developed (Fig. 4).

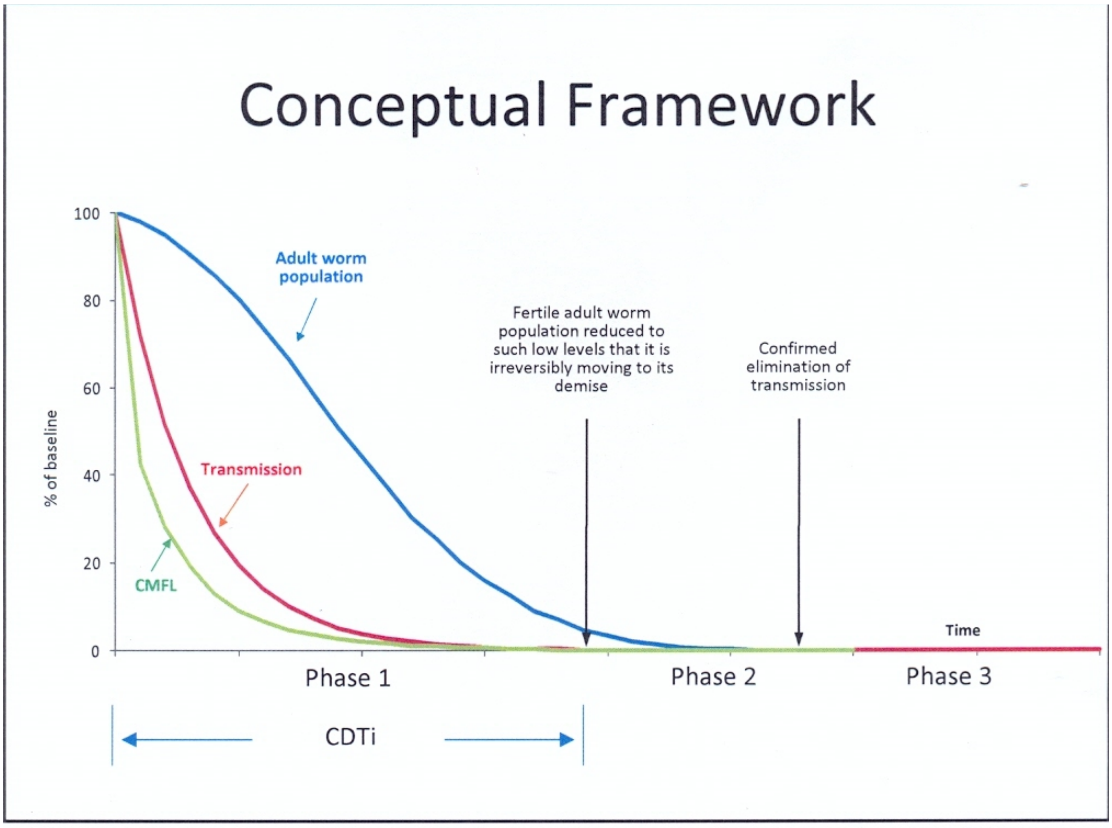

Fig. 4: Conceptual framework of onchocerciasis elimination showing the 3 phases of elimination [38]

Break-point

The concept of break-point was also introduced by the Expert Group: And this is operationally important: it means that infection and transmission do not have to be completely zero before treatment can be safely stopped. This concept has been proven in practice. In Senegal and Mali, there were still several microfilaria-positive people in each of the three river systems but when treatment was stopped, there was no renewed transmission and infection. The same was observed in the Onchocerciasis Control Programme (OCP) in West Africa where the prevalence of infection was still greater than zero in each river basin where vector control was stopped but, again, the cessation of control did not lead to renewed transmission and the infection died out [39].

Procedures and Indicators of when to Stop Treatment

The Informal Consultative Experts meeting on the Elimination of Onchocerciasis Transmission approved by the Technical Consultative Committee of APOC [39] also developed the technical and operational evaluation procedures and indicators of when to stop treatment (Table 2). There are three phases (phases 1[1a and 1b], 2 and 3) according to WHO/APOC [39].

Phase 1a Assess the decline in infection towards breakpoint

This involves an epidemiological survey to assess the levels of *O. volvulus* infection in sample communities selected from high-risk locations near the river and the vector breeding sites and should be communities for which pre-control epidemiological data (skin snip survey or REMO) exist. The survey should be done 11-12 months after the last treatment and just before the next ivermectin treatment rounds.

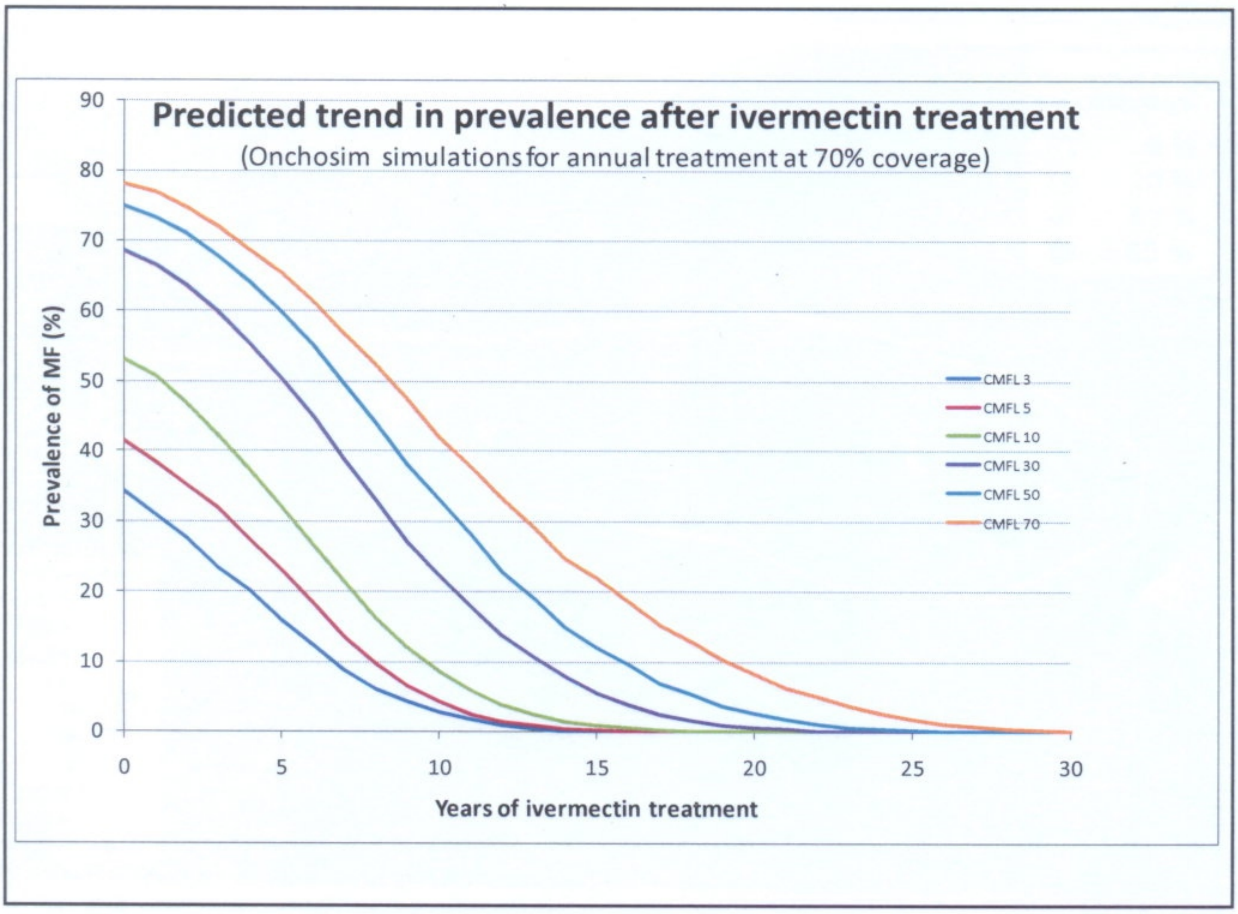

Fig. 5: Predicted trend in prevalence after ivermectin treatment [39]

Interpreting the result of the epidemiological survey is done by referring to ONCHOSIM prediction (the APOC onchocerciasis transmission model) (Fig. 5) of the expected trends in prevalence for different pre-control endemicity levels. The evaluation results are classified into satisfactory and unsatisfactory: it is satisfactory when the observed prevalence is equal or lower than the predicted prevalence and unsatisfactory when the observed prevalence is greater than the predicted prevalence.

Phase 1b. Confirm that the breakpoint has been reached and treatment can be safely stopped

This involves detailed epidemiological and entomological evaluations to assess the residual infection and transmission levels and confirm that these are below defined elimination thresholds. Epidemiological evaluation is the same as in phase 1a but with a wider spatial coverage (sample communities selected along the main rivers and effluents at a distance of no more than 20-30 km between communities). This is to ensure that infection levels throughout the transmission focus are below the threshold. Entomological evaluation is based on pool screening of biting back flies collected throughout the breeding season from selected high-risk locations along the principal rivers near major breeding sites of the vector. Preserved flies are sent to a reference laboratory for analysis, using an *O. volvulus*-specific DNA probe. Based on experience with the cessation of onchocerciasis control in West Africa (vector control in the OCP and ivermectin treatment in the study in Senegal and Mali), together with ONCHOSIM predictions, the threshold for elimination for the epidemiological and entomological indicators have been provisionally defined as shown in Table 2.

Table 2: Evaluation Objectives and Indicators of Elimination [39]

PHASE	EVALUATION OBJECTIVE	INDICATOR	TARGET
1	a. Assess decline towards elimination break-point	Prevalence of mf	<predicted prevalence
	b. Confirm that the break-point has been reached and treatment can be stopped	Prevalence of mf	<5% in all the surveyed villages <1% in all 95% of surveyed villages
		Vector infectivity rate	<0.5 infective flies per 1000 flies
2.	Confirm there is no recrudescence of infection or transmission	Prevalence of mf	No increase
		Vector infectivity rate	<0.5 infective flies per 1000 flies
3.	Detect possible recrudescence of infection or transmission	Prevalence of infection	<1% in all villages
		Vector infectivity rate	<0.5 infective flies per 1000 flies

Phase 2: Confirmation of Elimination
This phase is to confirm that the decision to stop treatment was correct and that this has not resulted in the recrudescence of infection and transmission. Phase 2 should last at least three years and involve entomological evaluation using the same methodology and catching point in Phase 1, and the final round of epidemiological evaluation. The epidemiological surveys are to be done at the end of the three years in a sample of first-line communities located at high-risk locations along the rivers.

Phase 3: Routine Surveillance
In this phase, there is routine epidemiological and entomological surveillance undertaken every 3 to 5 years. It is carried out to timely detect any possible recrudescence of onchocerciasis infection in man or transmission by black flies

Transmission Zone
Another challenge was to determine where exactly treatment can be stopped. That is to define the geographical area where treatment is needed to move from control to elimination. The Expert Group then introduced the concept of a transmission zone (Fig.6). This is defined as a "geographical area where transmission of *Onchocerca volvulus* occurs by locally breeding vectors which can be regarded as a natural ecological and epidemiological unit for intervention." [38]

"The core of a typical transmission zone (Fig. 6) is a river with vector breeding sites, with endemic communities located close to the river, and infection levels failing with decreasing distance from the breeding sites till they become negligible or reach another transmission zone"

Evaluation of APOC Projects for Onchocerciasis Elimination
Introduction
Following the proof of the principle from Senegal and Mali study, the first question was to what extent these findings could be extrapolated to the rest of Africa, and if elimination would be feasible in APOC projects in different endemic countries. The objective of the first epidemiological evaluation was to assess the impact of repeated ivermectin distribution on the

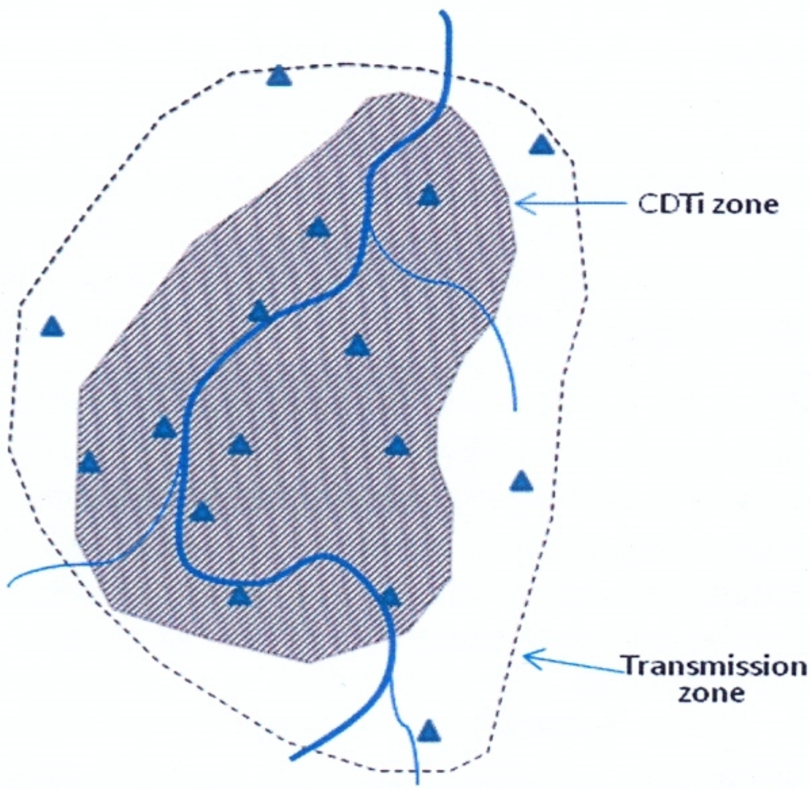

Fig. 6: Schematic example of an onchocerciasis transmission zone [39]

reduction of infection rates in endemic communities towards elimination thresholds. For the first evaluations, in 2008/2009, projects selected had at least 10 years of treatment and for which it was believed that treatment coverage has been satisfactory (the criteria for selection of the first evaluation sites are shown in box 1). In 2010, other epidemiological surveys were also carried out in APOC project areas (Table 3).

Criteria for Selection of first evaluation sites [39]

BOX 1: CRITERIA FOR SELECTION OF FIRST EVALUATION SITES [38]
a) At least 10 years of ivermectin treatment a) Complete geographical coverage b) Therapeutic coverage >70% c) Treatment coverage data available b) Relatively isolated area a) At least 20 km from other endemic areas where treatment started later c) High level of pre-treatment endemicity level a) Nodule prevalence rate >40% b) Where parasitological are available (prevalence of mf >65% or CMFL >40 mf/s)

In each selected site, skin snip surveys were done in a sample of 10 communities, selected from high-risk locations along the vector breeding sites. Skin nips were taken from up to 300 adult residents. Between 2008 and 2010, epidemiological evaluations were completed in 18 foci in Nigeria, Cameroon, Chad, Uganda, Tanzania and the Democratic Republic of Congo (DRC) (Table 3).

- The results from 15 foci were classified as satisfactory, with the prevalence of mf equal to or less than the predicted prevalence.
- In six (6) of these foci, it appeared that elimination of onchocerciasis has already been achieved with the prevalence of mf equal to zero in all sample villages, and
- Another five (5) foci appear to be very close to the break-point suggesting that treatment could be stopped in the next few years
- These initial evaluation results confirmed that onchocerciasis elimination is feasible in APOC projects with annual treatment with ivermectin in most areas. Since these evaluations, a lot more epidemiological and entomological evaluations have been carried out in APOC projects; and the results have been impressive.
- Again, the results of the entomological evaluation have shown a break in disease transmission in foci with zero prevalence.

Summary of WHO/APOC [40] supported

Table 3: WHO/APOC epidemiological survey to assess progress towards elimination of onchocerciasis [39]

S/N	COUNTRY	NUMBER OF FOCI SURVEYED	
		2009	2010
1.	Nigeria	5	3
2.	Cameroon	-	2
3.	Chad	2	-
4.	Democratic Republic of Congo	-	1
5	Tanzania	1	1
6.	Uganda	1	2
	TOTAL	9	9

epidemiological results in Nigeria.

In Nigeria, multi-site studies on the feasibility of onchocerciasis elimination with ivermectin treatment (sponsored by WHO/APOC) were carried out (2008-2012) in some endemic foci of Zamfara, Ebonyi, Kaduna, Taraba, Cross River, Edo and Delta States.

The following were the summary of the epidemiological results from communities of the five States of Zamfara, Ebonyi, Kaduna, Taraba, Cross River and Edo/Delta focus

Acknowledgements

(a) Zamfara State

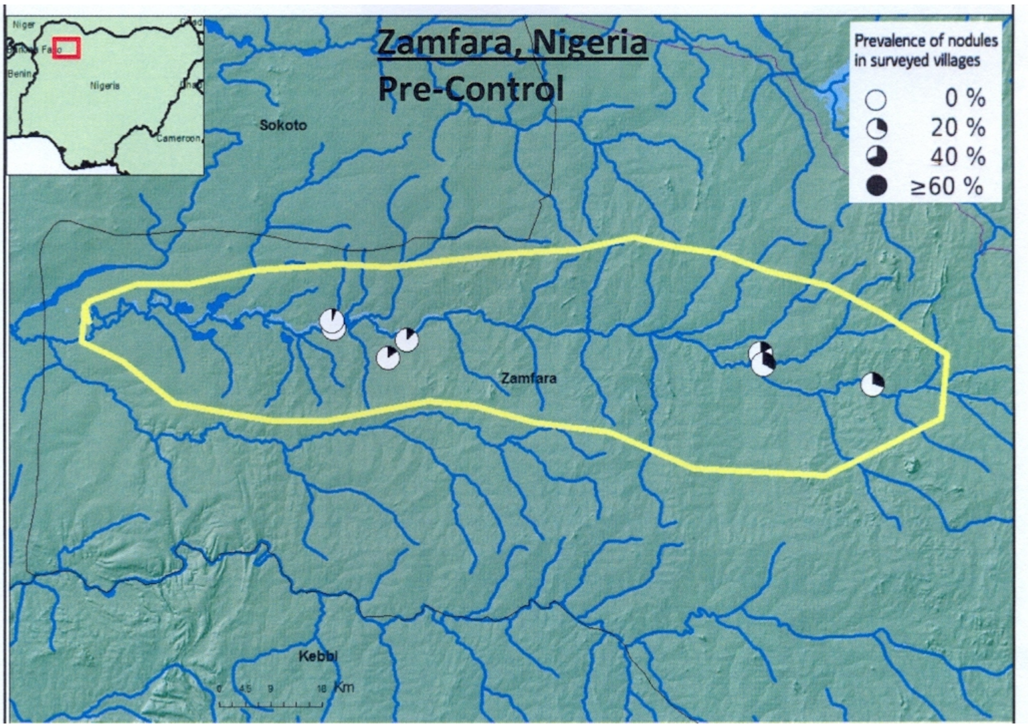

Fig. 7: prevalence of onchocerciasis infection in focus Zamfara, Nigeria [39]

Table 4: Predicted and observed prevalence of mf in Zamfara focus, Nigeria [39]

S/N	COMMUNITY	PRE-CONTROL PREVALENCE OF NODULES(%)	PRE-VALENCE OF MF IN 2010	
			PREDICTED	OBSERVED
1.	Yarsabaya	10	0.0	0.0
2.	Wuya	20	0.0	0.0
3.	Bimin Wajje	7	0.0	0.0
4.	Gabiya	10	0.0	0.0
5.	Zuramai	9	0.0	0.0
6.	Masaman	8	0.0	0.0
7.	Yarsabaya 1	10	0.0	0.0

(b) Ebonyi State

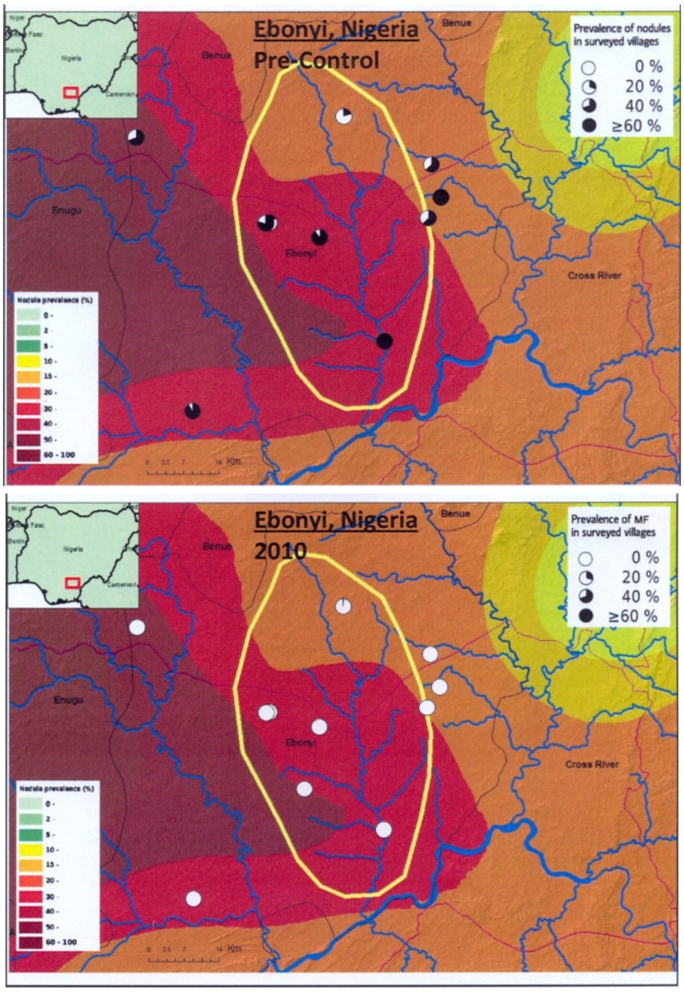

Fig. 8: Prevalence of onchocerciasis infection in Ebonyi focus, Nigeria [39]

Table 5: Prevalence and observed prevalence of mf at Ebonyi focus, Nigeria [39]

S/N	COMMUNITY	PRE-CONTROL PREVALENCE OF NODULES (%)	PREVALENCE OF MF IN 2010 (%)	
			PREDICTED	OBSERVED
1	Obegu Izzi	60	24.0	0.0
2	Opefia	38	10.0	0.0
3	Isie Gwudalegu	42	14.0	0.0
4	Ezekwe	10	0.0	0,0
5	Isiofia	48	16.0	0.0
6	Ugbodo Achara	62	26	0.0
7	Odeligbo	54	20	0.0
8	Achara	12	0.0	1.0
9	Amechi	56	22	0.0
10	Oferekpe	38	10.0	0.0

(C) Kaduna State

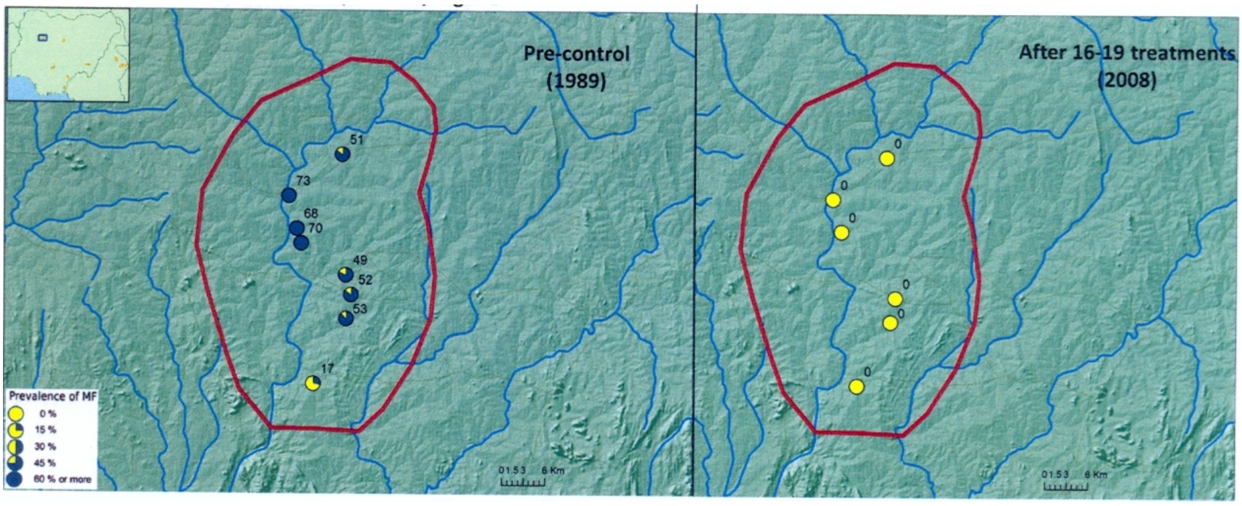

Fig. 9: Prevalence of onchocerciasis infection at Birnin Gwari focus, Kaduna Nigeria [39]

Table 6: Prevalence of mf at Birnin Gwari focus, Kaduna, Nigeria [39]

S/N	COMMUNITY	PRE-CONTROL		RESULT OF 2008/2009 EPIDEMIOLOGICAL SURVEY		
		% mf +ve	CMFL (mf/snip)	Number examined	% MF +ve	Predicted prevalence
1.	Ishiwai	73.0	8.9	115	0.0	0.0
2.	Kimbi	51.5	5.2	118	0.0	0.0
3.	Kurbau	52.9	4.9	91	0.0	0.0
4.	Randagi	17.2	0.5	81	0.0	0.0
5.	Ung. Bawa	67.5	4.8	51	0.0	0.0
	TOTAL			456	0.0	0.0

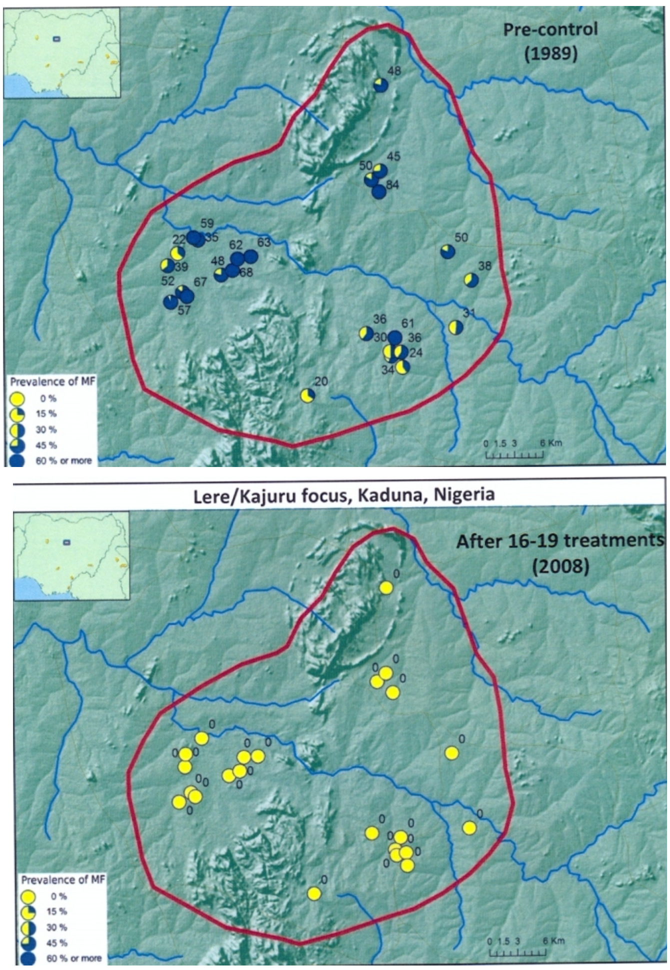

Fig. 10: Prevalence of onchocerciasis infection at Lere/Kajuru focus, Kaduna Nigeria [39]

Table 7: Prevalence of mf at Lere/Kauru focus, Kaduna Nigeria [39]

S/N	COMMUNITY	PRE-CONTROL PREVALENCE		RESULT OF 2008/2009 EPIDEMIOLOGICAL SURVEY		
		Mf +ve (%)	CMFL (mf/snip)	Number examined	Mf +ve (%)	Predicted prevalence
1,	Galadimawa	48.3	2.9	235	0.0	0.0
2.	Garamadi	52.3	4.4	155	0.0	0.0
3.	Garamadi Hayin	38.6	2.9	103	0.0	0.0
4.	Jankasi	63.3	3.9	118	0.0	0.0
5.	Kaguta	67.4	8.9	82	0.0	0.0
6.	Kuba Bauchi	59.1	2.3	196	0.0	0.0
7.	Madam	68.4	8.0	117	0.0	0.0
8.	Sabon Layi	61.6	3.8	117	0.0	0.0
9.	Sayama	21.9	1.1	127	0.0	0.0
10.	Dan Alhaji	30.9	2.2	69	0.0	0.0
11.	Kakidare	20.2	0.9	182	0.0	0.0
12.	Kudaru	48.1	4.6	224	0.0	0.0
13.	Kuduru	36.4	1.2	90	0.0	0.0
14.	Shaman	49.5	5.4	162	0.0	0.0
15.	Ung Tanimu	60.6	6.0	77	0.0	0.0
16.	Buzu	84.2	4.9	140	0.0	0.0
17.	Kurama	34.5	3.6	141	0.0	0.0
18.	Pahausawa	29.7	1.8	181	0.0	0.0
19.	Taimako	24.1	1.2	375	0.0	0.0
20.	Were I	50.1	3.7	67	0.0	0.0
21.	Were II	44.7	1.6	167	0.0	0.0
22.	Zarangi	35.8	2.4	260	0.0	0.0
	TOTAL			3,385	0.0	0.0

(d) Taraba State

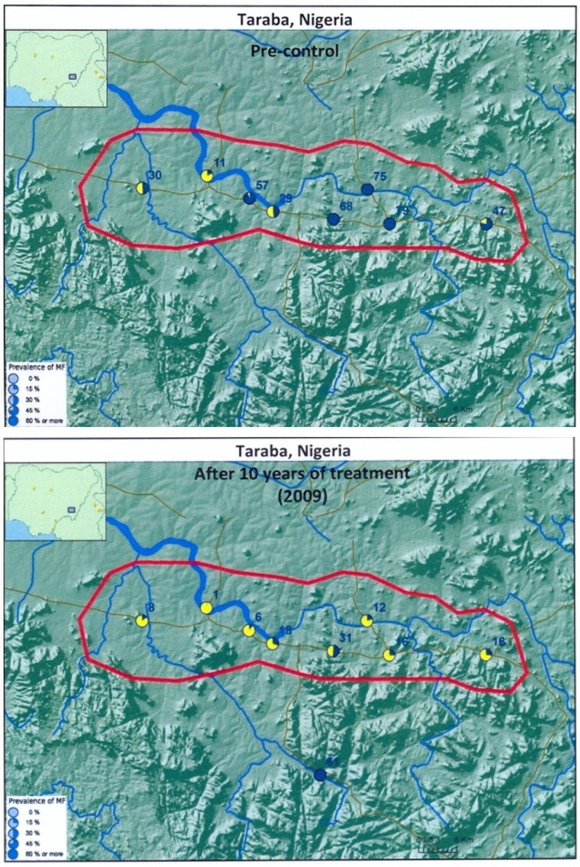

Fig 11: Prevalence of onchocerciasis infection at Taraba focus, Taraba Nigeria [39]

Table 8: Prevalence of mf at Taraba focus, Nigeria [39]

S/N	COMMUNITY	PRE-CONTROL PREVALENCE		RESULT OF 2008/2009 EPIDEMIOLOGICAL SURVEY		
		Mf +ve (%)	CMFL (mf/snip)	Number examined	Mf +ve (%)	Predicted prevalence
1.	Jamtari	47.3	25.7	119	16.0	20.0
2.	Gayam	79.2	60.3	167	15.6	36.0
3.	Gazabu	29.5	9.4	201	8.5	8.5
4.	Garbabi	56.8	43.5	181	6.1	29.0
5.	Kabarin Bature	28.7	13.2	247	18.2	10.0
6.	Bali	10.6	2.6	192	1.0	2.5
7.	Gangum	75.4	105.2	187	12.8	55.0
8.	Kunfan	Na	Na	62	30.6	Na

(e) Cross River State

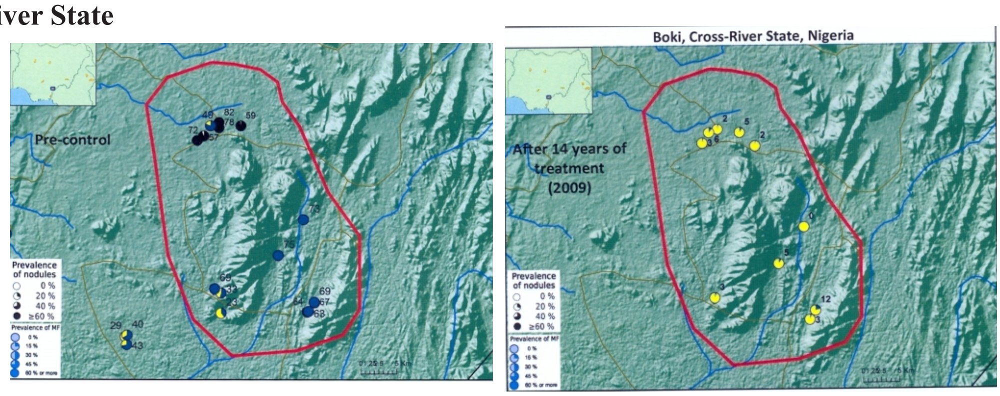

Fig 12: Prevalence of onchocerciasis infection at Boki focus, Cross River, Nigeria [39]

Table 9: Prevalence of mf at Boki focus, Cross Rivers Nigeria [39]

S/N	COMMUNITY	PRE-CONTROL PREVALENCE		RESULT OF 2008/2009 EPIDEMIOLOGICAL SURVEY		
		Mf +ve (%)	CMFL (mf/snip)	Number examined	Mf +ve (%)	Predicted prevalence
1.	BUANCHOR	75.2	14.6	143	4.9	2.7
2.	EBRANTA	69.4	13.5	183	3.3	72.3
3.	KABIESU	48.9	4.9	101	5.9	0.3
4.	KANYANG 1	63.3	6.8	103	2.9	0.7
5.	KANYANG 2	69.1	10.6	123	12.2	1.2
6.	OLUM	72.9	13.5	153	0,0	2.0
7.	BANKPOR	NA	NA	128	2.3	NA
8.	BEKPOR	NA	NA	132	5.3	NA
9.	KATCHUAN	NA	NA	161	2.6	NA
10.	OKUBUCHI	NA	NA	180	1.7	NA

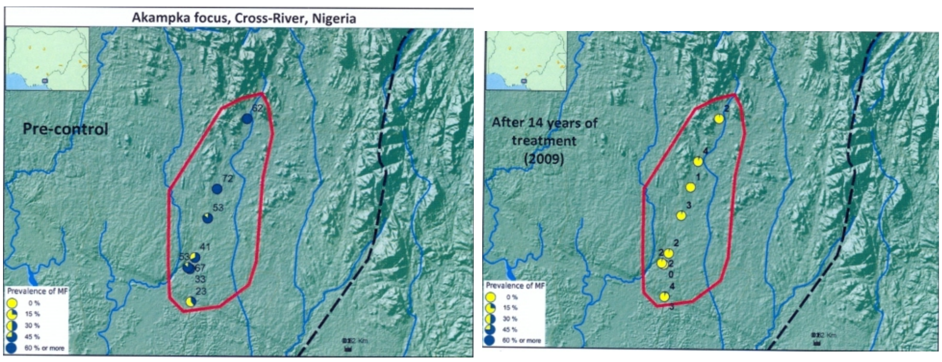

Fig 13: Prevalence of onchocerciasis infection at Akamkpa focus, Cross River, Nigeria [39]

Table 10: Prevalence of mf at Akamkpa focus, Cross River State, Nigeria [39]

S/N	COMMUNITY	PRE-CONTROL PREVALENCE		RESULT OF 2008/2009 EPIDEMIOLOGICAL SURVEY		
		MF +VE (%)	CMFL (mf/snip)	Number examined	Mf +ve (%)	Predicted prevalence
1.	ANINGEJE	33.2	NA	154	0.0	0.2
2.	EKONG	71.7	NA	141	0.7	6.8
3.	KWAFALLS	67.2	NA	98	2.0	5.5
4.	MFAMOSING 1	23.2	NA	78	3.9	0.0
5.	MFAMOSING 2	23.2	NA	127	3.1	0.0
6.	NJIKOKA	41.3	NA	103	1.9	0.4
7.	NTUISE	53.0	NA	127	2.4	1.3
8.	MANGOR	NA	NA	101	2.0	NA
9.	OBAN	NA	NA	161	3.7	NA

(f) Edo/Delta focus

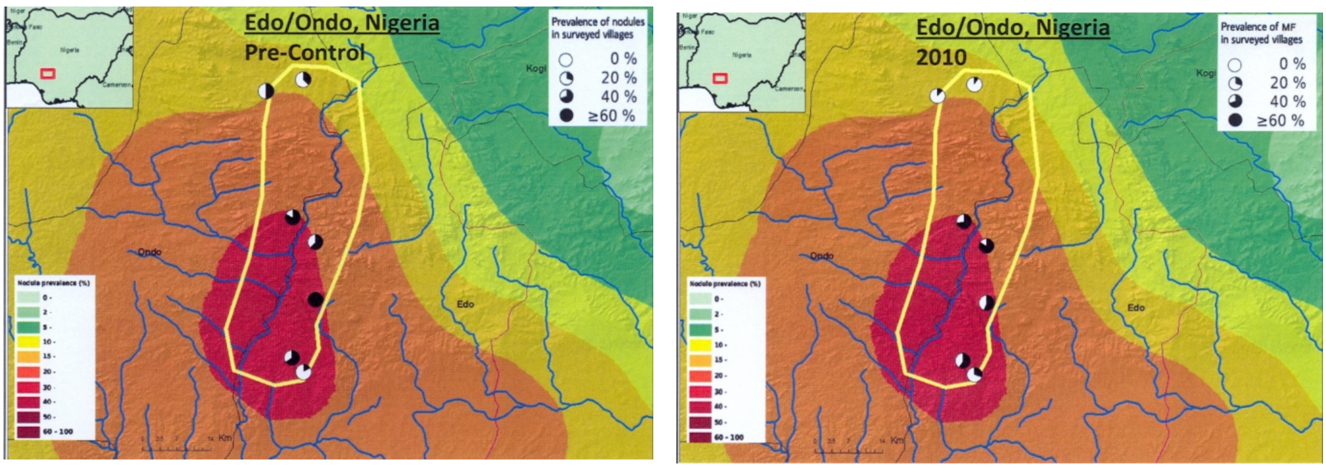

Fig. 14: Prevalence of onchocerciasis infection at Edo/Delta focus, Nigeria [39]

Table 11: Prevalence of onchocerciasis infection at Edo/Delta focus, Nigeria [39]

S/N	COMMUNITY	PRE - CONTROL PREVALENCE OF NODULES (%)	PREVALENCE OF MF IN 2010	
			PREDICTED	OBSERVED
1.	Auga	22	1	5
2.	1boropa	30	3	8
3.	Idogon	50	29	44
4.	Ijaja	37	11	51
5.	Ikhin	60	33	34
6.	Iloje	40	15	35
7.	Ivbiughuru	11	0	19

As observed in Mali and Senegal, epidemiological studies from these endemic areas in Nigeria also showed that large-scale treatment with ivermectin stopped further infections, especially in areas where there was a high percentage of treatment coverage. However, results from Edo/Ondo sites where ivermectin coverage was less than 65% showed that onchocerciasis elimination with ivermectin treatment was unsatisfactory. Since after these initial studies, other epidemiological surveys were conducted in other foci in the country. Again, entomological and epidemiological surveys have been conducted by NOCP in collaboration with APOC staff at those foci where MDA has been carried out for more than 14 years. The entomological results of 18,486 *Simulium* flies collected during 2011/2012 survey processed at the WHO/APOC molecular laboratory at Ouagadougou, Burkina Faso were satisfactory. None of the flies was positive for *Onchocerca volvulus*. L3 parasite samples from standard catches and dissection from Kaduna were non-volvulus [39]. This is consistent and similar to Mali and Senegal results. This is the end of this era in the control of onchocerciasis in Nigeria.

Table 12: Summary of onchocerciasis elimination evaluation in Nigeria, 2008 – 2012 [39]

S/N	TRANSMISSION FOCUS	PRE-CDTI ENDEMICITY	YEAR OF TX	NO OF COMMUNITY SAMPLED	NO PERSON EXAMINED	NO INFECTED (%) AND RANGE OF INFECTION	PROGRESS IN ONCHO ELIMINATION
1.	Zamfara	Low	13	7	1,065	0 (0.0) 0	Satisfactory. Elimination is probably achieved
2.	Ebonyi	High	13	5	3,239	5 (0.2) 0-1	Satisfactory. Elimination is probably achieved
3.	Birim Gwari, Kaduna	Medium	17	5	456	0 (0.0) 0	Satisfactory. Elimination is probably achieved
4.	Lere/Kajuru, Kaduna	Medium	17	22	3,385	0 (0.0) 0	Satisfactory. Elimination is probably achieved
5.	Taraba	Very high	10	8	1,696	214 (12.7) 1 – 30.6	Satisfactory. Still, some way to go, but on track
6.	Boki, C/River	Medium to	14	10	1,601	81 (3.0)	Satisfactory.
7.	Akamkpa, C/River	high	14	9	1,118	0 – 12.0	Close to elimination
8.	Edo/Delta	Medium to high	13	7	1,660	424 (28.0) 5 – 51	Not satisfactory. Far behind expectation (prediction)

It is worthy to acknowledge and appreciate the then Honourable Minister for Health, Federal Ministry of Health and Social Services, Prof. Olukoye Ransome-Kuti for establishing the National Onchocerciasis Control Programme (NOCP) in 1982. He also initiated the first-ever extensive and intensive nationwide prevalence survey of onchocerciasis using the skin-snip method. It is important to note that it was the result of this survey that gave the United Nation Agencies and the international community the pattern and seriousness of the disease in the country, hence their interest in the control programme.

We want to appreciate Merck, Sharp and Dohme (MSD) (today called Merck) for their decision on October 21, 1987, to supply Mectizan® free for the mass treatment of onchocerciasis to anyone who needed it, for as long as necessary. This was a remarkable breakthrough, which revolutionized the fight against river blindness in Nigeria.

We acknowledge and appreciate the pioneering commitment of Africare and Sight Savers International (then through the National Eye Centre led by Prof. Adenike Abiose who started the partnership with NOCP Nigeria to commence the pilot project of mass ivermectin distribution in endemic communities of Kwara (now in Kogi) and Kaduna States in 1988/89 respectively. With the support of UNICEF/Nigeria, the Ivermectin Distribution Programme (IDP) commenced in February 1991 in Benue, Oyo, and Bauchi States.

Ivermectin Distribution Programme (IDP) progressively spread to other endemic parts of the country with the support and partnership of the NGDO Coalition, which started in 1992. The impressive partnership with the River Blindness Foundation, Lions Clubs International, German Technical Co-operation Agency (GTZ), International Foundation for and Self Help (IFESH), Christofel Blinden Mission (CBM), International Eye Foundation (IEF), MITOSATH and Helen Keller International is highly recognized and appreciated.

We thank TDR/WHO Operational Research for supporting Rapid Epidemiological Assessment (REA) and UNICEF Nigeria for sponsoring the first-ever Rapid Epidemiological Mapping of Onchocerciasis in Nigeria, which was later refined by the African Programme for Onchocerciasis Control (APOC).

The history of this era in the control of onchocerciasis in Nigeria cannot be complete without appreciating the outstanding support and successful contribution of the African Programme for Onchocerciasis Control (APOC). The launching of the African Programme for Onchocerciasis Control (APOC) in 1995 and the introduction of community-directed treatment with ivermectin (CDTI) by APOC revolutionized onchocerciasis control in Nigeria. The epidemiological and entomological evaluations driven by APOC in partnership with NOCP and NGDO coalition in Nigeria were what provided the evidence that long-term sustained mass ivermectin distribution in endemic had the potential to interrupt transmission and or eliminate onchocerciasis. For all these and more we will ever remain grateful to APOC.

Ethical Considerations
Not Applicable

Conflict of Interest
None

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None

Authors' Contributions
NBEB conceptualized the manuscript and wrote the initial draft. ANM, CC, EUF, IAE, MMA, MHB, ME, ME, OKN and FR reviewed the draft and made contributions. All the authors approved the final draft of the manuscript.

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