THE
CARTER CENTER

Waging Peace. Fighting Disease. Building Hope.

SUMMARY
2019 VIRTUAL PROGRAM REVIEW
RIVER BLINDNESS ELIMINATION PROGRAMS
ETHIOPIA, NIGERIA, OEPA, SUDAN, AND UGANDA
MARCH 19-30, 2020
THE CARTER CENTER
ATLANTA, GA

SEPTEMBER 2020

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And to many others, our sincere gratitude.

**The Reaching the Last Mile Fund, housed within The END Fund, is a multi-donor fund, initiated and led by His Highness Sheikh Mohamed bin Zayed Al Nahyan, the Crown Prince of Abu Dhabi*

TABLE OF CONTENTS

ACRONYMS

APOC	African Program for Onchocerciasis Control
ARV	At-Risk Village
ATP	Annual Transmission Potential
CAICET	NE Venezuela and the South Focus
CAR	Central African Republic
CDD	Community Directed Distributors
CDTI	Community Directed Treatment with Ivermectin
COVID-19	2019 novel coronavirus disease
CS	Community Supervisor
DBS	Dried Blood Spots
DEC	Diethylcarbamazine
DRC	Democratic Republic of Congo
EOEEAC	Ethiopia Onchocerciasis Elimination Expert Advisory Committee
ELISA	Enzyme-linked immunosorbent assay
ESPEN	Expanded Special Project for Elimination Neglected Tropical Diseases
FLHF	Frontline Health Facility
FMOH	Federal Ministry of Health
FTS	Filarial Test Strip
HDA	Health Development Army
HEW	Health Extension Worker
IACO	InterAmerican Conference on Onchocerciasis
IHA	Indigenous Health Agent
IRB	Institutional Review Board
KAP	Knowledge Attitude & Practices
LF	Lymphatic Filariasis
LGA	Local Government Areas
LLIN	Long-lasting Insecticidal (Bed) Nets
MDA	Mass Drug Administration
MDP	Mectizan Donation Program
Mectizan®	Ivermectin (Merck & Co., Inc., product name)
MITOSATH	Mission to Save the Helpless
MMDP	Morbidity Management and Disability Prevention
MMN	Madi-Mid North
MOH	Ministry/Ministries of Health
MSD	Merck & Co., Inc., Kenilworth, N.J. USA
NGDO	Non-Governmental Development Organization
NOEC	National Onchocerciasis Elimination Committee
NTD	Neglected Tropical Disease
OEPA	Onchocerciasis Elimination Program for the Americas

ACRONYMS

OTS	Onchocerciasis Technical Subgroup/Subcommittee
PAHO	Pan American Health Organization
PCC	Program Coordinating Committee of OEPA
PCR	Polymerase Chain Reaction
PTS	Post-Treatment Surveillance
QGIS	Geographical Information System
RB	River Blindness
RBEP	River Blindness Elimination Program
REMO	Rapid Epidemiological Mapping of Onchocerciasis
RPRG	Regional Program Review Group
RSS	Republic of South Sudan
RTI	Research Triangle Institute
S&C	Slash and Clear
SCH	Schistosomiasis
SE/SS	South East/South South
SIZ	Special Intervention Zone
SNNPR	Southern Nations, Nationalities and People's Region
STH	Soil-Transmitted Helminths
TAS	Treatment Assessment Survey
TCC	The Carter Center
UOEEAC	Ugandan Onchocerciasis Elimination Expert Advisory Committee
USAID	United States Agency for International Development
USF	University of South Florida
UTG	Ultimate Treatment Goal
WER	Weekly Epidemiological Record
WHO	World Health Organization
YFA	Yanomami Focus Area

EXECUTIVE SUMMARY

The 24th Annual Review Meeting of the Carter Center (TCC) River Blindness Elimination Program (RBEP), scheduled for March 11-13, 2020, in Atlanta, was canceled in the wake of the emerging 2019 novel coronavirus disease (COVID-19). The RBEP Atlanta staff held abbreviated virtual reviews between March 19 - 30, 2020, with each RBEP-assisted country's staff and, in some countries, Ministry of Health (MOH) officials, focusing on the 2019 achievements, challenges, operational research, and recommendations for 2020 activities.

The goal of the RBEP is to assist MOH in six countries[1] to eliminate river blindness (RB) transmission. The strategy for elimination in RBEP programs is mass drug administration (MDA) with ivermectin (Mectizan®, donated by Merck & Co., Inc., Kenilworth, N.J. USA), given twice-per-year, and in some cases, four-times-per-year. This strategy has been highly successful in the Americas, resulting in World Health Organization (WHO)-verified national elimination of onchocerciasis from Colombia (in 2013), Ecuador (2014), Mexico (2015), and Guatemala (2016). The Abu Hamad Focus in Sudan was the first focus in Africa to eliminate onchocerciasis disease and its transmission in accordance with WHO guidelines, and since then, seven foci in Uganda have followed. The approach to RB elimination is defined by WHO guidelines, which provide three milestones (shown by the vertical lines in Figure ES1): 1) transmission suppressed; 2) transmission interrupted and MDA halted; and 3) transmission eliminated after three to five years of post-treatment surveillance (PTS).

As a result of our RB elimination partnership, 6.9 million people no longer need Mectizan® treatment in Carter Center-assisted areas in ten countries (Figures ES2 and ES3).

In 2019, The Carter Center assisted in a total of 41,608,910 mass ivermectin treatments for RB (onchocerciasis) in the Americas, Ethiopia, Nigeria, Sudan, and Uganda, reaching 77% of the 2019 treatment target (Figures ES4). The first round of twice-per-year RB treatment in Nigeria was not administered due to drug shipment delays. A goal of 68 million treatments has been set for 2020 (Figure ES5); however, it is unclear when MDA will occur due to the uncertainty surrounding COVID-19.

RBEP's cumulative treatments since 1996 have now reached 425 million (Figure ES6). Figures ES7 and ES8 show our assisted treatments and annual coverage geographically. RBEP aims to exceed 90% reported treatment coverage of the eligible population (which excludes children under five years of age) in each treatment round, except in the Americas, where the goal is at least 85% coverage.

RBEP is an integrated program that includes lymphatic filariasis (LF), schistosomiasis (SCH) and soil-transmitted helminthiasis (STH). In 2019, 18,914,001 ivermectin and albendazole (donated by GSK) treatments for LF (85% of the 2019 treatment target) were provided in Ethiopia and Nigeria, while 2,390,729 praziquantel (donated by Merck KGaA, Germany) treatments for SCH (46% of the treatment target) and 5,808,340 mebendazole (donated by Johnson & Johnson) or albendazole (GSK) treatments for STH (61% of the treatment target) were provided in Nigeria. These low coverages were due to delay in supply of praziquantel and mebendazole. RB treatments represented 50% of the 83 million MDA treatments for neglected tropical diseases (RB, LF, SCH, STH and trachoma) assisted by The Carter Center in 2019 (Figure ES9).

[1] Brazil, Ethiopia, Nigeria, Sudan, Uganda, and Venezuela.

Our work would not be possible without a grassroots network of community-directed drug distributors (CDDs) who provide the treatments along with health education. A combined 358,186 CDDs were trained in 2019, all of whom were trained and mentored by MOH personnel working in affected districts assisted by TCC (Figure ES10).

The 2019 Review highlighted challenges in some cross-border transmission areas that we have termed ‘Special Intervention Zones’ (SIZs). Transmission must be simultaneously tackled on both sides of the SIZ if the elimination initiative is to be successful. One side cannot be left behind, and engaging both sides involves not only technical activities but political and diplomatic engagement as well. SIZ issues are relevant both in the Americas (Yanomami area) and in Africa, which include the Ebola outbreak in the Democratic Republic of Congo (DRC) related to Lhubiriha focus in Kasese District in Uganda, and security concerns in Kajo Keji area in the Republic of South Sudan (RSS) bordering Madi-Mid North (MMN) focus of Uganda. Also, security concerns were the main challenges in Radom focus in South Darfur state of Sudan as well as Khor Yabus focus shared by Ethiopia, Sudan and RSS (Figure ES11).

2020 GENERAL RECOMMENDATIONS FOR CARTER CENTER RIVER BLINDNESS ELIMINATION PROGRAMS

In collaboration with the host governments, RBEP helps to interrupt onchocerciasis transmission in Carter Center-assisted RBEP areas in Africa and the Americas. TCC/RBEP work includes:

- Helping to empower national onchocerciasis elimination committees to review their data and inform national decisions that demonstrate progress toward elimination, such as: enhancing interventions, expanding treatment, stopping interventions, and conducting PTS. Decisions should be guided by (but not restricted to) WHO guidelines.

- Conducting new assessments to help delimit the precise borders of African onchocerciasis transmission zones ('foci') (and buffer zones between transmission zones) that can assist our elimination agenda in TCC/RBEP-assisted areas.

- Defining areas of active onchocerciasis transmission, including within the so-called 'hypoendemic' onchocerciasis areas that have traditionally not been targeted for ivermectin treatment under previous WHO/African Program for Onchocerciasis Control (APOC) disease control policy.

- Enhancing interventions (two- or four-times-per-year ivermectin treatment, vector control, etc.) where transmission persists or in new foci where treatments have never been given.

- Where active onchocerciasis transmission spans borders, working with authorities on both sides of internal or international boundaries to establish 'SIZs and encouraging the needed collaboration on both sides to stop transmission.

- Monitoring the impact of interventions using sensitive and specific tools. Consider integrated monitoring especially in RB/LF overlap areas when stop MDA decisions are being considered.

COVID-19 PANDEMIC. As a result of the pandemic, the 24th TCC/RBEP Program review scheduled for March 11-13, 2020 was canceled. At the time of the abbreviated virtual meetings (late March 2020), TCC noted the WHO recommendation to member states that they halt Neglected Tropical Disease (NTD) MDA activities (training, health education, and drug distribution) community-based surveys, and active case-finding activities. TCC also noted national decisions in the countries assisted by RBEP to limit all travel, meetings, and direct community engagement. That notwithstanding, the following 2020 recommendations are made to TCC/RBEP assisted programs, and the original treatment numbers and trainings proposed before COVID-19 constraints have been retained.

TCC/RBEP encourages improved collaboration and transparency among stakeholders to reduce drug supply delays and supply inaccuracies.

Programs should collect more information to explain when they have communities with low coverage indicated on the Likert scale coverage graphic.

The Carter Center international offices should conduct treatment coverage surveys, in consultation with HQ and MOH.

There should be special reports on MDA activities among refugees and internally displaced persons.

TCC/RBEP encourages Ministries of Health to submit drug applications to WHO and the Mectizan Donation Program (MDP) as early as possible; timely drugs are critical, particularly for twice-per-year treatment areas. Programs in Africa should actively pursue collaboration with Ministries of Health on application preparation, and target an April 30 submission, to receive drugs on time. Drug inventories submitted with applications can be interim but must be included. Assist the national programs with submissions. Keep TCC/RBEP Atlanta office informed on the process.

Seek to increase training, supervision, involvement of kinship groups, and gender balance among CDDs and community supervisors (CSs).

The Carter Center website should house key public domain documents from National Onchocerciasis Elimination Committees (NOECs) of Ethiopia, Nigeria, and Uganda. The Onchocerciasis Elimination Program for the Americas (OEPA) domain should house the InterAmerican Conference on Onchocerciasis (IACO) meeting conclusions and recommendations.

TCC/RBEP will maintain laboratories for OV16 serology, entomology, and parasitology (including O-150 Polymerase Chain Reaction [PCR] testing in vectors and skin snips), with technical support by Dr. Thomas Unnasch and his team at the University of South Florida (USF). In consultation with USF, international laboratories should send samples and/or data to USF for quality control purposes. Reagent and supply orders from these labs must be reviewed promptly by Dr. Unnasch or his staff so that TCC HQ can purchase and ship in a timely manner. For the time being, TCC will use as our principle OV16 test the 'OEPA' OV16 Enzyme-linked immunosorbent assay (ELISA). Review and consider, internally and with national onchocerciasis elimination committees, the frequent changes in recommendations being produced by the WHO Onchocerciasis Technical Subgroup (OTS), particularly as these relate to mapping of onchocerciasis in presumably hypoendemic areas. These recommendations at times are causing considerable confusion for the programs and implying resource expenditures that The Carter Center is unable to support at this time.

Through national mechanisms, TCC/RBEP offices should monitor government, Expanded Special Project for Elimination Neglected Tropical Diseases (ESPEN), and other partners' financial contributions for elimination efforts in RBEP-assisted areas.

Carter Center program staff must complete or renew their Emory Institutional Review Board (IRB) certification if they are to be involved with work that is considered research.

TCC/RBEP encourages the Ministries of Health to revise complex village rollup forms that must be completed by CDDs and health workers that require recording treatment data by gender and age groups. TCC/RBEP seeks technological solutions for improving accuracy and speed of village level and district level roll up data reporting.

In fulfillment of the second pillar of the Global Programme to Eliminate LF, ensure that CDDs collect and report LF morbidity data in LF-endemic areas. Begin reporting these data as part of annual program reports.

TCC's RB, LF, SCH and STH Programs propose to assist ministries of health to provide 109 million treatments for NTDs in 2020.

Based on the successful experience with virtual TCC Program Reviews in 2020 due to the COVID-19 outbreak, consider having virtual linkages in future TCC Program Reviews so that additional TCC international personnel might view some of the proceedings live or as recorded media.

2020 Treatment and Training Objectives:

UTG = Ultimate Treatment Goal
UTG2 = Twice-per-year Treatment Goal
UTG4 = Four-times-per-year Treatment Goal

2020 River Blindness			
Annual (UTG)	Semiannual (UTG2)	Quarterly (UTG4)	Total
6,779,049	61,983,231	62,160	**68,824,440**

2020 Lymphatic Filariasis	
Annual (UTG)	Total
23,456,885	**23,456,885**

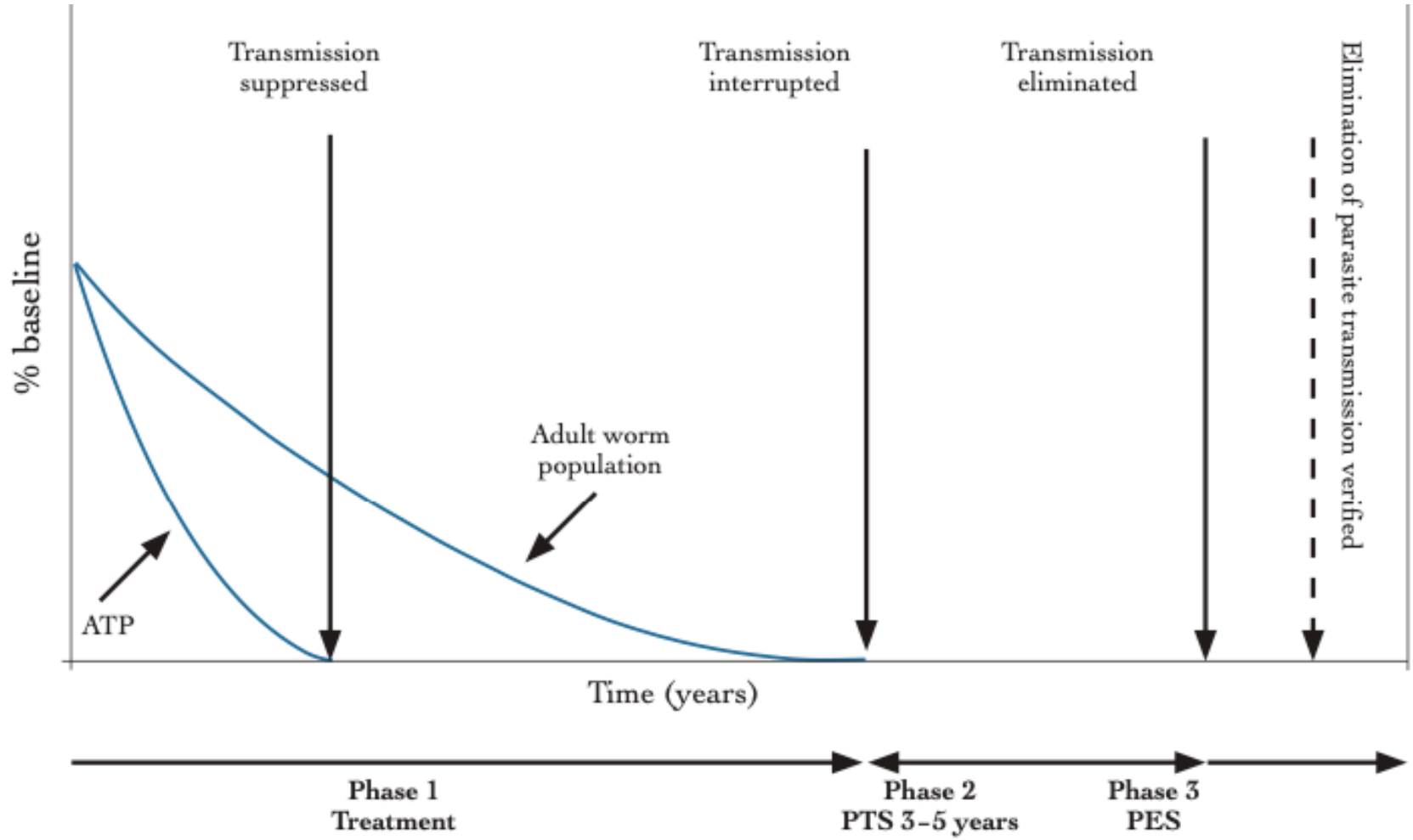
2020 Schistosomiasis	
Annual (UTG)	Total
5,583,186	**5,583,186**

2020 Soil-Transmitted Helminths		
Annual (UTG)	Semiannual (UTG2)	Total
7,276,782	3,832,977	**11,109,759**

2020 Training Objectives	
CDDs	368,416
CSs	109,877

Figure ES1

Phases of the Elimination of Onchocerciasis (2016 WHO Guidelines*)



ATP, annual transmission potential; PES, post-elimination surveillance; PTS, post-treatment surveillance

*WHO (2016). Guidelines for stopping mass drug administration and verifying elimination of human onchocerciasis: criteria and procedures (document WHO/HTM/NTD/PCT/2016.1). Geneva, World Health Organization. http://www.who.int/onchocerciasis/resources/9789241510011/en/

Figure ES2

Population Currently and Previously Targeted for Mectizan® Treatment

6.9 million people in ten Carter Center-assisted countries no longer need treatment as a result of our river blindness elimination partnership

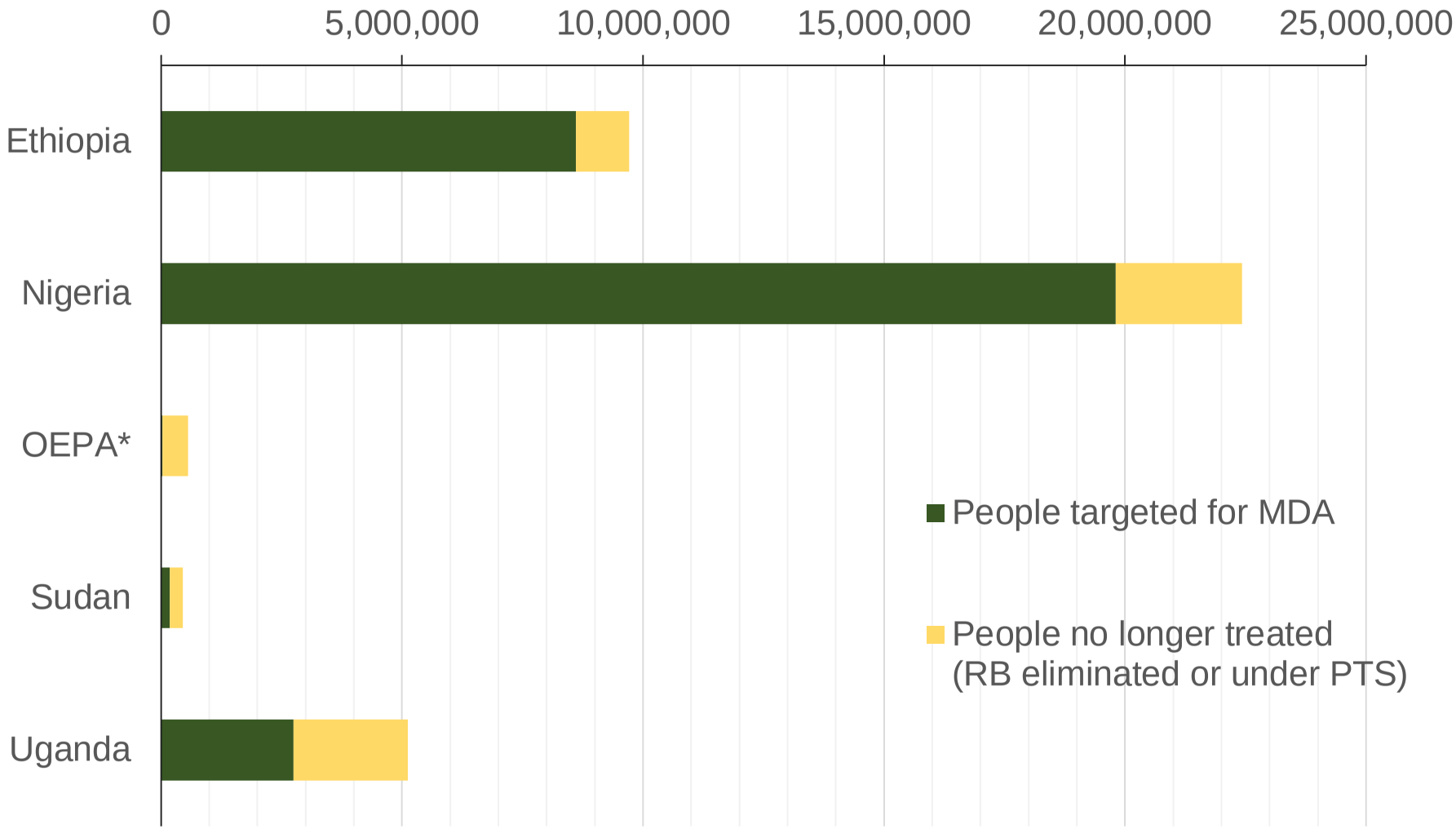


Figure ES3

Inventory of 'Stop MDA' for River Blindness (RB) and Lymphatic Filariasis (LF) in Carter Center-Assisted Programs

RIVER BLINDNESS		
Country	Total Population residing in areas where MDA stopped 2009-2019	Stopped MDA in 2019
ETHIOPIA	1,100,000	
OEPA[1]	538,517	
NIGERIA	2,618,861	
SUDAN	264,811	
UGANDA[2]	2,367,204	608,219
TOTAL	**6,889,393**	**608,219**

[1]Representing Brazil, Colombia, Ecuador, Guatemala, Mexico and Venezuela.
[2]Excludes the eliminated Victoria focus (not TCC-assisted, eliminated in the 1970s), population 2.8 million.

LYMPHATIC FILARIASIS		
Country	Populations NOT on MDA in 2019 (both eliminated and in PTS)	Stopped MDA in 2019
ETHIOPIA	552, 376	138,881
NIGERIA	7,258,307	
TOTAL	**7,810,683**	**138,881**

Figure ES4

2019 Mectizan® Mass Treatment Figures for TCC-assisted Areas and %UTG in Africa and Latin America (OEPA)

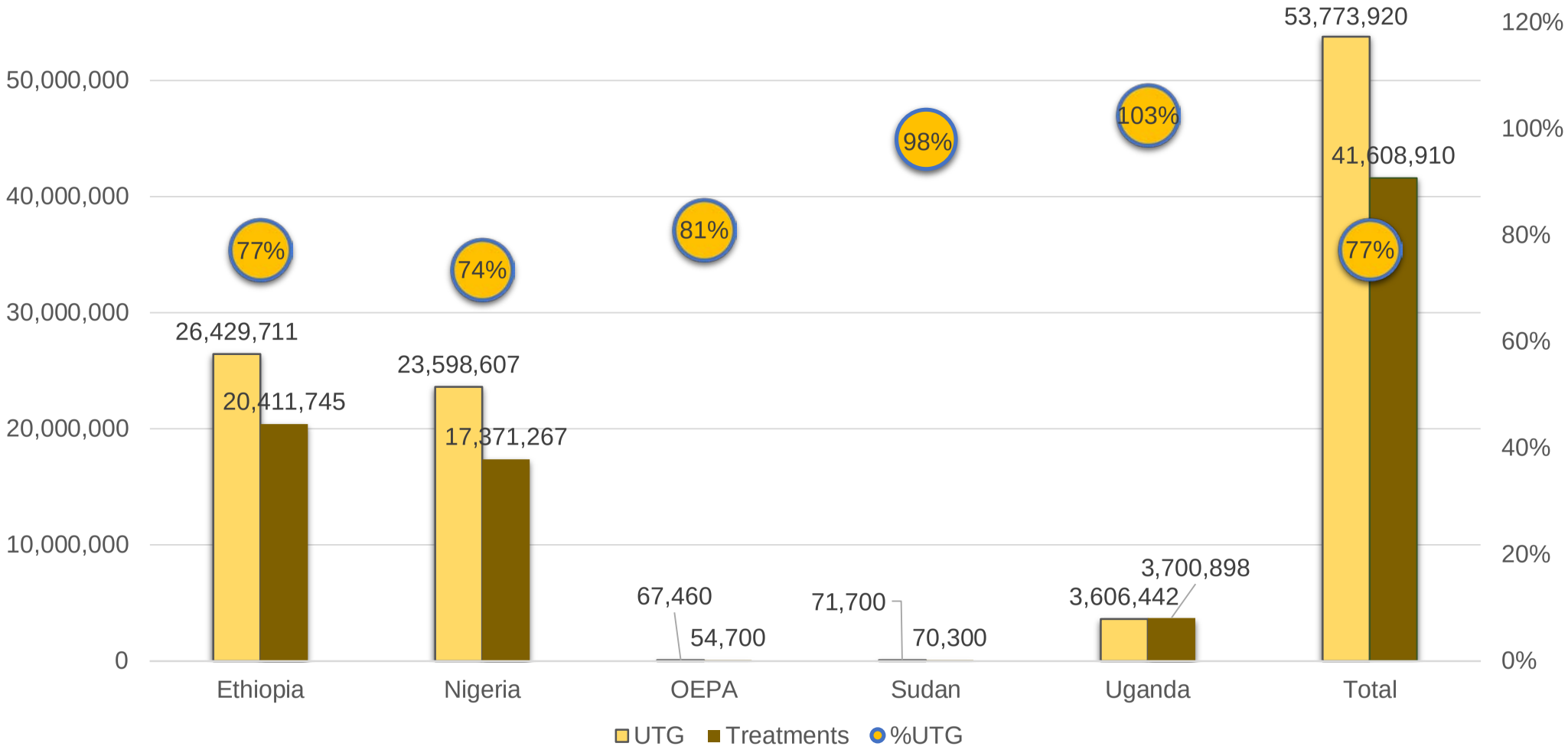
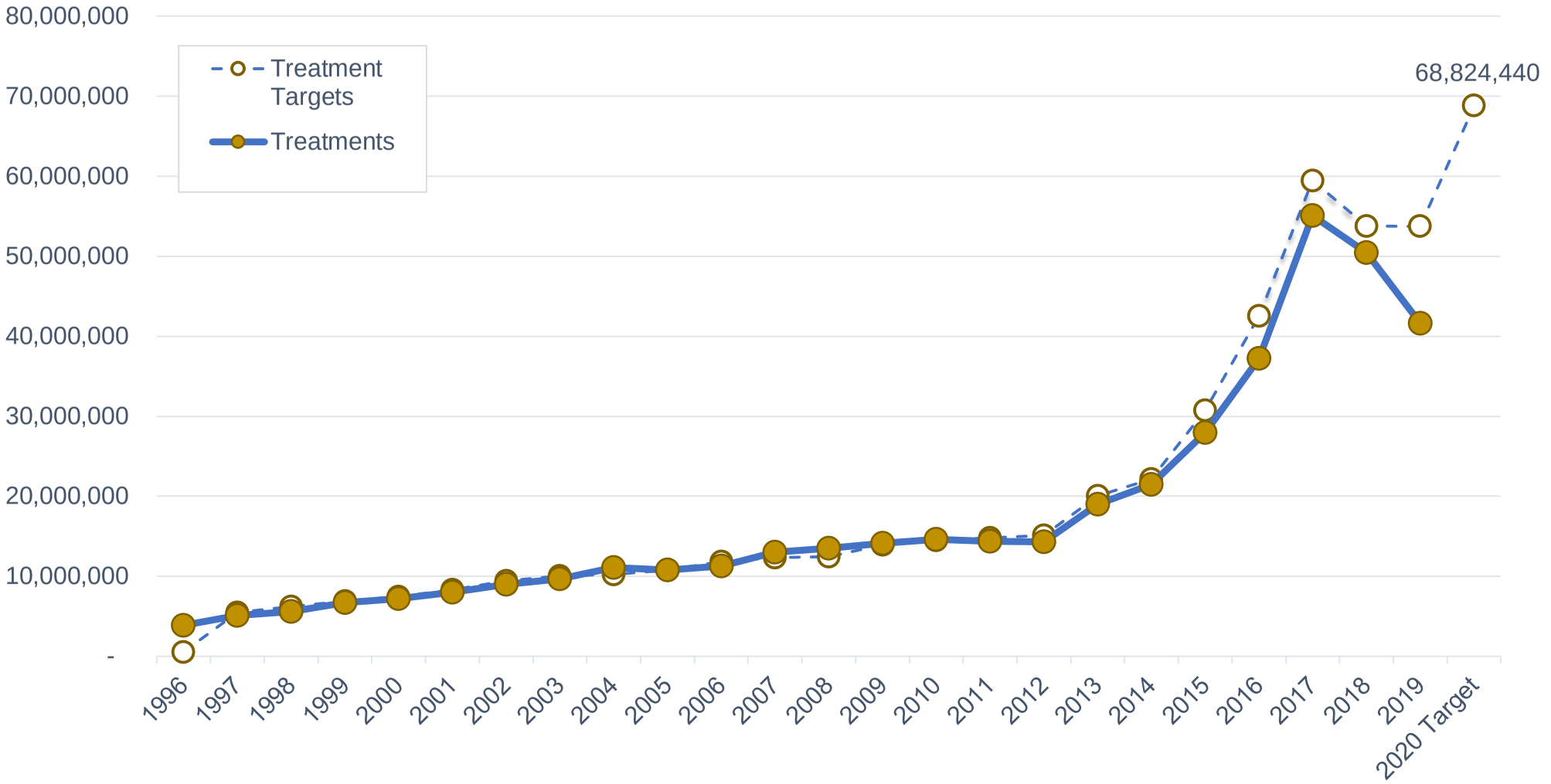
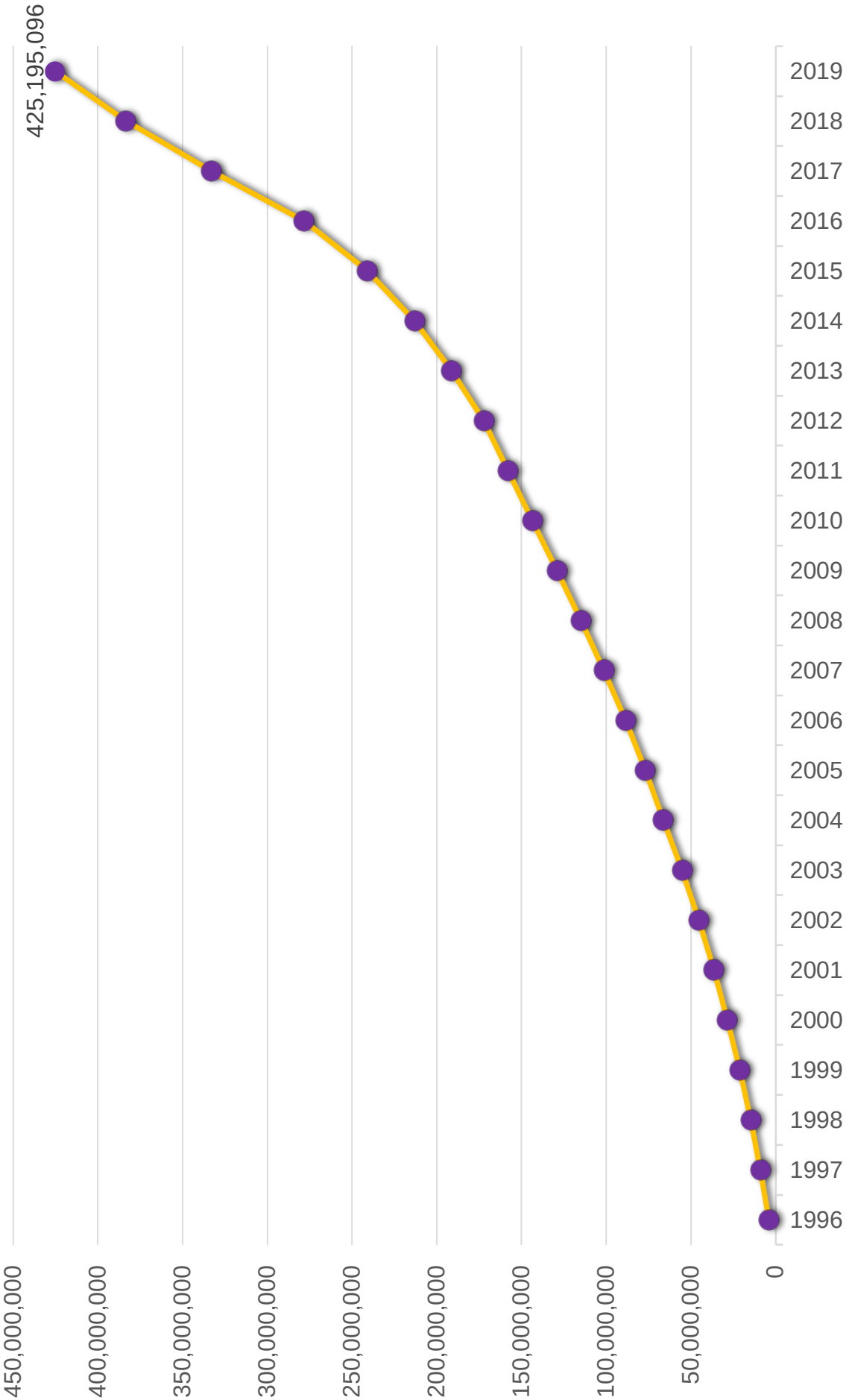


Figure ES5

RBEP-Assisted Programs: Mectizan® Treatments and Targets 1996 – 2020




425,195,096
2019
2018
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2001
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1997
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450,000,000
400,000,000
350,000,000
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250,000,000
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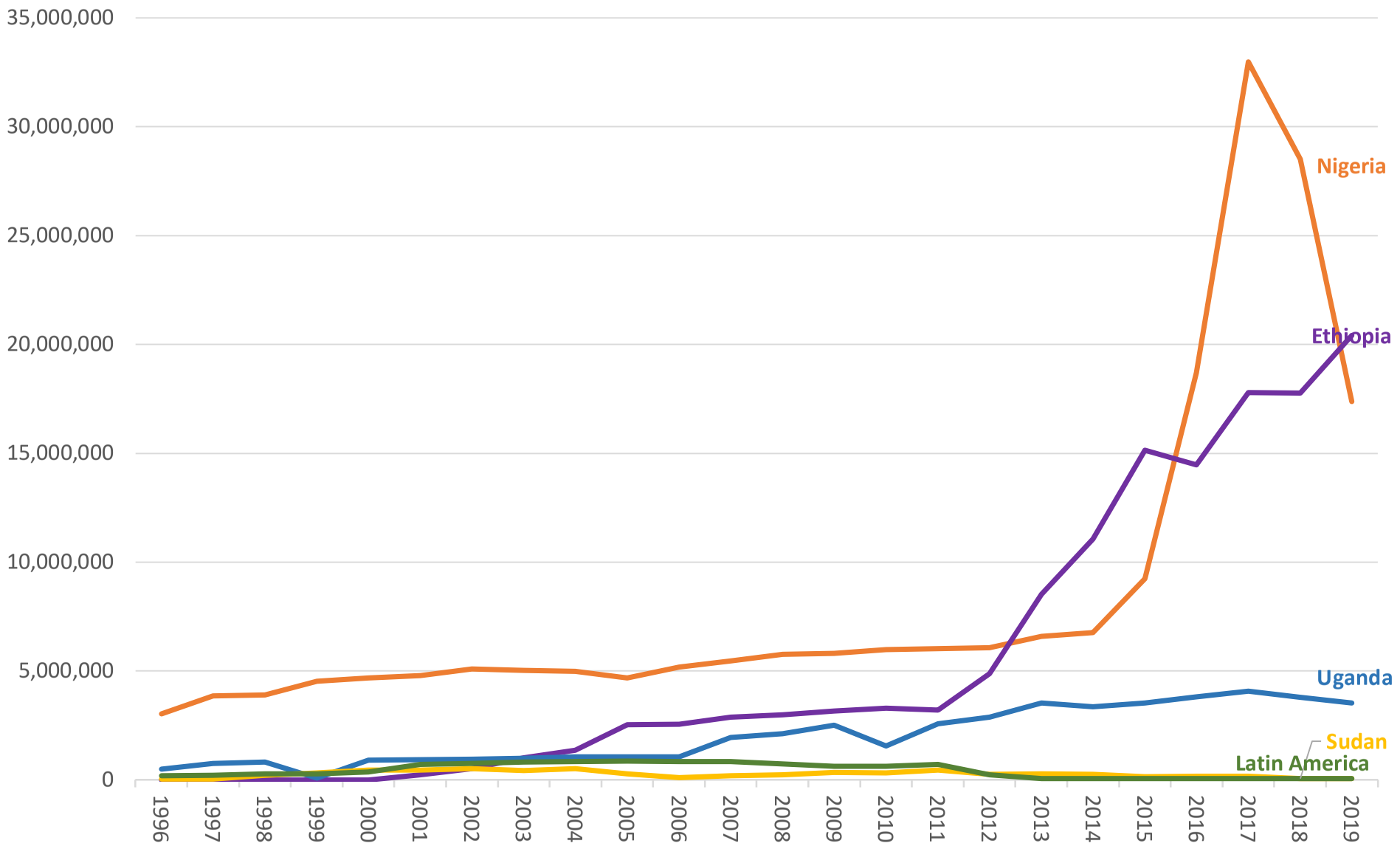
150,000,000
100,000,000
50,000,000
0

Figure ES6

Figure ES7


35,000,000
30,000,000
25,000,000
20,000,000
15,000,000
10,000,000
5,000,000
0
1996
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1999
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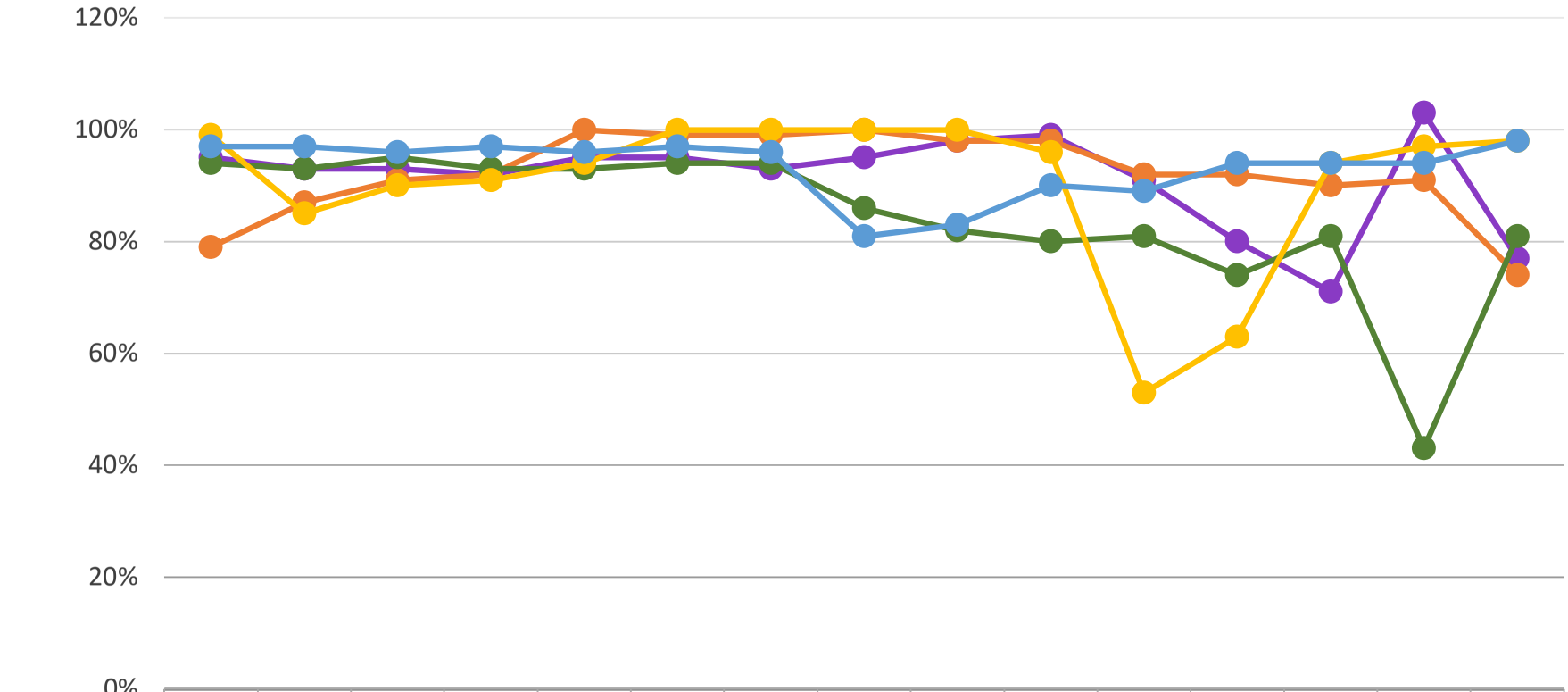
2011
2012
2013
2014
2015
2016
2017
2018
2019
Nigeria
Ethiopia
Uganda
Sudan
Latin America

Figure ES8

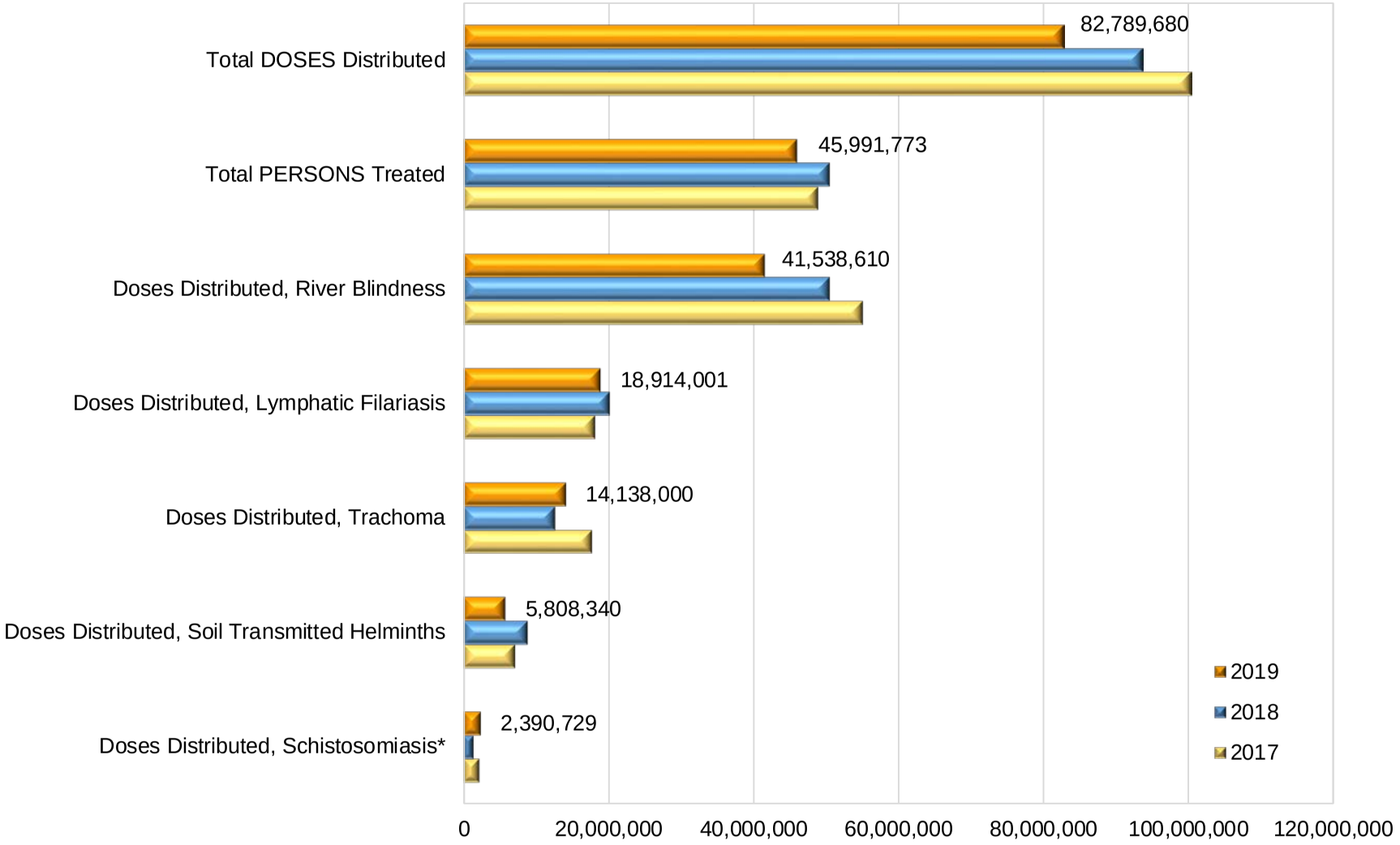
River Blindness Program: Reported Treatment Coverage (Eligible Population) by Project: UTG, UTG(2), or UTG(4) 2005 – 2019



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Ethiopia	95%	93%	93%	92%	95%	95%	93%	95%	98%	99%	91%	80%	71%	103%	77%
Nigeria	79%	87%	91%	92%	100%	99%	99%	100%	98%	98%	92%	92%	90%	91%	74%
OEPA	94%	93%	95%	93%	93%	94%	94%	86%	82%	80%	81%	74%	81%	43%	81%
Sudan	99%	85%	90%	91%	94%	100%	100%	100%	100%	96%	53%	63%	94%	97%	98%
Uganda	97%	97%	96%	97%	96%	97%	96%	81%	83%	90%	89%	94%	94%	94%	98%

Figure ES9

Carter Center-Supported Treatment Doses and Persons Treated for Neglected Tropical Diseases, 2017 – 2019



The Carter Center is grateful for our Ministry of Health partners and the many donors and pharmaceutical companies who have made financial and in-kind contributions to make these treatments possible.

** The decrease in treatment between 2018 and 2019 is attributable to a Mectizan delay in Ethiopia and Nigeria.*

Figure ES10

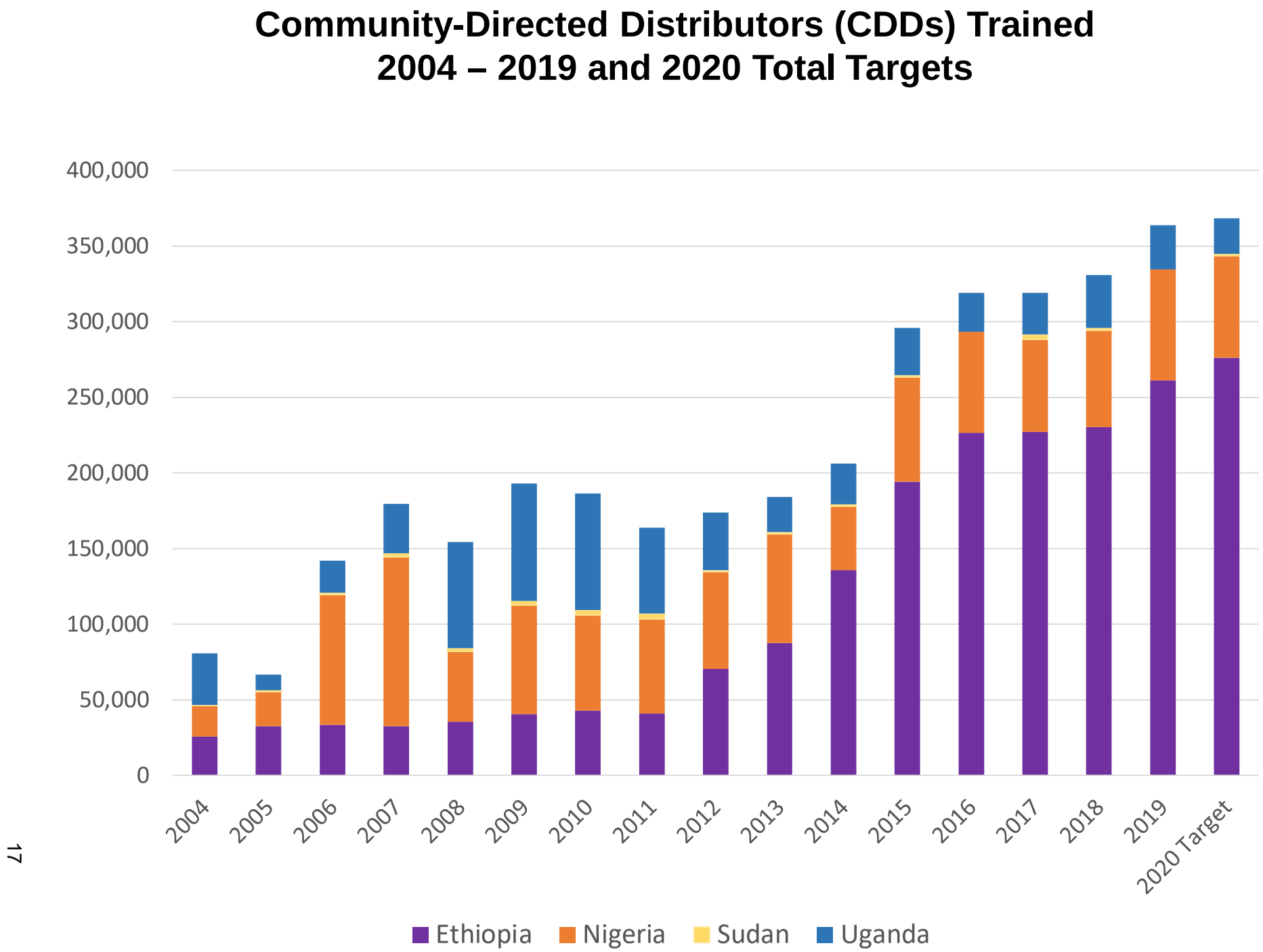
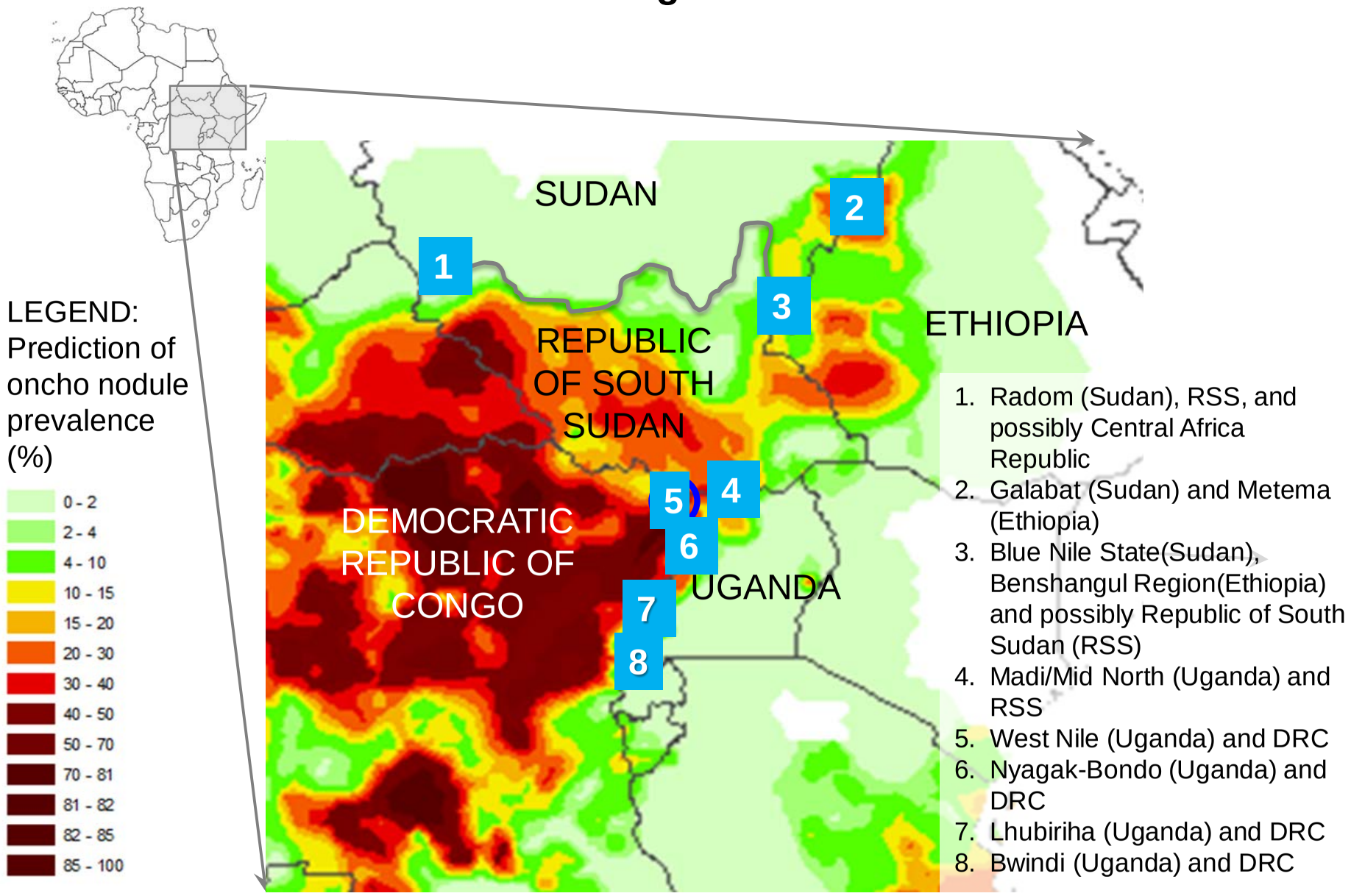

Community-Directed Distributors (CDDs) Trained
2004 – 2019 and 2020 Total Targets
400,000
350,000
300,000
250,000
200,000
150,000
100,000
50,000
0
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
2019
2020 Target
Ethiopia
Nigeria
Sudan
Uganda

Figure ES11

Carter Center Assisted Special Intervention Zones in Ethiopia, Sudan, and Uganda



Map source: APOC

Figure ES12

Geographic Distribution and Transmission Status of Onchocerciasis in the Americas in 2020

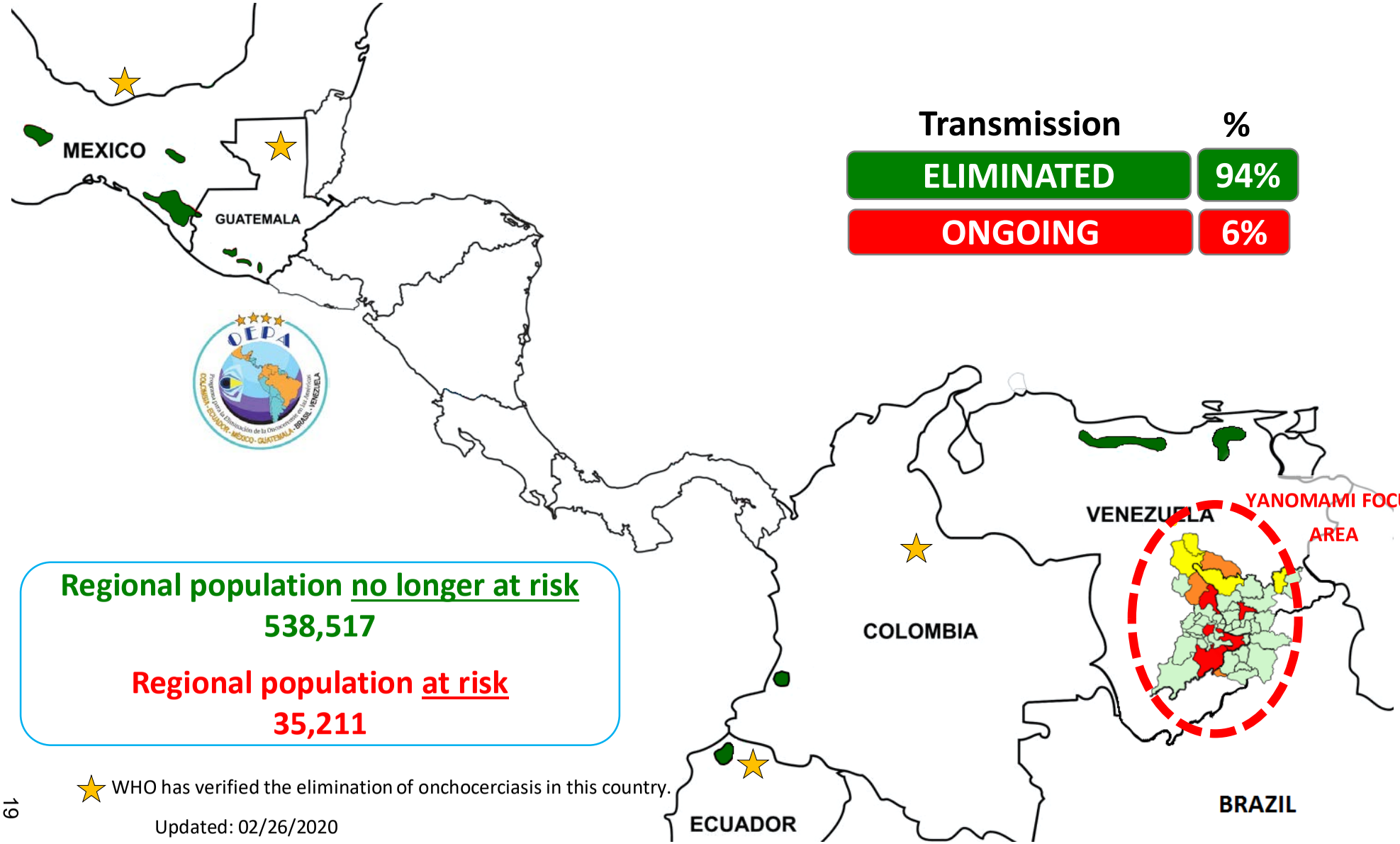


Figure ES13

Mectizan® Treatment History in the Americas
1989 - 2019

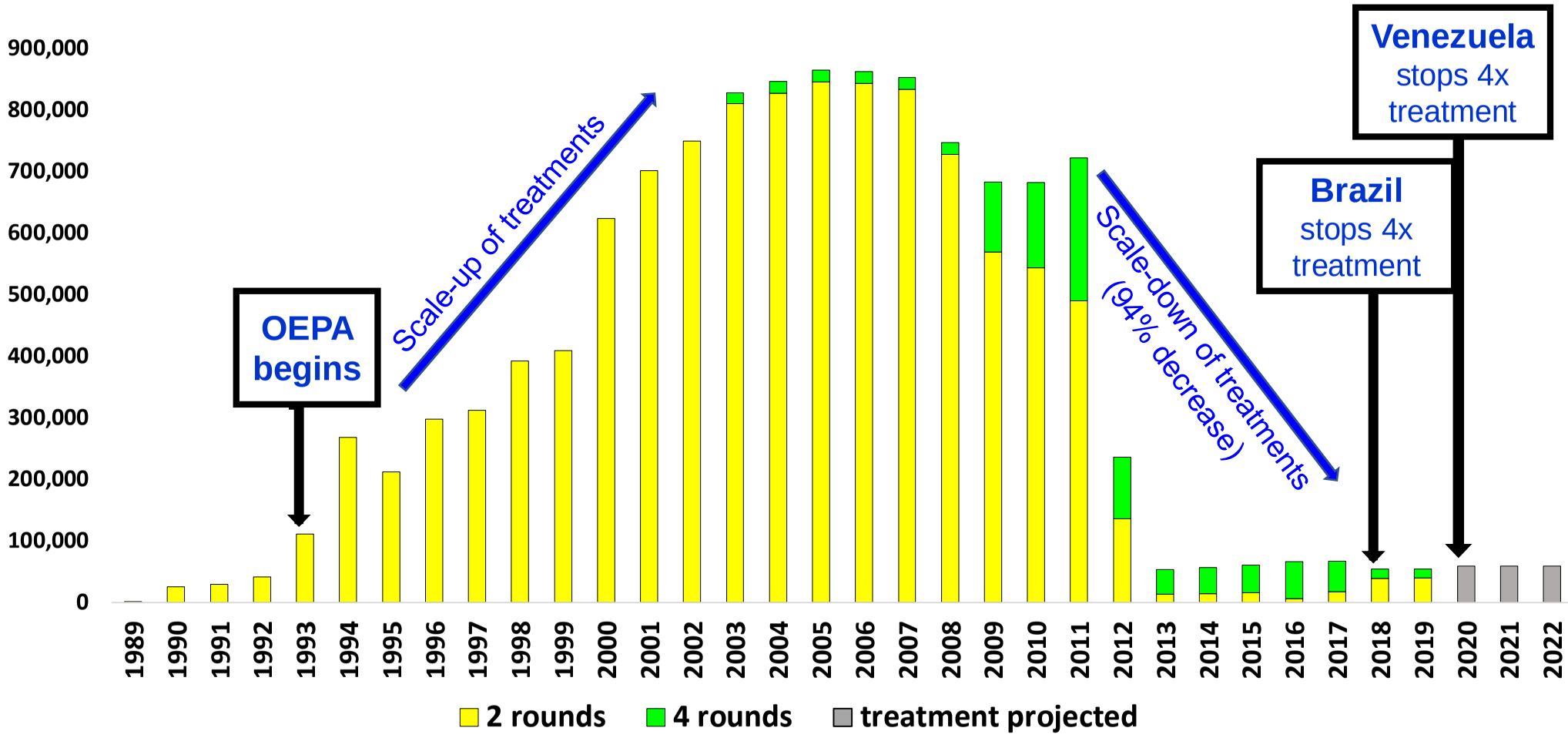


Figure ES14

OEPA, Regional Population-at-Risk, No Longer at Risk and Eligible for Treatment in 2020

Focus	Number of communities	Population at risk	Population out of risk	Population eligible for treatment	Transmission status
Lopez de Micay-COL	1		1,366	★	Eliminated in 2010 Verified in 2013
Esmeraldas-ECU	119		25,863	★	Eliminated in 2012 Verified in 2014
North Chiapas-MEX	13		7,125	★	Eliminated in 2010, 2011, 2014 Verified in 2015
Oaxaca-MEX	98		44,919		
South Chiapas-MEX	559		117,825		
Escuintla-GUA	117		62,590	★	Eliminated in 2010, 2010, 2011, 2014 Verified in 2016
Santa Rosa-GUA	37		12,208		
Huehuetenango-GUA	43		30,239		
Central-GUA	321		126,430		
Northcentral -VEN	45		14,385		Eliminated in 2013
Northeast -VEN	465		95,567		Eliminated in 2017
South-VEN	**373**	**17,502**		**15,229**	Ongoing
Amazonas-BRA	**272**	**17,726**		**14,358**	Ongoing
Regional total	**2,463**	**35,228**	**538,517**	**29,587**	

★ *WHO has verified elimination*

Figure ES15

Evolution of Transmission Status in the Yanomami Focus Area 2009 - 2019

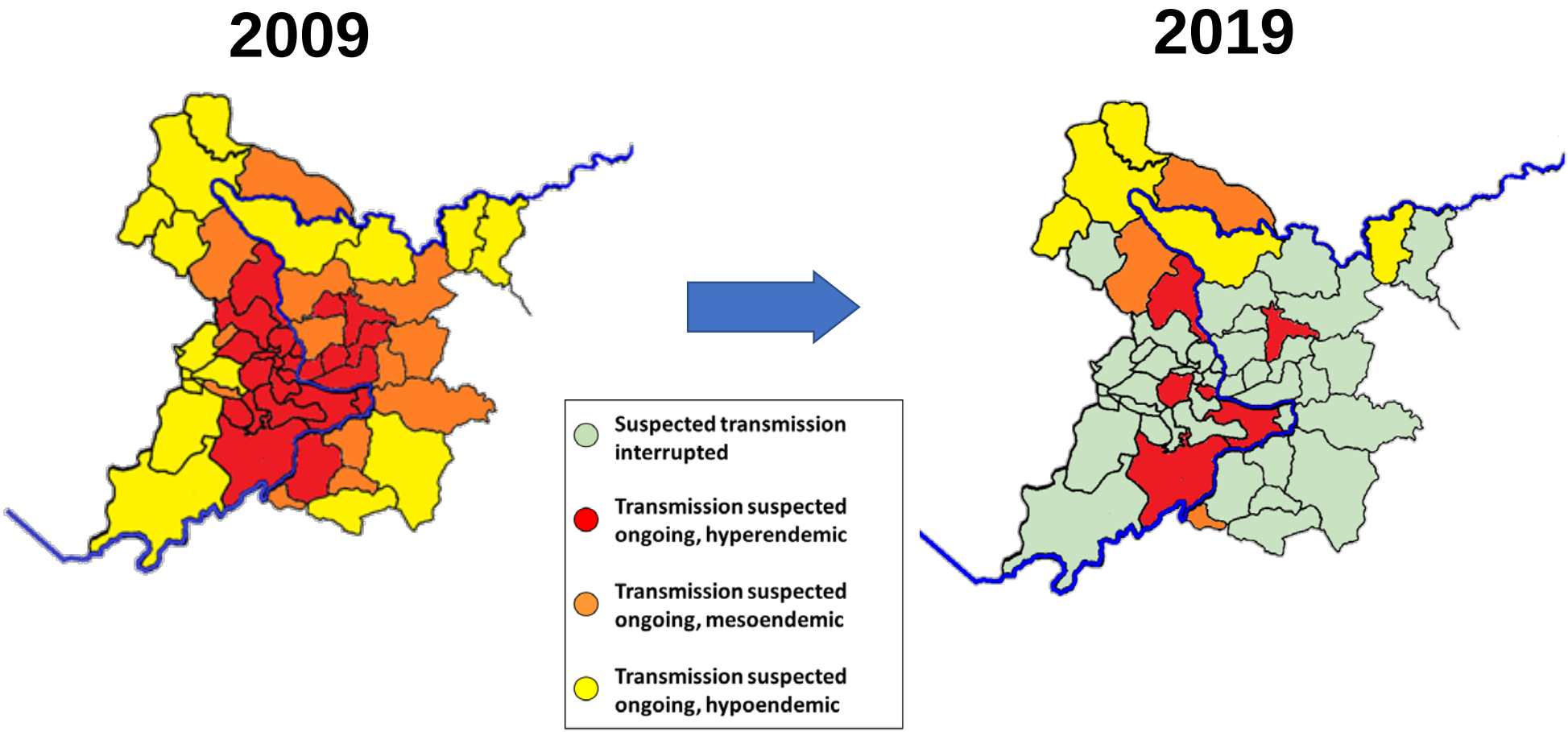


Figure ES16

Ethiopia: Carter Center Assisted River Blindness (RB) and Lymphatic Filariasis (LF) Treatments and Targets 2012 – 2020

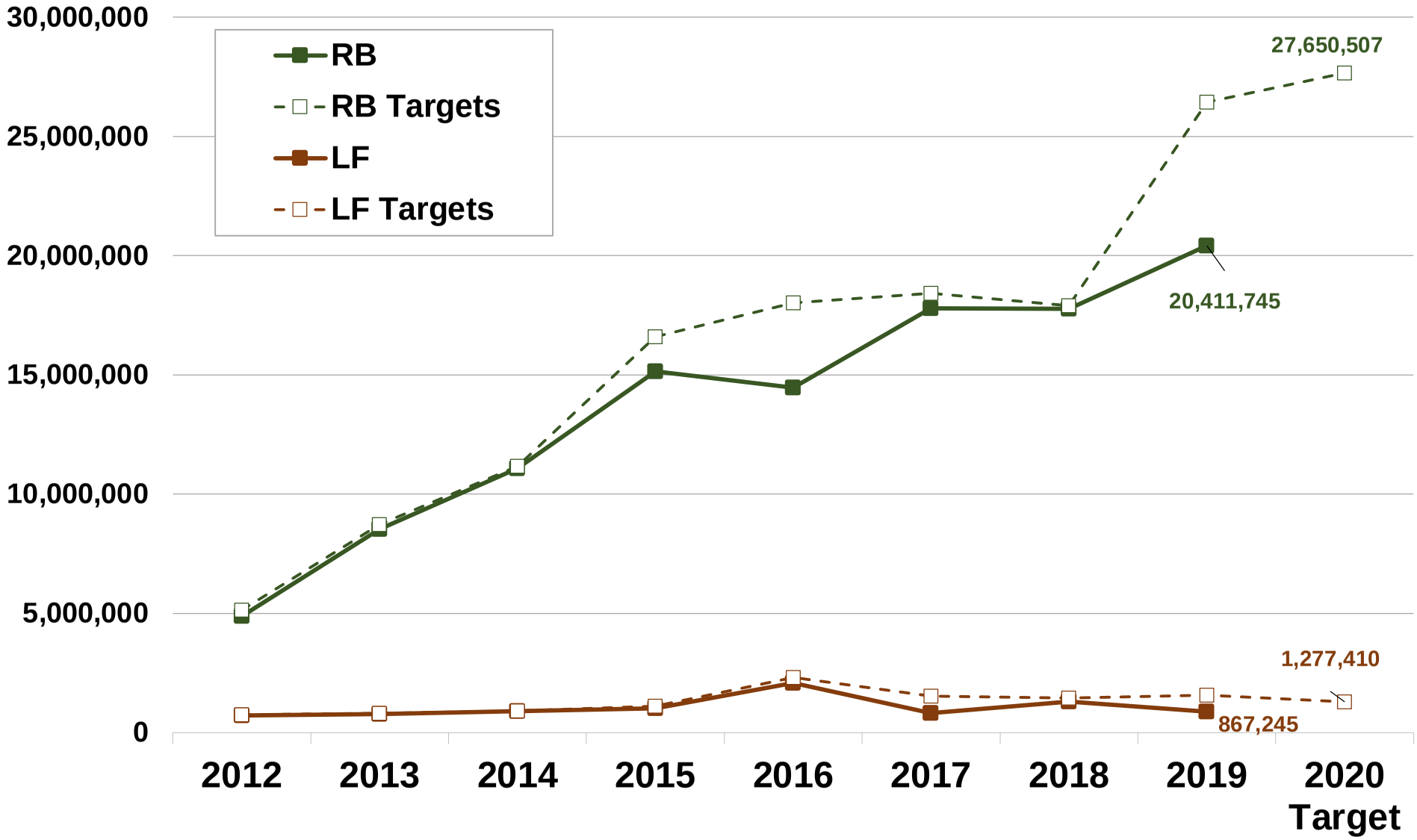


Figure ES17

Lymphatic Filariasis Elimination Progress by Woreda (district) in Ethiopia

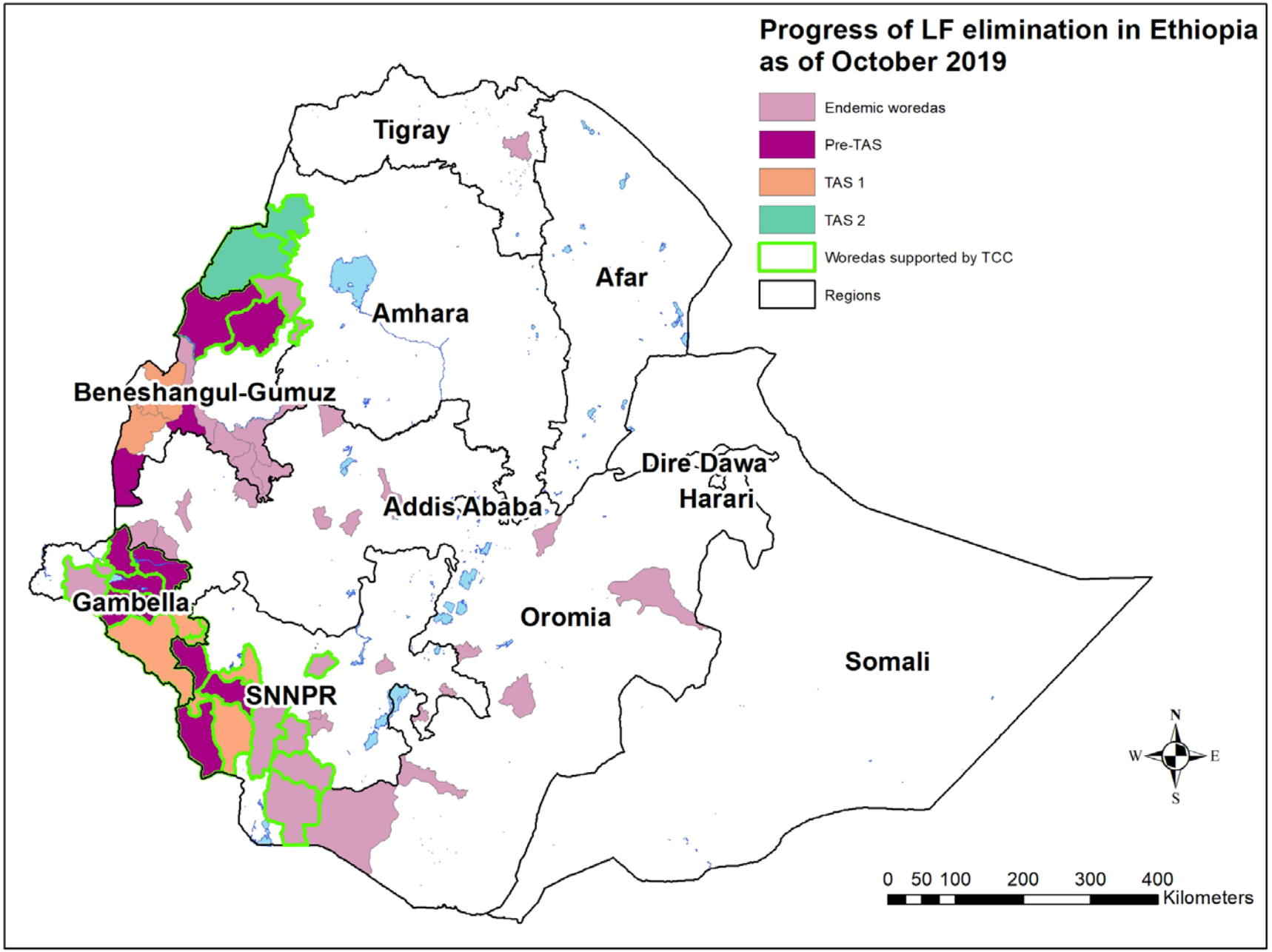
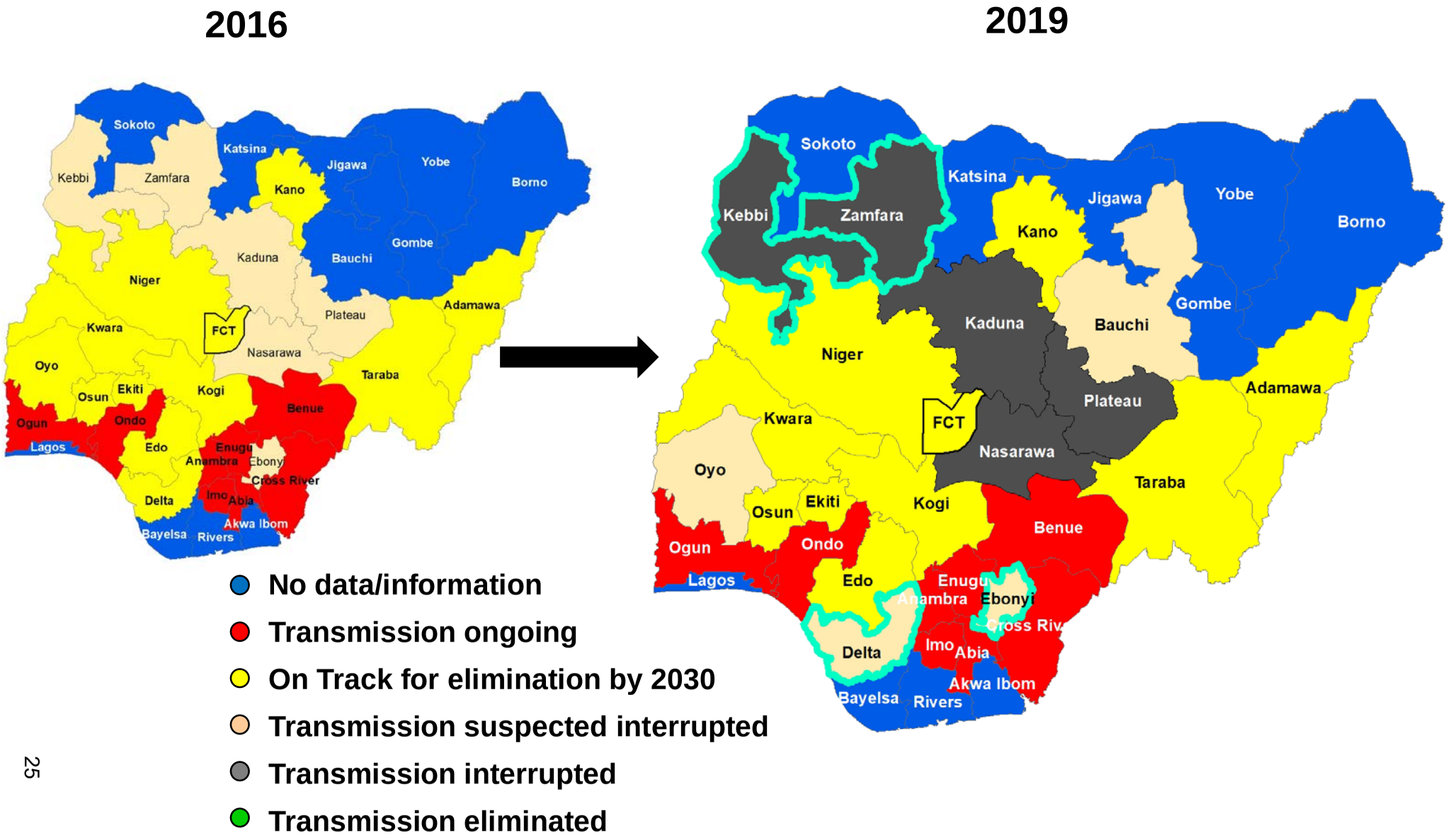


Figure ES18

Progress of Onchocerciasis Elimination in Nigeria



*States changing status in 2019 are outlined in green highlight.

Figure ES19

Nigeria: Carter Center Assisted River Blindness (RB), Lymphatic Filariasis (LF), Soil Transmitted Helminths (STH) and Schistosomiasis (SCH) Treatments and Targets 2012 – 2020

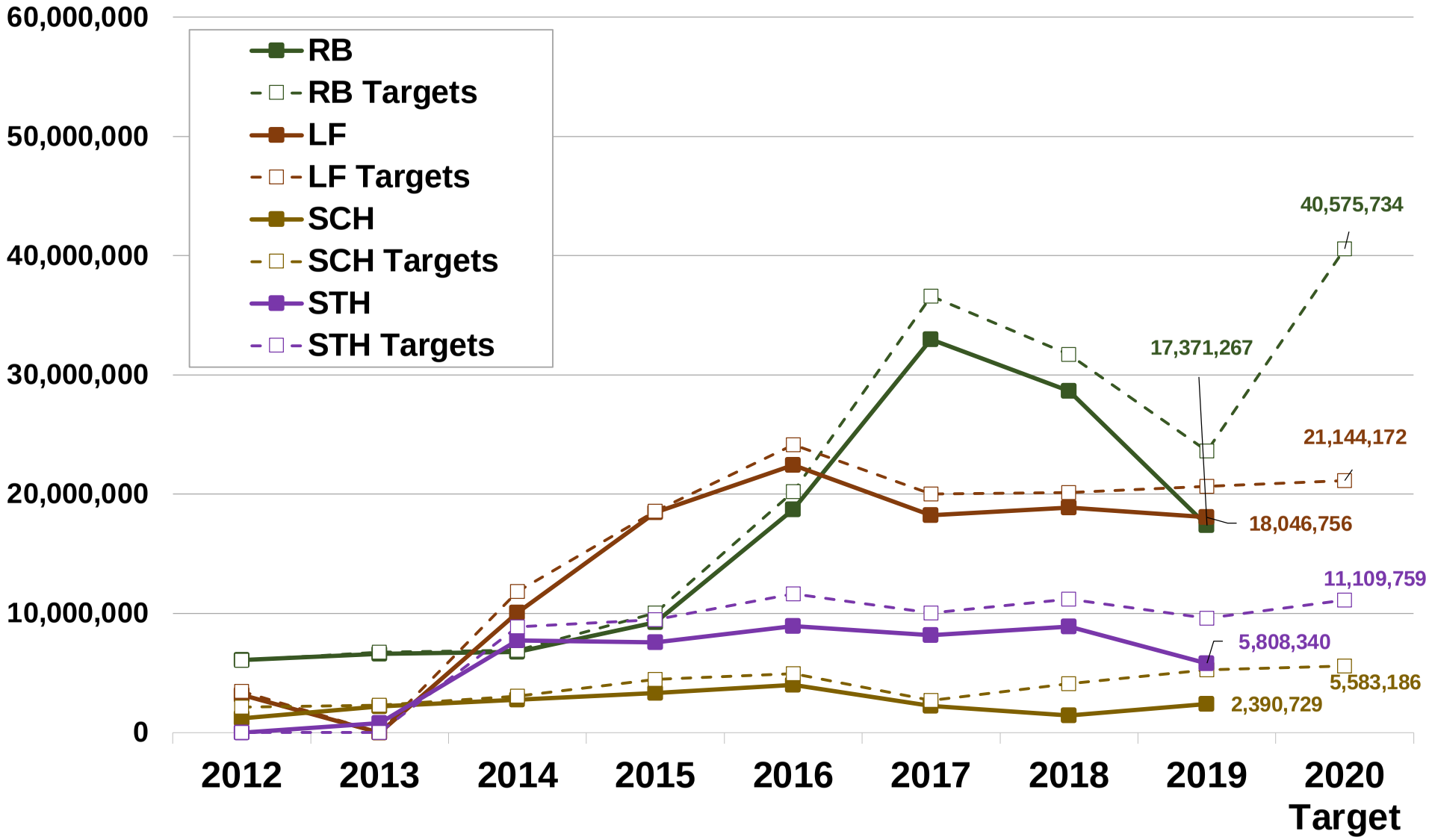


Figure ES20

Nigeria: Annual and Semiannual Mectizan® Treatments in RBEP-Assisted Areas*

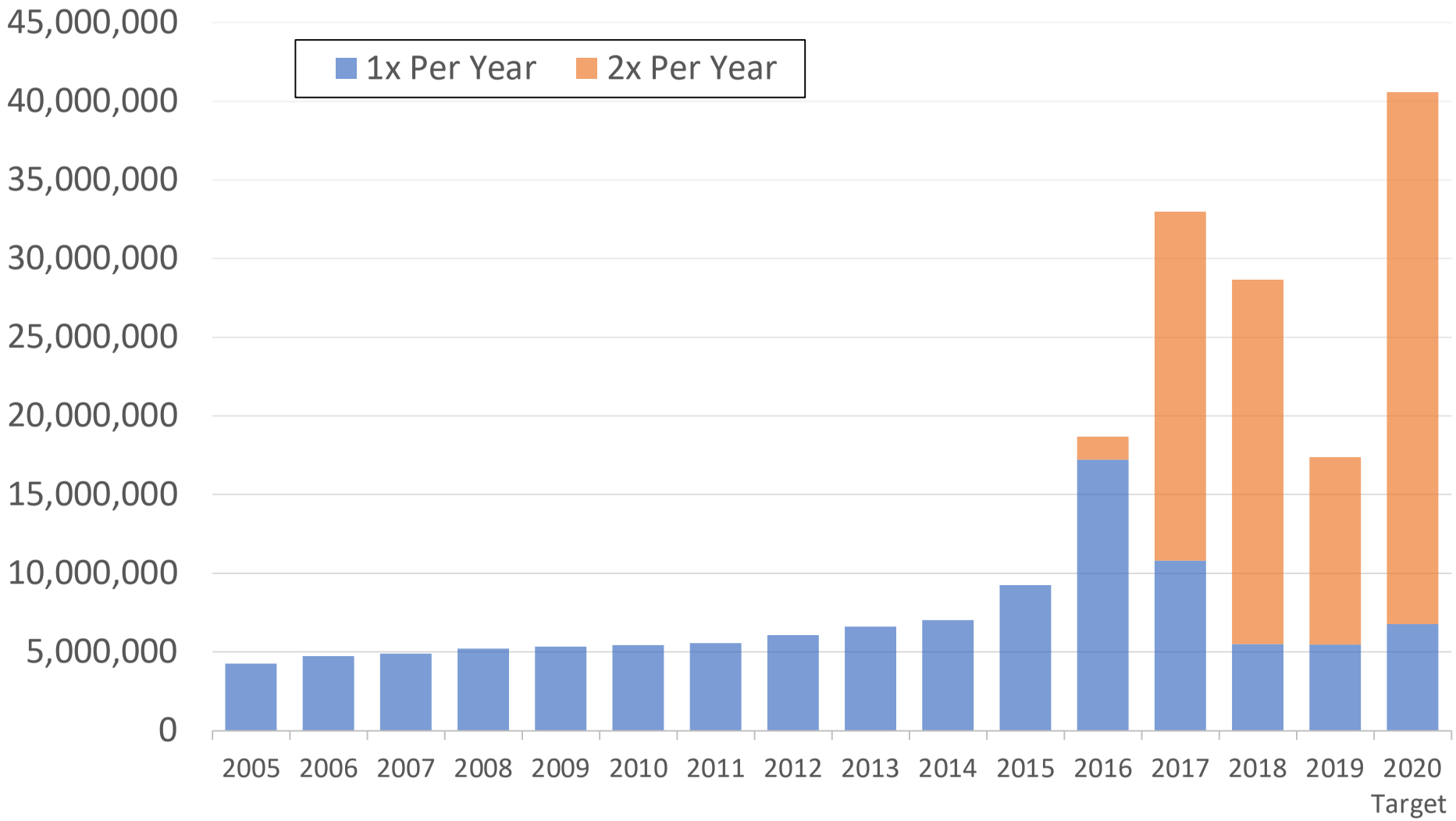
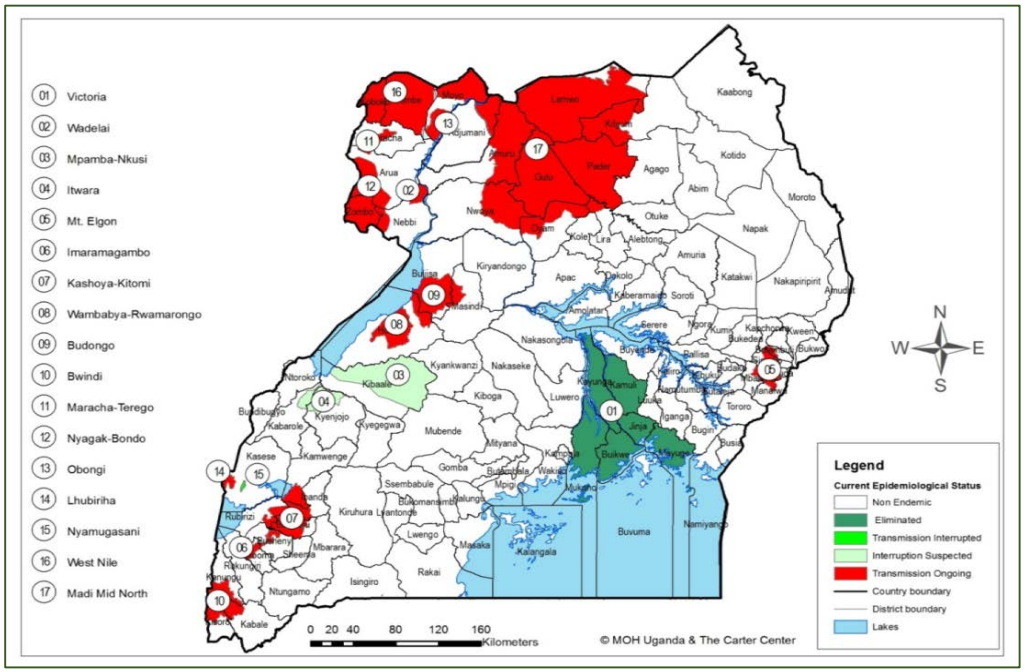


Figure ES21

Uganda: Twelve Years of Progress in Eliminating Onchocerciasis Transmission

2007



2019

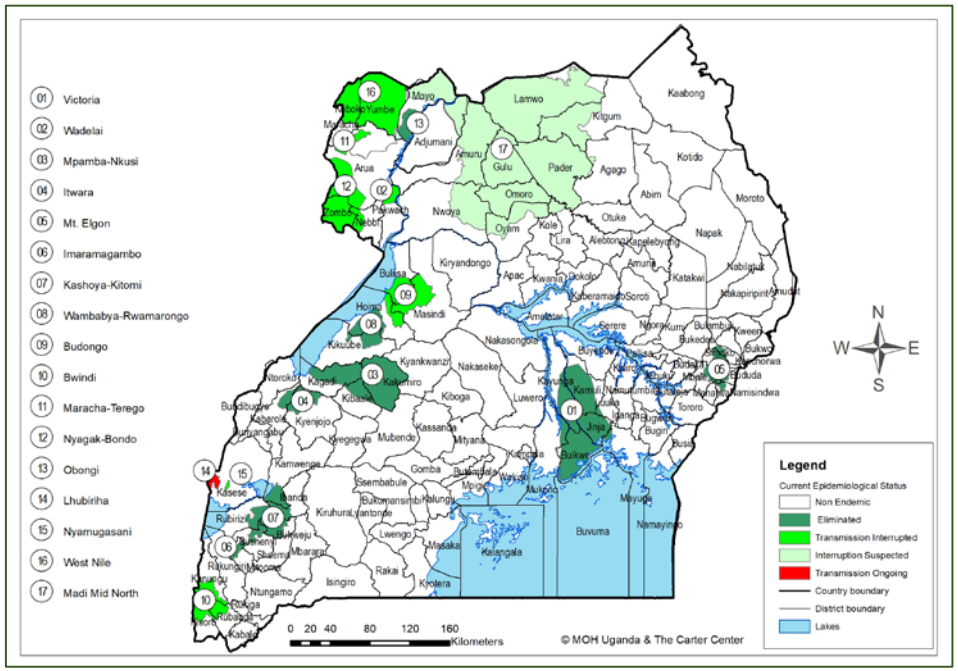
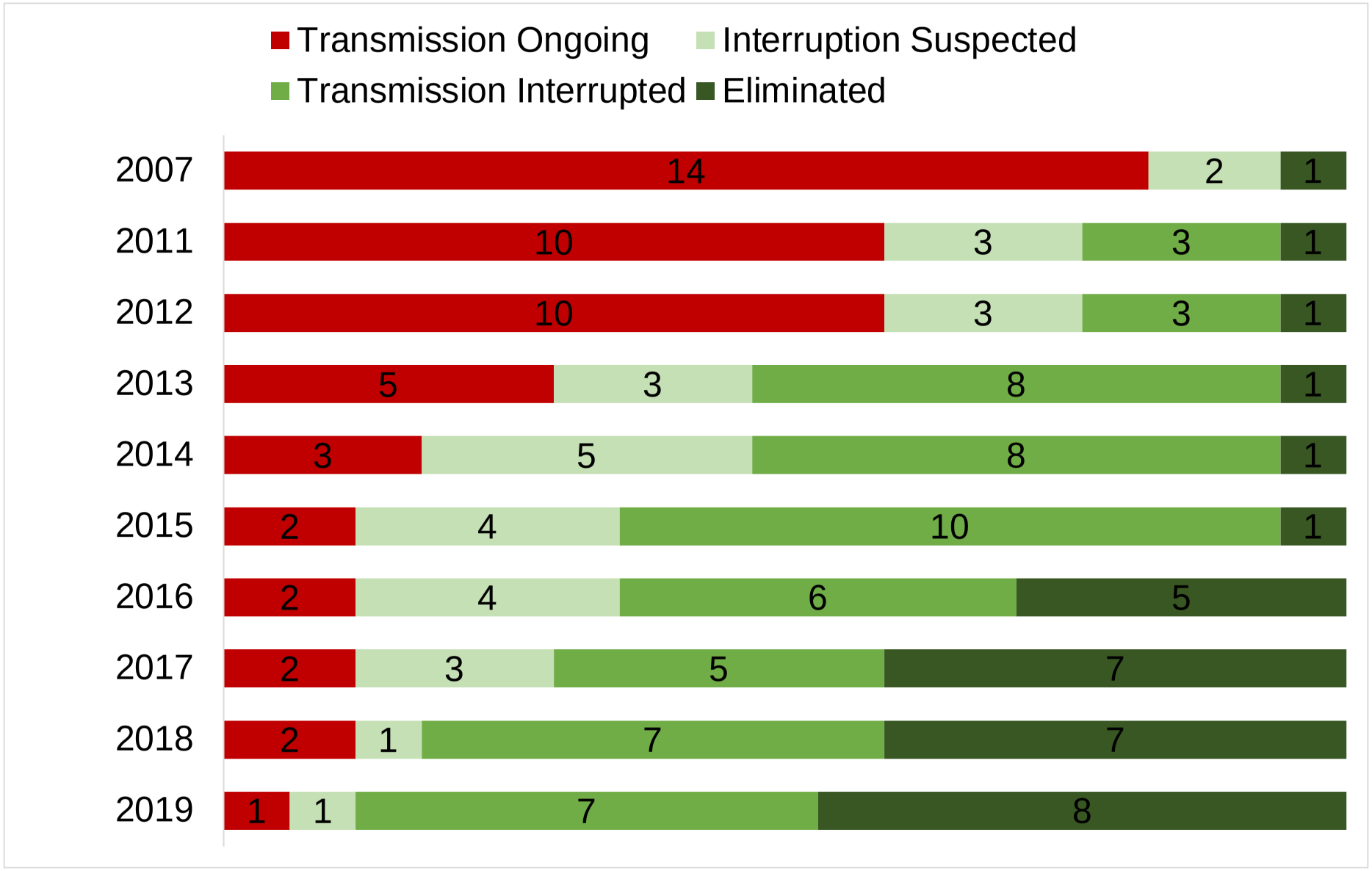


Figure ES22

Uganda Progress in Eliminating Onchocerciasis Transmission (Change in Endemic Status in Foci) 2007-2019



THE AMERICAS

OEPA is a coalition led by The Carter Center that includes the ministries of health of the affected countries in the Americas, the Pan American Health Organization (PAHO)/WHO, and other partners. The OEPA initiative has stopped treatments in 94% of the population once endemic for the disease, and four countries have received WHO verification of elimination: Colombia (2013), Ecuador (2014), Mexico (2015), and Guatemala (2016). In 2017, PTS was completed in the Northeast Focus of Venezuela, once the third largest transmission zone of the region in terms of population. See Figure ES12 for a map of the region. The OEPA treatment history over almost two decades shows a scaling up of MDA treatments followed by a scaling down treatments as elimination was achieved in an increasing number of areas (Figure ES13).

OEPA is a coalition led by The Carter Center that includes the ministries of health of the affected countries in the Americas, the Pan American Health Organization/WHO, and other partners. The OEPA initiative has stopped treatments in 94% of the population once endemic for the river blindness, and four countries have received WHO verification of elimination (Figure ES14). The last active transmission zone is in the Amazon rainforest bordering Brazil and Venezuela, called the 'Yanomami Focus Area' (YFA) after the indigenous people residing there. The challenge with the YFA lies in the remoteness of its population, the lack of high-level coordination between Brazil and Venezuela, and especially the deteriorating political situation in Venezuela. In 2019, OEPA assisted Brazil and Venezuela in 54,700 Mectizan® treatments, representing 81% of the 2019 treatment target. Some of the Yanomami people from the endemic communities of both Brazil and Venezuela serve as Indigenous Health Agents (IHAs) and are proving vital to the program to provide health services in this challenging area. Despite the political, humanitarian and health crises of Venezuela, Venezuelan teams supported by The Carter Center were able to provide ivermectin MDA as well as vaccinations, malaria treatments, and other health services. Additionally, the program has conducted 20 rounds of successful high-coverage treatment in 61% of the communities of the YFA, which means that transmission in these communities is likely interrupted (Figure ES15). In 2019, the OEPA program received financial support from the United States Agency for International Development (USAID), Merck & Co., Inc., the Lions Clubs International Foundation, and the Carlos Slim Foundation.

The countries and TCC staff are trying to creatively surmount the problems of extreme isolation and difficult access to the Yanomami area. In Venezuela, the program is using satellite imagery to locate communities, rehabilitating or building airplane landing strips, and training Yanomami health workers to actively help provide ivermectin treatment as well as other health care. About 59,000 treatments are planned in the Yanomami Area in 2020.

2020 RECOMMENDATIONS FOR THE ONCHOCERCIASIS ELIMINATION PROGRAM FOR THE AMERICAS (OEPA)

GENERAL:

- The programs should work to reach high treatment coverage (>85%) in each treatment round.

- Train more IHAs and continue the important advances in participation of Yanomami women.

- The use of doxycycline treatment in a carefully selected group of patients is underway in both Brazil and Venezuela and may be an important ancillary approach in the final stages of elimination.

- The Venezuela scoring system should be maintained and further refined despite the end of the 4x/year approach. Brazil should continue its development of a scoring system, noting that Brazil has fewer data on individual communities than does Venezuela. A common community scoring system for the overall Yanomami Area should be developed in the near future based on common data variables collected, especially effective treatment rounds, baseline endemicity, most recent assessment results and prevailing vector species.

- Continue to invite all six OEPA country representatives to IACO regardless of verification of elimination status.

- The midyear Program Coordinating Committee of OEPA (PCC) meeting may need to be postponed due to the COVID-19 epidemic.

- If the COVID-19 pandemic allows, hold IACO 2020 in Antigua, Guatemala. Promote the highest level of political support from Venezuela and Brazil and representation at IACO if the present adverse political environment in both countries allows. Encourage the Lions Clubs International Foundation to maintain support to a Lions representative from each of the six countries to attend IACO.

- Refine the geographical information system (QGIS), the common mapping platform of the two countries' technical teams working separately, tracking community treatment performance and epidemiological indicators and keeping coordinates as current as possible.

- Continue the anthropologist consultancies that are helping the program to understand Yanomami movements and cultural outlooks pertinent to the treatment program, and to further improve the training approach for IHAs if budget permits.

Venezuela:

- The 4x-per-year treatment scheme was abandoned in 2019. A remaining issue is whether the program will still require four trips per year to the endemic areas to reach >85% treatment coverage in all villages.

- Continue using remote sensing to monitor and identify communities in the South

Venezuela Focus of the Yanomami Area. New communities (previously unrecognized by the program) need to have 1) a confirmatory 'fly-over' or site visit to confirm they are inhabited; 2) an epidemiological assessment; and 3) if the village is confirmed to be onchocerciasis endemic, Mectizan treatment should be started immediately.

- Seek new ways to channel funding to support activities in NE Venezuela and the South Focus (CAICET).

- The Venezuela scoring system should be maintained and further refined despite the end of the 4x/year approach. Brazil should continue its development of a scoring system, noting that Brazil has less baseline endemicity, and fewer data on individual communities than does Venezuela. A common community scoring system for the overall Yanomami Area should be developed, based on common data variables collected, especially effective treatment rounds, baseline endemicity, most recent assessment results and prevailing vector species.

- Source airplane fuel in Venezuela so that the recovered airstrips can be visited before they become overgrown again. Complete work on the partially constructed airstrip in Venezuela's Siapa river valley.

- Continue to support identification and training of Yanomami residents as IHAs who will take part in treatment activities, including Mectizan® distribution and malaria treatment. Track the number of IHAs in each program and establish common indices to monitor their performance (such as ratio of IHAs: persons treated, IHAs/community, number of female IHAs, etc.).

- Seek medical commodities from PAHO country delegations in Brazil and Venezuela (especially vaccines and malaria diagnostics and therapeutics) for the medical teams visiting the Yanomami area, to provide these urgently needed services to as many people as possible.

Brazil:

- Engage the four new supervisors in Brazil and follow their progress.

- Conduct epidemiological assessments (serology, entomology) in non-sentinel areas.

2020 OEPA Treatment Targets	
Semiannual (UTG2)	59,148

ETHIOPIA

Ethiopia is now in its third year of conducting primarily twice-per-year treatments for RB to aggressively pursue its policy of onchocerciasis elimination by 2020. In 2019, Ethiopia delivered a total of 20,411,745 Mectizan treatments, representing 77% of the 2019 treatment target (Figure ES16). The TCC-assisted LF program provided 867,245 annual treatments with Mectizan and albendazole, representing 56% of the 2019 treatment target. A total of 261,278 CDDs were trained, about 31,012 more than in 2018 (Figure ES10). Ethiopia's RBEP is aiming for 24 million treatments in 2020. The Carter Center's work in Ethiopia is based on a longstanding partnership with the Federal Ministry of Health (FMOH), The Lions Clubs International Foundation, The Lions Clubs of Ethiopia, The END Fund/Reaching the Last Mile Fund[2], and other donors.

2020 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, ETHIOPIA

Work toward a target ratio of at least 1 CDD:50 people, 1 CS:5 CDDs, and 1 CS per village nationwide.

Consider publication of the remarkable success in improving gender ratios among CDDs.

Onchocerciasis

Review and confirm the negative PCR results in 2019 in the Wude Gemzu 'hot spot' in the Metema sub-focus. Consider publication of findings.

Maintain good coverage in the four-times-per-year MDA in the Wude Gemzu 'hot spot' as best as possible given security issues there.

Complete all 'first stage' mapping activities as resources and security allow and in consultation with The Carter Center Atlanta office and FMOH. Leave second stage mapping to FMOH, ESPEN or other partners. Before further MDA expansion, discuss at the 2020 Ethiopia Onchocerciasis Elimination Expert Advisory Committee (EOEEAC) meeting, the new 2019 WHO OTS recommendations, which we understand will call for a change from current OTS and EOEEAC guidance of ≥2%.

Establish twice-yearly MDA in 13 districts (11 new and two additional new districts in adjacent areas) in Amhara, Oromia, and Southern Nations, Nationalities and People's Region (SNNPR).

Provide financial and administrative support for the 2020 EOEEAC meeting.

Complete entomological assessments in East and West Hararge, finish testing dried blood spots (DBS) taken from children, and clarify results from skin snip PCR. Consider publishing findings.

Work with USF resolve the issues with the PCR test in the Ethiopia lab.

Encourage EOEEAC to issue a press release following each meeting and the chair to brief the minister of health after each meeting.

The program should provide updates on treatment of refugees in border areas assisted by TCC,

[2] The Reaching the Last Mile Fund, housed within the END Fund, is a multi-donor fund, initiated and led by His Highness Sheik Mohamed bin Zayed Al Nahyan, the Crown Prince of Abu Dhabi.

especially in Gambella.

Lymphatic Filariasis

In consultation with HQ and FMOH-NTD secretariat, conduct pre-Treatment Assessment Surveys (pre-TAS) and TAS studies (Figure ES17).

Obtain DBS for OV-16 testing during TAS studies, if indicated.

Publish 2019 TAS-OV16 study showing utility of this approach for gathering information on onchocerciasis.

Await direction from FMOH (preferably after consultation with LF Regional Program Review Groups [RPRGs]) before conducting further LF remapping/reassessments. Ideally the RPRG would provide the filarial test strips (FTS) through the FMOH for such assessments.

2020 Ethiopia River Blindness Treatment Targets		
Semiannual (UTG2)	Quarterly (UTG 4)	Total
24,930,186	52,160	24,992,346

2020 Ethiopia Lymphatic Filariasis	
Annual UTG	1,161,243

2020 Training Objectives	
CDDs	CSs
275,985	90,722

NIGERIA

Thanks to NTD funding from USAID's ENVISION project and Act to End NTDs | East program, both led by Research Triangle Institute (RTI) International, and funding from the IZUMI Foundation and other generous donors, the program assisted 43.6 million treatments for RB, LF, SCH, and STH.

The Carter Center currently assists river blindness and LF treatments in seven southern states in Nigeria (Figure ES18); Plateau and Nasarawa states in central Nigeria stopped MDA for LF and RB in 2013 and 2018, respectively. Unfortunately, Nigeria's RBEP only assisted in 17,371,267 Mectizan treatments for river blindness in 2019 (Figure ES19), a 39%decrease from 2018 and only about 74% of the target, due to ivermectin importation delays that precluded the first round of the twice-per-year treatment regimen (Figure ES20). However, the national elimination program continues to make progress, as Delta and Ebonyi states changed status to "transmission suspected interrupted" and two Sight Savers-assisted states (Kebbi and Zamfara) changed status to "transmission interrupted" per the Nigeria Onchocerciasis Elimination Committee (Figure ES18). Our Nigeria LF program assisted 18,046,756 treatments in 2019 reaching 85% of the target. The 2020 targets for RB and LF are 41 and 21 million, respectively (Figure ES19). The NTD programs in Nigeria were supported in large part by the USAID's ENVISION project and Act to End NTDS | East program, both led by RTI International.

The Carter Center assisted in 2,390,729 praziquantel treatments for schistosomiasis in the nine states in Nigeria in 2019. The SCH program follows WHO guidelines that target some areas only every other year or every three years, and 2019 was a high-target year with a 69% increase from 2018. However, our programs reached less than half (46%) of our target for 2019 due to importation delays that affected praziquantel supply. Praziquantel is donated to The Carter Center through the WHO by Merck KGaA, Germany. The Izumi Foundation also supported this program in 2019. Our target in 2020 is 6 million praziquantel treatments (Figure ES19).

Treatments in 2019 for STH were 5,808,340, representing 61% of the 2019 treatment target. The 2020 target is 11 million treatments. The medicines used for STH treatment are donated by GSK (albendazole) or Johnson & Johnson (mebendazole).

2020 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, NIGERIA

Overarching for the three programs:

Rolling surveys should be smaller in scale and budget than those promoted by WHO. Coverage evaluations of any kind should inform programmatic decisions, so they should be directed to areas where there is concern about the quality of MDA or where an epidemiological study is planned.

Whenever possible, add LF and/or RB sentinel villages to the sample in any population-based survey activities being conducted (in these SVs' states or local government areas [LGAs]). This would help us to conduct serial monitoring of SVs.

Continue providing awards in each state to the best CDD, teacher, frontline health facility (FLHF) worker, village leader and CS.

The ratio of CDDs per persons treated has increased with treatment expansion far beyond the

national 1:250 limit. Increase the number of CDDs as budgets allow, working to reach the target ratio of at least 1 CDD:250 people, 1 CS:5 CDDs and 1 CS per village. When calculating population served per CDD, remove urban populations from the equation since these are typically served directly by health workers.

Complete the analysis of the pilot CDD attrition study (based on Kaplan-Meier survival methodology). Review final analysis with HQ and then make plans to expand the study by establishing the number of CDDs that will be studied (with good gender representation). Explore the relationship of increasingly complicated registers and roll-up forms to CDD attrition rates, perhaps using focus groups of CDDs and their supervisors.

Work with the different levels of government to effectively track drug supply, including reverse supply logistics.

Due to tragedy of a child who died by choking on a tablet administered by his siblings, work with all levels of government to reinforce CDD training (as well as all other levels of training) such that treatment must be directly observed by CDDs or health workers (in the case of urban distribution) and treatments may not be left with families. Include this enhanced messaging in a Standard Operating Procedures document provided to all CDDs

Design an evaluation to determine whether the roll-up forms The Carter Center Nigeria office designed to improve tallying of household treatment data has indeed been effective in improving data accuracy.

Lymphatic Filariasis/Malaria:

The program in Plateau and Nasarawa should complete the LF morbidity case search and the assessments of the ability of the states' health care system to take care of morbidity that has resulted from past LF infections, in accordance with WHO requirements. Our objective should be to assure that we have done the required level of Morbidity Management and Disability Prevention (MMDP) work to prepare the dossier supporting the two states' claim to have 'eliminated LF as a public health problem.' With Izumi support and in close consultation with the Atlanta office, launch MMDP activities in Plateau and Nasarawa states that includes 1) assessment of burden, 2) strengthening of primary care support for patients with lymphedema/elephantiasis/acute attacks and hydrocele, 3) establishing more Hope Clubs, and 4) hydrocele surgical camps that include referral systems for more severe cases. Consider publishing the results of hydrocele assessment surveys that reviewed high rates of inguinal hernia.

In the South East/South South (SE/SS) states, conduct assessments of LF morbidity case burden during LF MDA or pre-TAS/TAS assessments. Support other MMDP work in LGAs that have stopped MDA (after passing TAS-1). It is important to note that USAID's Act to End NTDs | East program, led by RTI International, does not support MMDP work, so budgetary constraints limit the degree of our TCC support for MMDP.

Complete the final report of the Wb123 and OV16 research to the Task Force for Global Health; consider publishing these results.

Continue entomological collections in LF sentinel villages in Plateau and Nasarawa but start again to dissect *Anopheles* mosquito specimens for *W. bancrofti* larvae.

Conduct pre-TAS in 49 LGAs in seven states, and TAS1 in 16 LGAs in three states. Where TAS1

indicates MDA can cease, conduct Health Education to prepare the populations for an end of MDA, and advise the state MOH that TCC support for SCH and STH will soon cease (see below).

In Plateau and Nasarawa states develop a plan for staged mainstreaming of SCH/STH that includes a monitoring and evaluation element on how mainstreaming might affect the program, positively or negatively.

Discuss with FMOH, NOEC, WHO and other authorities the FMOH LF policy demanding that pre-TAS and TAS not be done until 6 months after MDA; these policies are a threat to the states where twice-per-year ivermectin treatment is being implemented for RB elimination (the 'red states').

Onchocerciasis:

As soon as possible, meet and/or speak with FMOH NTD drug supply personnel to determine if the Mectizan for the first round of 2020 RB MDA (as well as the belated second-round 2019 Mectizan) will be shipped.

Collect samples from at least 3,200 children in every TCC-assisted red state to determine which states are ready to advance to the next color, and perhaps proposed to NOEC for stop-MDA surveys.

Conduct stop-MDA entomology assessments in NOEC-selected sites, as well as in RB sentinel sites, in Delta state. Have results ready in time for the December 2020 NOEC meeting.

Publish the hypoendemic onchocerciasis mapping study (from the 2016 *Loa loa* study, L Rakers first author) that used OV16 RDTs (compared with an ELISA subset). Prepare a presentation for the December NOEC.

Complete PTS entomology activities in Plateau and Nasarawa. Include some new fly collection at selected cross border sites. Consider publishing the experience with treating migrants and the PTS health education campaign and site-specific posters. Conduct a knowledge attitude and perceptions (KAP) study in a sample selected from the 'oncho' LGAs.

Provide entomological lab support for halting MDA for RB in Kebbi and Zamfara states (assisted by Sightsavers), if specimens are provided. Provide OV16 lab support to Mission to Save the Helpless (MITOSATH) for DBS collected in Ondo state. Obtain USF training for TCC lab technician on PCR in skin snips.

All SE/SS states should continue prospecting the entomological sites preselected by the NOEC for future stop-MDA entomological assessments. Those sites that are not producing sufficient numbers of vectors will need to be replaced by better sites (and permission for site changes made to NOEC). Maintain good records so that the coordinates can be assessed in a proposed remote sensing study to assess productivity of entomological sites in Nigeria. In consultation with the Atlanta office, calibrate black fly collection by traps with nearby collections by human attractants so that Annual Transmission Potential (ATP) calculations are possible.

Encourage the NOEC to begin to classify certain states (Ondo, Taraba) by LGA to capture that some LGAs are 'red' (treating twice per year). Begin to show this on the NOEC map.

Provide financial and administrative support for the 2020 NOEC.

Schistosomiasis (SCH) and Soil Transmitted Helminthiasis (STH):

Due to an anticipated reduction in funding of SCH/STH work by USAID in future years, The Carter Center is beginning a process to incrementally transition ownership of SCH/STH to the federal, state and local governments. In LGAs where RB or LF community-wide MDA is ongoing, integrate the STH/SCH treatments into the RB or LF platform, co-administering drugs. Where the RB or LF community-wide platform is being lost due to stop-MDA determinations, the SCH/STH programs should be mainstreamed into a school-based program such that national funds will transition over a short time period to fully support the program. We should monitor this process carefully for evidence of decreasing MDA coverage in the school-aged target population.

Publish in a peer-reviewed journal the results of the SCH/STH impact assessment in Plateau and Nasarawa that includes intensity of infection determinations.

2020 Nigeria River Blindness Treatment Targets		
Annual (UTG)	Semiannual (UTG2)	Total
6,779,049	33,796,685	**40,575,734**

2020 Nigeria Lymphatic Filariasis	
Annual (UTG)	**21,144,172**

2020 Nigeria Schistosomiasis	
Annual (UTG)	**5,583,186**

2020 Nigeria Soil-Transmitted Helminths		
Annual (UTG)	Semiannual (UTG2)	Total
7,276,782	3,832,977	**11,109,759**

2020 Training Objectives			
CDDs	CSs	HWs	Teachers
67,583	12,901	7,340	4,701

SUDAN

During 2019, 70,300 treatments were provided in Sudan, 45,000 treatments in Radom, South Darfur along with 25,300 treatments among refugees, representing 98% of the 2019 treatment target. Sudan aims to give about 403,750 treatments in 2020 in their Radom focus, security permitting.

2020 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, SUDAN

Work toward a target ratio of at least 1 CDD:100 people, 1 CS:5 CDDs and 1 CS per village.

Although TCC is not assisting the Sudan LF program, a report on that program was given. LF endemicity is much more expansive in Sudan than that of RB, with 14 states, 59 districts and 7.9 million persons eligible for treatment. MDA with ivermectin and albendazole has been launched but the numbers of treatments given in 2019 was not reported at the Review. It was noted that the RB program is under considerable pressure to integrate with LF and that ivermectin orders for RB were being mixed up with LF ivermectin order.

Galabat Focus in Gedaref State

Conduct the 3rd year Post Treatment Surveillance exercise focusing (in accord with WHO guidelines) on the entomological assessments. However, in the PTS evaluation of the cross-border regions adjoining Ethiopia's Wudi Gemzu hot spot, serology (OV16) assessments are also needed.

Radom

It was noted that (annual) treatments have been dramatically increasing from 50,000 in 2014 to 176,000 in 2019; 400,000 treatments are projected in 2020, to begin in May. Increases are due to inward migration (including gold miners), and refugees from RSS and Central African Republic (CAR).

If the Peace Program at The Carter Center or the Sudan government are able to secure a stable peace where increased activities are feasible in Radom, seek funds to launch the expanded MDA program that would include twice per year treatments. Further assessments to determine the new limits of the Radom focus are also needed. All of these activities should involve detailed discussions with the Atlanta office.

Blue Nile State (adjacent to RB transmission zones in Ethiopia)

If the security situation in Blue Nile allows, seek funding to evaluate the status of onchocerciasis transmission in Khor Yabus, Wad Elmahi and Geissan districts of Blue Nile state. Data suggests that there are few breeding sites in these areas and that infections may be acquired in Ethiopia. Additional surveys should be done in coordination with similar surveys in corresponding areas across the border in Ethiopia. TCC can help with activities on the Ethiopia side primarily in those areas where RBEP Ethiopia assists (which does not include Assosa and Kemashi).

Disease assessment surveys in Khor Yabus, and possibly El Mahi and Geissan, will be a challenge, with many roads in Khor Yabus known to still be landmined. Assessments should take place after population movements returning to their old villages have stabilized such that the

assessments give a good account of human infection rates. Entomological surveys will be important given the reports of few breeding sites having been identified.

2020 Sudan Treatment Targets	
Semiannual (UTG2)	403,750

2020 Training Objectives		
CDDs	CSs	HWs
1,360	86	40

UGANDA

In 2007, Uganda declared a goal of RB transmission elimination from all its 17 transmission zones (foci). The program made further progress in 2019. The Ugandan Onchocerciasis Elimination Expert Advisory Committee (UOEEAC) meeting recommended the Obongi focus be reclassified as eliminated based on the WHO elimination guidelines. The Nyagak-Bondo focus, with a population of over 600,000 people was reclassified as having interrupted transmission. The MMN focus has been reclassified as interrupted-suspected. There is one focus, Lhubiriha, that still has ongoing transmission (Figures ES21 and ES22). Uganda administered a total of 3.7 million Mectizan treatments in 2019, all under the twice-per-year strategy, representing 103% of the 2019 treatment target. For 2020, the target is 2.8 million treatments, which will take place in the large MMN focus that encompasses 11 districts, many of which border with South Sudan. Uganda also has important cross-border foci shared with the DRC. The Ugandan MOH onchocerciasis elimination program is supported by TCC, USAID's Act to End NTDs | East program, led by RTI International, ELMA Philanthropies, and Sightsavers.

The Slash and Clear (S&C) approach to vector control has proven effective in controlling *Simulium* vectors of onchocerciasis in Uganda. Therefore, the program plans to establish community-driven S&C activities in all first-line communities close to rivers where the vectors are breeding. Every affected community will be responsible for S&C activities along the river 1 to 2 kms on either side of the community.

2020 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, UGANDA

MDA has stopped in the Nyagak-Bondo focus; inform communities why MDA has halted and launch Post-treatment Surveillance.

Where health education involves new approaches such as art, singing, and dancing, document some of the events with professional videography.

Continue PTS in Bwindi, Budongo, Nyamugasani, Wadelai and West Nile foci.

Maracha-Terego onchocerciasis focus, where transmission was interrupted in 2012, has yet to begin PTS due to ongoing LF MDA. Follow results of planned TAS1 evaluations in 2020, which if successful would allow for stop LF MDA so that PTS for onchocerciasis may commence.

After the WHO-mandated period for interruption of transmission of Ebola is completed, given that all indicators suggest there has been successful control of Ebola in DRC, TCC should assist the Uganda MOH in cross-border activities between the Lhubiriha focus in Uganda, and adjacent areas in DRC (Health Zones of Beni, Kamango, Mutwanga, and Oicha).

Provide financial and administrative support for the 2020 UOEEAC meeting.

Conduct a study to determine what the former RB CDDs in eliminated foci are doing now that onchocerciasis interventions have been halted.

Madi-Mid North (MMN) and Lhubiriha

Report at the 2020 UOEEAC meeting the results from serological and entomological assessments conducted in the border 'fringe areas' of MMN, per UOEEAC recommendations.

Continue to report MMN results by district with specific calculations of rounds of effective coverage. The important indicator is rounds of effective (>85%) semiannual treatment ≥13, ideally sequential effective treatments.

Conduct treatment coverage surveys in consultation with the Atlanta office.

Support the Uganda MOH in its joint cross-border activities with DRC and RSS in SIZs and provide a report that includes number of treatment rounds, numbers of treatments, and coverage in DRC and RSS border areas at the 2020 UOEEAC and Program Review.

Implement community-directed S&C activities in FMOH-selected communities of MMN that were not part of the USF research program. A KAP study conducted in communities that are part of the USF study showed that money paid to 'slashers' was a constraint to community implementation of S&C, and that future community interventions must have a strong health education component. Consider using new health education approaches that include performances, song and dancing in those health education interventions.

2020 Uganda Treatment Targets	
Semi-annual (UTG2)	2,793,462

2020 Training Objectives				
CDDs	CSs	HWs	Parish Supervisors	Local Leaders
23,488	6,168	97	900	2,282

ANNEX 1: BACKGROUND

Human onchocerciasis, an infection caused by the parasitic worm *Onchocerca volvulus,* causes eye lesions that can progress to visual loss or complete blindness. In addition to severe eye disease, onchocerciasis causes papular or hypopigmented skin lesions and intense itching. The parasite is transmitted by certain species of *Simulium* black flies, with the most common vector being *Simulium damnosum* sensu lato (sl). *Simulium* species black flies breed in rapidly flowing rivers and streams, thus leading to the common name for the disease, “river blindness”.

In humans, the adult worms cluster in subcutaneous fibrous onchocercomas (commonly referred to as ‘nodules’) that are often visible and/or palpable. In these nodules, fertilized females release first-stage larvae (microfilariae [mf]) that migrate in the sub dermis and eye, causing immune reactions that result in the major morbidities associated with the infection. Some mf are picked up when the vector flies take a blood meal. In the flies, the mf eventually develop into the third stage larvae (L3) that are infectious to humans on subsequent blood meals. In the humans, the larvae then develop into adult worms and so continues the life cycle. There are no known environmental or epidemiologically important animal reservoirs of *O. volvulus*.

The World Health Organization (WHO) estimates that 20.9 million people are infected and 1.15 million had vision loss. Approximately 205 million people live in endemic areas worldwide and are therefore at risk of infection; more than 99% of those at risk live in sub-Saharan Africa. Onchocerciasis also exists in Latin America. Periodic mass drug administration (MDA) with oral Mectizan® (ivermectin, donated by Merck) tablets prevents eye and skin disease caused by *O. volvulus,* and may also be used to reduce or even interrupt transmission of the disease depending on the duration and frequency of treatment, the efficiency of the vector, and the extent of the infected population, the vector, and MDA distribution programs. An WHO update on the global onchocerciasis initiative was provided in the Weekly Epidemiological Record (WER) in September 13, 2019 (No 37, 2019, 94, 415–420).

The Carter Center (TCC) River Blindness Elimination Program (RBEP) is dedicated to safe and sustainable mass distribution of Mectizan (together with health education) to eliminate onchocerciasis transmission. The distinction between control (of disease) and elimination (of transmission) is important. In the control approach, Mectizan is distributed only once-per-year in areas where the eye and skin disease from the infection is greatest (the so-called ‘meso/hyperendemic’ areas where nodule rates are $\geq$ 20%). In control programs, MDA will likely need to continue indefinitely because onchocerciasis transmission persists, and people continue to get new infections (‘open system’); sustainability of control programs and indefinite effectiveness of the drug are vital in this scenario. In the elimination approach, Mectizan treatment is used more intensively to ‘close the system’ to eventually break transmission. Treatment is given twice-per-year and included areas where nodule rates are <20% (hypoendemic areas). At a point when the residual parasites in the human population are so compromised as to be unable to recover their reproductive capacity, MDA can be stopped because there is no animal or environmental reservoir of infection. Before 2013, the elimination of onchocerciasis was the program goal in the Americas, Uganda and Sudan, but not in Nigeria and Ethiopia. By 2013, national onchocerciasis transmission elimination had become the stated goal of all the governments where RBEP assists. At that time, RBEP set a new goal to stop transmission in all its assisted areas.

A historical barrier to treatment in some parts of Nigeria where TCC works has been co-endemicity of the parasitic worm *Loa loa*; Mectizan treatment in a person with high *Loa loa* parasite loads (>20,000 *Loa loa* microfilaria per ml blood) can result in serious central nervous system adverse

reactions, with complications that can lead to coma or death. In partnership with the federal and local governments of Nigeria, The Carter Center conducted a large survey in Nigeria in 2016 using a recently developed technology called the 'LoaScope' and determined that microfilaria levels of *Loa loa* were not sufficient in our supported areas to preclude treatment (of over 10,000 persons examined with the LoaScope, the highest count observed was under 12,000 mf per ml blood). Our results (published in 2018 by Emukah *et al.* in *AJTMH*) were reviewed by the Mectizan Expert Committee and the Federal Ministry of Health of Nigeria, and both gave their permission to use ivermectin MDA treatment in *Loa loa* areas in Nigeria that are ivermectin-naïve and hypoendemic for onchocerciasis.

A major focus of TCC is reaching the best possible treatment coverage, monitored through routine monthly reports by assisted programs, periodic coverage surveys, and impact on RB transmission indicators. Annex 3 is a discussion of this reporting process, as well as treatment indices used by the program and in this report. Important coverage terms include: the Ultimate Treatment Goal (UTG), which is the census-based, calculation of treatment-eligible people living in a program area (persons >5 years of age); UTG(2) and UTG(4), which are the multiplication of the UTG by 2 or by 4, respectively, and are used by elimination programs in areas where semi-annual or quarterly treatments are required to break transmission; and full coverage, which is defined as >90% achievement of the UTG, UTG(2), or UTG(4) (85% for OEPA). It is important not to confuse coverage reported in this Program Review with coverage calculated based on Total Population (often called 'therapeutic coverage') that includes children. The difference in the denominators between these two calculations can amount to 10-20%.

Mectizan tablets are distributed in Africa at the community level by grassroots community volunteers known as Community Directed Distributors (CDDs) through a process known as Community Directed Treatment with Ivermectin (CDTI). CDTI was perfected by the Tropical Disease Research program of WHO and was broadly introduced into the African Programme for Onchocerciasis Control's (APOC) supported project areas throughout Africa in the late 1990's. In some areas, TCC's RBEP focuses on "kinship/family/neighborhood-enhanced CDTI," an approach that seeks to train more CDDs than is done in classic CDTI, and which TCC developed and pioneered in Uganda. In kinship-enhanced CDTI, CDDs serve within their own kinships/family or neighborhoods, and decisions and treatment activities are handled at the sub-community level. A similar approach is used in Ethiopia, where the Health Development Army (HDA) system is based in communities' Health Development Units, with five households/families of about 30 people served by at least one CDD from the HDA. The ratio of CDDs per population that our programs have pursued historically has been at least 1 CDD per 100 persons to be treated. Ethiopia, using its Health Development Army, has moved towards supporting a ratio of 1 CDD:50 persons. Uganda is steadily increasing its concentration of CDDs with an ultimate goal of 1 CDD:60 persons.

CDDs are supervised by Community Supervisors (CSs). These are often but not always district level health personnel. In Ethiopia they are the Health Extension Workers (HEWs). The desired ratio is 1 CS:5 CDDs.

Our MDA strategy seeks to increase the active participation of members of affected communities by: 1) training as many inhabitants of endemic villages as possible to serve as distributors; 2) encouraging the involvement of women; 3) reducing the demand for financial or other "incentives"; and 4) allowing community members to choose their own distributors and the time and location of treatments. Monitoring indices of the kinship approach include: 1) community selection of CDDs

in every kinship/neighborhood zone in the community; 2) sustained treatment coverage of at least 90% of treatment-eligible persons; 3) increasing involvement of women as CDDs; and 4) the presence of at least two community-selected supervisors in every community.

The CDDs and community supervisors are often also highly engaged in other community-based health interventions, such as water provision and sanitation, malaria control, immunization, and integrated neglected tropical disease (NTD) control efforts.

ANNEX 2: A Timeline of the River Blindness Campaign at The Carter Center

- **2019:** Problems with the importation of Mectizan into Nigeria in 2019 resulted in an inability of RBEP-assisted programs to provide twice-per-year MDA for onchocerciasis; all RBEP-assisted Nigeria programs provided a single round of treatments. Just over 600,000 treatments were halted in Uganda after successful stop MDA assessments were conducted. The large Madi-Mid North focus bordering the Republic of South Sudan was reclassified as 'transmission suspected interrupted.' Cross-border activities between Uganda and the Democratic Republic of Congo (DRC) were halted however, because of the DRC Ebola outbreak. Onchocerciasis Elimination Mapping in Ethiopia provided data that led the national committee to recommend treatments be launched in several new areas of the country. The lymphatic filariasis (LF) elimination program in Ethiopia stopped about 117,000 treatments after successful Transmission Assessment Surveys (TAS). The OEPA program held the 29th InterAmerican Conference on Onchocerciasis (IACO) in Brasilia, with the theme "Brazil approaching the elimination of onchocerciasis." The conference praised the Indigenous Heath Agents (IHAs) involved in both the Brazil and Venezuela elimination programs. In 2019, RBEP authors published papers on vegetation clearance (slash and clear) as a non-chemical based vector control in Uganda, the role of OEPA as a model for Africa RB elimination programs, MDA coverage surveys in Uganda and Cameroon, and use of doxycycline treatment as an endgame strategy in the Americas.
- **2018:** Three papers (on topics of Uganda, OEPA and National Onchocerciasis Elimination Committees) are published by RBEP authors in a special supplement on Onchocerciasis Elimination in the journal International Health. In Nigeria a schistosomiasis and soil transmitted helminth impact evaluation was conducted among 9,660 children; a reduction in prevalence of infection compared to a 2013 baseline was demonstrated in many areas. In the East and West Harage zones of eastern Ethiopia, a new onchocerciasis focus was identified in OV16 surveys in an area previously believed to be non-endemic. In Uganda, MDA for onchocerciasis was recommended to be halted among more than 335,000 persons with declaration of transmission interruption in two foci. The OEPA program celebrated its 25th anniversary as it struggled to operate in Venezuela amidst political and financial turmoil.
- **2017:** The most successful year ever for numbers of RBEP-assisted Mectizan® treatments (over 55 million) delivered. Decisions to stop treatments at the end of 2017 in 3.8 million persons resident in RBEP-assisted areas in three African countries (Ethiopia, Nigeria, and Sudan), believed to be the largest number of persons for whom RB MDA has been stopped in a given year. Sudan and Ethiopia jointly declare a stop ivermectin MDA decision for 1.2 million persons in the cross-border Galabat/Metema onchocerciasis transmission zone. Nigeria halts MDA among 2.2 million persons in Plateau and Nasarawa States. Uganda halts MDA among 421,000 persons in two foci. Venezuela completes PTS in its largest focus (the Northeast focus) and transmission there is declared eliminated.
- **2016:** WHO verifies that Guatemala has eliminated onchocerciasis transmission. Uganda declares river blindness transmission eliminated in four foci. The Carter Center celebrates its ½ billionth treatment for NTDs. Nigeria Onchocerciasis Expert Committee (NOEC) releases a plan of action for elimination of river blindness in Nigeria. The Carter Center is selected as a semi-finalist in the MacArthur Foundation's *100&Change* grant competition with a proposal to support the NOEC plan, but is not ultimately the grant recipient.
- **2015:** WHO verifies that Mexico has eliminated onchocerciasis, and Guatemala requests verification. The Carter Center provides technical and financial assistance to help establish a national onchocerciasis expert advisory committee in Nigeria. Sudan announces that transmission has been eliminated in Abu Hamad Focus.
- **2014:** WHO verifies that Ecuador has eliminated onchocerciasis. ITFDE reviews RB/LF in Africa again (*WER* 2014). The Carter Center provides technical and financial assistance to help establish a national onchocerciasis expert advisory committee in Ethiopia.
- **2013:** The name of TCC's River Blindness Program changes to The Carter Center's River

ANNEX 2: A Timeline of the River Blindness Campaign at The Carter Center - *continued*

Blindness Elimination Program (RBEP) to reflect the paradigm shift to focusing efforts on eliminating RB transmission everywhere we work. Colombia is the first country in the world verified by WHO to be free of onchocerciasis. Ecuador applies to WHO for verification of elimination.

- **2012:** Sudan announces interruption of transmission in Abu Hamad Focus (Higazi 2013). TCC's River Blindness Program obtains our Board of Trustees' approval for an eight-year plan to interrupt RB transmission everywhere we assist by 2020. The WHO sends a verification team to Colombia to determine if the country has eliminated onchocerciasis.
- **2011:** TCC's International Task Force for Disease Eradication (ITFDE) reviews the RB and LF elimination efforts in Africa, applauds the move by APOC from RB control to elimination, and calls for better coordination of RB and LF interventions as well as with malaria bed net distribution efforts (*Weekly Epidemiological Record* 2011). An expert committee (with Frank Richards, the TCC RBP Director, as a member), meeting under the auspices of the World Bank, recommends an elimination goal for ten African countries by 2020, including Nigeria, Uganda, and Ethiopia. In late 2012, the World Bank/APOC governing board recommends onchocerciasis elimination now be APOC's goal.
- **2010:** TCC reports considerable success in RB elimination efforts in the Americas (series of *Weekly Epidemiological Record* articles) and parts of Africa. However, Katabarwa (TCC/RBP) notes a need to expand treatment into the so-called hypoendemic areas excluded by APOC's treatment strategies. He also challenges the Diawara report by noting failures of once-per-year treatment with ivermectin alone for 17 years in TCC-assisted North Province, Cameroon; TCC calls for twice-per-year treatment in these areas (Katabarwa 2011). At an international conference, TCC reports an analysis of the impact of annual ivermectin and albendazole (for lymphatic filariasis) on onchocerciasis transmission elimination in many areas of Plateau and Nasarawa States of Nigeria.
- **2009:** A key Gates Foundation-supported WHO/TDR study by Diawara (2009) conducted in Senegal and Mali (derived as an outcome of the 2002 Conference on Eradicability) proves RB elimination is possible with 17 years of ivermectin alone under some conditions in Africa. Gates, MDP, TCC, and APOC all call for "Shrinking the Map" in Africa (WHO 2009). Rakers (TCC/RBP) reports that RB programs in Nigeria would collapse without external support, questioning the 'sustainability' theory (*The Lancet* 2009).
- **2008:** The Carter Center provides technical and financial assistance to help establish a national onchocerciasis expert advisory committee in Uganda with seed support from Mr. John Moores.
- **2007:** TCC's International Task Force for Disease Eradication reviews RB eradicability and notes evidence that ivermectin alone may interrupt transmission in Africa, but that the challenge of *Loa loa* needs to be resolved. (WHO 2007). TCC/RBP agrees to assist Uganda in its new goal of national RB elimination.
- **2006:** TCC agrees to assist Sudan's declaration of national elimination, starting with enhanced efforts in the Abu Hamad focus on the River Nile (Higazi 2011, 2013).
- **2005:** Paper published by Hopkins, Richards, and Katabarwa ("Whither Onchocerciasis Control in Africa?") challenges the feasibility of indefinite RB control in Africa without continued external support; calls for governments to do more to fund their programs; and calls for further research into RB elimination in Africa (Hopkins 2005).
- **2003:** Richards co-authors a paper on mass treatment decision-making in *Loa loa* areas where onchocerciasis occurs (Addis 2003).
- **2002:** The Carter Center and WHO (with Gates Foundation support) co-host the Conference on RB Eradicability that concludes RB can be eliminated in the Americas but not yet throughout Africa with current tools (ivermectin alone). The challenge is noted of the parasite *Loa loa*, which occurs in some areas that have RB: ivermectin given to a person having *Loa*

ANNEX 2: A Timeline of the River Blindness Campaign at The Carter Center - *continued*

loa infection can result in severe nervous system reactions, including coma. The conference calls for further study in Africa and for implementers to 'go for transmission elimination' in Africa where feasible (Dadzie 2003). The Gates Foundation, in part as a result of the findings of the conference, shortly thereafter provide major grants to TCC in support the OEPA program and TDR to study using Mectizan® alone to eliminate onchocerciasis transmission in Mali and Senegal.

- **2000:** OEPA needs a 'definition of success' endorsed by WHO; with a push from President Carter to WHO DG H Gro Brundland, WHO agrees to hold an important meeting to establish certification criteria for onchocerciasis elimination (WHO 2001), which had great utility for programs in the Americas and Uganda. Richards, writing in *The Lancet*, notes the importance of the LF program in advancing the RB elimination agenda and challenges the African program to move toward onchocerciasis transmission elimination in a model similar to that in the Americas.
- **1998:** Richards, with other TCC authors (Miri and Sauerbrey), writes about opportunities for RB elimination in a special edition of the Bulletin of WHO entitled "Global Disease Elimination and Eradication as Public Health Strategies". He also writes about the history of launching of the OEPA initiative (Bull PAHO).
- **1997:** Carter Center Vice President of Health Programs, Dr. Donald Hopkins, and Richards publish "Visionary Campaign: Eliminating River Blindness" in the 1997 Encyclopedia Britannica Medical and Health Annual.
- **1996:** The Carter Center (TCC) assumed country program activities of RBF in the Americas, Nigeria, Cameroon, Sudan, and Uganda. (Ethiopia started in 2001.) Dr. Frank Richards is seconded from CDC to TCC as its RB technical director. RBF formally closes, and program funding in Africa becomes the responsibility of the newly launched African Programme for *Onchocerciasis* Control (APOC), which was jointly developed by NGOs (including RBF and TCC), WHO, and the World Bank with bilateral and multilateral donors.
- **1991:** The River Blindness Foundation (RBF) is launched by philanthropists John and Rebecca Moores of Houston, TX. RBF quickly becomes the largest source of support for Mectizan® distribution activities, funding NGOs such as Sightsavers, Helen Keller International, the International Eye Foundation, CBM, and others. It also launches the OEPA initiative in the Americas and supports the WHO-NGO coordination office for onchocerciasis in Geneva.

ANNEX 3: The Carter Center RBEP Reporting Processes

Treatment areas: An epidemiological mapping exercise is a prerequisite to identifying at-risk villages (ARVs) for mass Mectizan® treatment programs. The assessment techniques used in the mapping exercise in Africa varies from those used in the Americas. An overview of the two approaches follows.

In much of Africa, a staged village sampling scheme called Rapid Epidemiological Mapping of Onchocerciasis (REMO) was executed with assistance from the World Health Organization (WHO) to define endemic "zones" that should capture most or all villages having onchocercal nodule rates ≥ 20% in adults (which roughly corresponds to a microfilariae in skin prevalence ≥ 40%) for mass treatment. The mapping strategy is based on studies that have shown that most ocular and dermal morbidity from onchocerciasis occurs in villages where the nodule prevalence exceeds 20%.

In the first stage of REMO, survey villages are selected based on a review of large-scale maps of areas that appear to be environmentally able to support black fly breeding and, therefore, transmission of *O. volvulus*. In the second stage, villages located closest to what appears on maps to be rapidly flowing rivers (rivers near compressed contour lines on topographical maps) are called 'first line villages' and are priority for visits by field teams. In the first line villages, a convenience sample of 30-50 adults are examined for characteristic onchocercal nodules. The mean nodule prevalence for each village sample is then mapped in geographic information systems (GIS), which is used to define endemic zones where all villages are to be treated by community-directed treatment with ivermectin (CDTI). As noted, CDTI treatment zones typically are defined to include all sample villages having nodule prevalence of ≥20%.

All villages within the CDTI treatment zone are offered mass Mectizan treatment annually. The approach of REMO excludes those endemic villages from CDTI where nodule rates are under 20% (the so-called "hypoendemic areas"). Here it is important to note again that not all persons infected with onchocerciasis (as defined by their having microfilariae in their skin) have nodules. On average, nodule prevalence is 50% of mf prevalence, although this varies by geographical location. Villages in hypoendemic areas with nodule rates of <20% could still have 30% microfilaria prevalence of onchocerciasis as determined by superficial skin biopsies ('skin snips') to identify *O. volvulus* microfilaria by microscopic examination.

As the policy in Africa has shifted towards elimination (and all Carter Center-supported countries have adopted an elimination policy), the role of hypoendemic areas in *O. volvulus* transmission is being critically re-examined. Any ivermectin untreated areas are being critically reevaluated in new mapping exercises based on new mapping guidelines set by that country's national onchocerciasis elimination committee, typically using OV16 serology. Most recently the new WHO Onchocerciasis Technical Subcommittee (OTS) has suggested that OV16 testing be conducted in samples of adult residents. Proposed serological thresholds launching mass drug administration range from 2% to 5%.[3]

In the Americas, the goal from early on has been to eliminate *O. volvulus* transmission. As a result, all endemic villages are offered mass Mectizan® treatment activities every three or six months. The Onchocerciasis Elimination Program for the Americas (OEPA) casts a much broader net for mass treatment, and the African concept of excluding hypoendemic villages has never been accepted. For the Americas, where the endemic foci are characteristically smaller and more defined than in Africa, every village in known or suspected endemic areas has a rapid epidemiological assessment of 50 adults, who have both nodule examinations and skin snip

[3] WHO *Weekly Epidemiological Record* 2018; 93(47): 633–648.

microscopy to identify *O. volvulus* microfilaria in skin. Villages in which one or more persons are positive (sample prevalence ≥2%) are considered "at risk" and are recommended for the twice per year (or four times per year) mass drug administration (MDA) program. Thus, the cutoff prevalence for treatment was much lower for the Americas compared to the original REMO mapping in Africa until elimination of transmission of onchocerciasis in Africa became the focus.

Data Reporting: The Carter Center country program offices report monthly to The Carter Center Atlanta office. These reports include: 1) number of at risk villages and persons treated during the previous month (treatment reports are updated quarterly for the Americas); 2) the status of the Mectizan® tablet supply; 3) training and health education activities; 4) epidemiological assessment, research, and program monitoring activities; and 5) administrative issues. Standardized tables and graphs are used across programs. The reported treatment data are recorded by hand in village-level registers during census and directly observed treatment activities by community drug distributors (CDDs) or national Ministry of Health (MOH) personnel. It is important to emphasize that these are MOH programs and MOH data.

The accuracy of these reports is routinely confirmed with random spot checks performed primarily by Carter Center and MOH personnel, supplemented by treatment coverage surveys, which are based on statistical sampling methods with household questionnaires administered by The Carter Center and MOH staff. Recently, these data have been collected on smart phones or tablets so that results can be rapidly compiled.

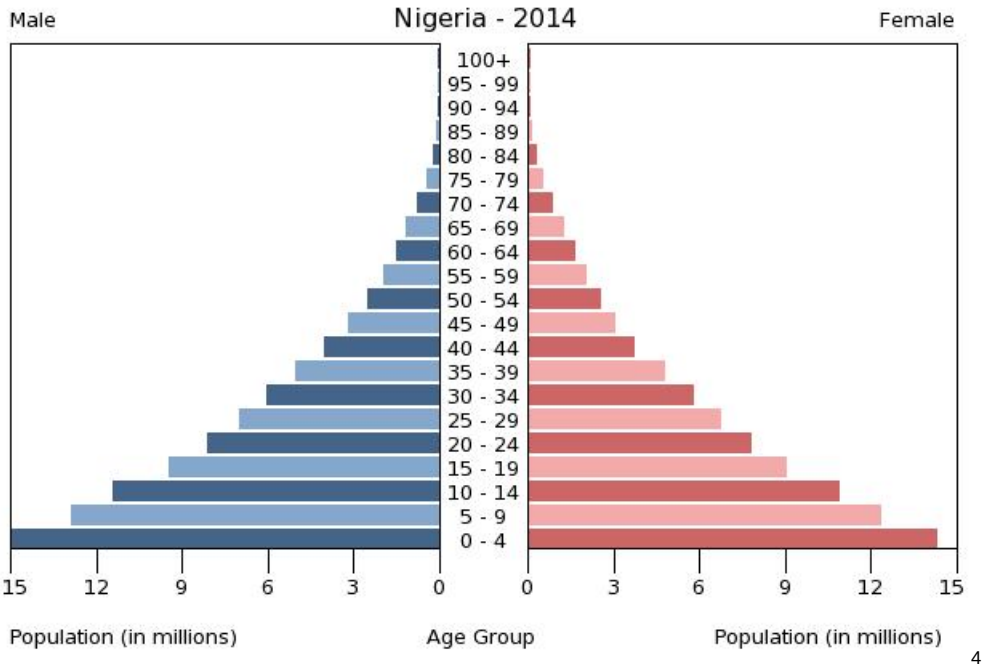
Summary reports of numbers of villages and persons treated are compiled from the village registers by the CDDs and their Community Supervisors, then forwarded to the district level. District-level summary reports are forwarded (whenever possible through MOH surveillance and reporting channels) to both the state MOH offices and the national Carter Center offices, which forward the data monthly to RBEP in Atlanta. In the Americas, the MOHs of Venezuela and Brazil report their treatments quarterly to the OEPA office in Guatemala City, which then provides a combined regional report to The Carter Center and to the Program Coordination Committee (PCC), InterAmerican Conference on Onchocerciasis (IACO) and the Pan American Health Organization (PAHO)/WHO in its regular meetings; OEPA updates are provided annually in WHO's *Weekly Epidemiological Record (WER)* articles (See Annex 9 for references to these publications). African MOHs report their annual results directly to WHO, which has recently begun producing annual summaries of African programs' onchocerciasis treatments.

The data from monthly reports are supplemented with additional information at the annual Carter Center RBEP Review held during the first quarter of the following year. At these reviews, all Carter Center program directors and partners convene to finalize treatment figures for the previous year, establish new treatment objectives for the coming year, and discuss results from monitoring and research initiatives. The Carter Center reports its final treatment figures to the Mectizan Donation Program (MDP), Merck, and the non-governmental development organization (NGDO) Onchocerciasis Coordination Group.

RBEP Treatment Indices: Treatments are reported as number of persons and number of ARVs treated for the month by district, focus, region, state, or zone, depending on the MOH's administrative structure of the country program. Cumulative treatment figures for the year are compared to Ultimate Treatment Goals (UTGs), i.e., the eligible at-risk population that is targeted for MDA. Treatment coverage is calculated with treatments as the numerator and UTG as the denominator. UTG figures assume full geographic coverage of the targeted area, and typically increase by about five percent annually to account for normal population growth. It is important to note that some programs report treatment coverage only of those villages that were reached,

rather that coverage based on all villages in the targeted area (e.g. both villages reached and those that were missed).

The eligible populations of ARVs targeted for mass distribution receive community-wide Mectizan treatment. The eligible at-risk population includes all persons living in ARVs who are eligible to receive Mectizan (i.e., those who are either ≥5 years of age, ≥15 kg in weight, or ≥90 cm in height, and who are in good health). Although RBEP mass treatment activities exclude pregnant women, these women should be treated later during the treatment year, as soon as one week or more after parturition; therefore, all adult women are included in the UTG calculation. In practice, the UTG should be established by census, adjusting from the most recent treatment rounds. The UTG is expected to be the same figure used in the annual request for tablets submitted to the Mectizan Donation Program. RBEP differs from the usual WHO approach of using total population as their treatment denominator; therefore, for standardization requirements RBEP also routinely reports both coverage of eligible population (UTG) and coverage of total population ("therapeutic coverage") in its tables to satisfy those programs' needs. The rationale for RBEP's focus on the UTG denominator has been published (Richards et al., *American Journal of Tropical Medicine and Hygiene* 2001; 65:108-14). In general, total population coverage is 16-20% less than UTG (eligible) population coverage, in accord with population pyramids in areas being served, where up to 20% of the population is under 5 years of age and so ineligible for Mectizan treatment (see example below, Nigeria where the under 5 population is 15%).



[4]

The UTG(2) and UTG(4) denominators are used by elimination programs where six-monthly ('semiannual') or quarterly treatments are delivered, respectively. The values are twice or four times the UTG and represent treatments targeted for the year, not persons. Full coverage in once-per-year treatment areas is defined as 90% achievement of the UTG. Full coverage for elimination programs is 90% of the UTG(2) in African projects, and 85% of the UTG(2) or UTG(4)

[4] Source: CIA Factbook. https://www.cia.gov/library/publications/the-world-factbook/geos/ni.html.

for OEPA. The differences in full coverage thresholds result from varying recommendations by the African and American expert committees.

In post-treatment scenarios, passive treatments with Mectizan are provided when patients present themselves in clinics within towns of endemic districts, or where large sections of the population are highly mobile and are often from non-endemic areas.

ANNEX 4: The Lymphatic Filariasis (LF) Elimination Program

Lymphatic Filariasis (LF) in Africa is caused by *Wuchereria bancrofti*, a filarial worm that is transmitted in rural and urban areas by *Anopheline* and *Culex sp*. mosquitoes, respectively. The adult worms live in the lymphatic vessels and cause vessel dysfunction, often leading to poor drainage of lymphatic fluid. Clinical consequences include a collection of lymph (lymphatic fluid) that results in swelling of limbs and genital organs (lymphoedema, "elephantiasis" and hydrocele), and painful recurrent bacterial infections ('attacks' of acute adenolymphangitis). The female worms release microfilariae, which are tiny embryonic worms that circulate in blood at night when the mosquito vectors bite. Microfilariae are picked up by mosquitoes, develop over several days into infective larvae, and are then able to be transmitted to another person when the mosquitoes bite again. Microfilariae are killed by annual single-dose combination therapy, with either Mectizan® (donated by Merck & Co., Inc.) and albendazole (donated by GSK/The Task Force for Global Health), or diethylcarbamazine (DEC, donated by Eisai Co., Ltd.) and albendazole (in areas where there is no onchocerciasis and/or *Loa loa* infection). Annual mass drug administration (MDA) prevents mosquitoes from becoming infected and, when given for a period of time (estimated to be five to six years), can interrupt transmission of *W. bancrofti* (which has no animal reservoir). In 2013, the World Health Organization (WHO) issued a 'provisional strategy' for *Loa loa* areas that includes the dual approach of albendazole monotherapy via MDA twice per year, together with long-lasting insecticidal (bed) nets (LLIN). Because of River Blindness Elimination Program (RBEP)-sponsored research, as of 2017, Nigeria has been excluded from this *Loa loa* policy and combination MDA with Mectizan®/albendazole can be used there (see below).

Nigerians suffer in disproportionate numbers from LF. Disease mapping of the country confirms that Nigeria is second globally (behind India) in human suffering from this parasite. With 761 out of 774 LGAs of 36 States and the Federal Capital Territory mapped, 572 LGAs (75%) are endemic and over 130 million Nigerians are at risk.

Elimination of LF as a Public Health Problem in Plateau and Nasarawa States: In Plateau and Nasarawa States, The Carter Center, working with the Federal Ministry of Health (FMOH) of Nigeria and with state and local government ministries, assisted in establishing an LF elimination program. The effort is based on a strategy of two pillars: 1) annual MDA combination therapy consisting of albendazole and Mectizan® to interrupt transmission of LF and 2) Morbidity Management and Disability Prevention (MMDP) programs for those suffering from lymphoedema, elephantiasis, hydrocele and adenolymphangitis. GSK and Merck donations in Nigeria allow pillar 1 MDA activities, which were the focus of the early years of the program. After disease mapping in 1998-99, the MDA program was launched in 2000. After years of high treatment coverage, together with LLIN distribution by the malaria program, LF transmission was broken in the two states in 2012. Subsequent transmission assessment surveys (TAS2 and TAS3) confirmed that children were not becoming reinfected during the post-treatment surveillance period. Additional entomology studies (showing no infected mosquitos) and LF antigen studies in adults showed that LF transmission had been eliminated. Seven million people are no longer at risk of LF as a result of a successful pillar 1 MDA program. Post-elimination surveillance continues in the two states, together with ongoing LLIN distribution, which will hopefully prevent reintroduction of the infection since the two states are surrounded by LF-endemic areas (see Figure 1 below).

The focus in Plateau and Nasarawa states is now shifting to the second pillar of the elimination of LF as a public health problem: clinical services to those suffering from LF morbidity. In 2019 RBEP began work with its ministry of health partners to quantify the burden of morbidity and to help the states strengthen primary care support and referral networks for management of

lymphedema and hydrocele surgery, as well as mental health needs (in 'Hope Club' support groups). These tasks are necessary to complete elements of the national dossier for WHO.

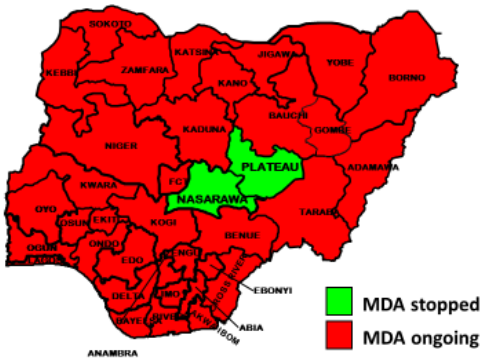


Figure 1: Elimination of LF in Plateau and Nasarawa states in 2017

***Scale-Up the LF Program in the Seven TCC-Assisted States in Southern Nigeria*:** LF treatments in Nigeria expanded to the seven states we assist in southern Nigeria as part of the United States Agency for International Development's (USAID) ENVISION project, led by Research Triangle Institute (RTI) International. Treatments started in 2014 in areas with an existing river blindness program and, in 2015, expanded to address all LF-endemic areas in the nine states. After two years of the provisional six-monthly albendazole-alone monotherapy (together with LLIN) due to *Loa loa* concerns, The Carter Center, in partnership with the federal and local governments of Nigeria, conducted a large survey in 2016. The study determined that levels of *Loa loa* were not sufficient in TCC-supported areas to preclude treatment (Emukah et al., *Am J Trop Med Hyg* 2018). Our results were favorably reviewed by the Mectizan Expert Committee; the program is now supporting annual ivermectin and albendazole MDA where needed in the seven states, rather than the less efficient and more costly twice-per-year albendazole-only approach.

LF and Malaria in Nigeria: Through a grant from the Bill & Melinda Gates Foundation, The Carter Center also conducted research on the use of LLINs alone to combat LF in Imo and Ebonyi States, areas where LF MDA with Mectizan® was at that time not possible due to the presence of *Loa loa*. Results showed that the LLINs had significant impact on mosquito infection (Richards et al., *Am J T Med Hyg* 2013). Thanks to The Global Fund Round 8 in the early 2010s, LLINs were distributed at a rate of two per household throughout the majority of Nigeria for malaria prevention; LLIN were shown to be synergistic with the MDA program in Plateau and Nasarawa states. The national malaria and lymphatic filariasis programs remain actively involved in The Carter Center-assisted program, and The Carter Center has assisted (in differing degrees) in the mass distribution of LLINs in all nine states where we work. Due in part to strong Carter Center advocacy, Nigeria launched its FMOH Guidelines for Malaria-Lymphatic Filariasis Co-implementation in Nigeria in June 2013. We continue to work on this important synergy in Carter Center-assisted states, although much less so after the Center's Malaria Program closed in 2014.

LF in Ethiopia: The much smaller LF program in Ethiopia was launched in 2008, in tandem with The Carter Center's Malaria Program, which was engaged in assisting the FMOH to distribute LLINs. The Ethiopian Malaria Program completed the mass distribution of LLINs throughout the malaria-endemic areas of Ethiopia just before the LF program (the first such program in Ethiopia) was launched. These LLINs undoubtedly have had an impact on LF transmission and the 'killing two birds with one stone' strategy of fighting malaria and LF with LLINs were the primary reason the FMOH decided to launch the LF MDA effort. With GSK support, The Carter Center assisted the Ministry of Health in launching a LF elimination pilot program in 2009 that provided roughly 75,000 treatments annually. Today, the program is delivering over 800,000 treatments each year, and several passed Treatment Assessment Surveys 1 (TAS1), stopped over 600,000 treatments and begun post-treatment surveillance (PTS) (TAS2 and TAS3).

ANNEX 5: The Schistosomiasis/Soil-Transmitted Helminthiasis Control Program

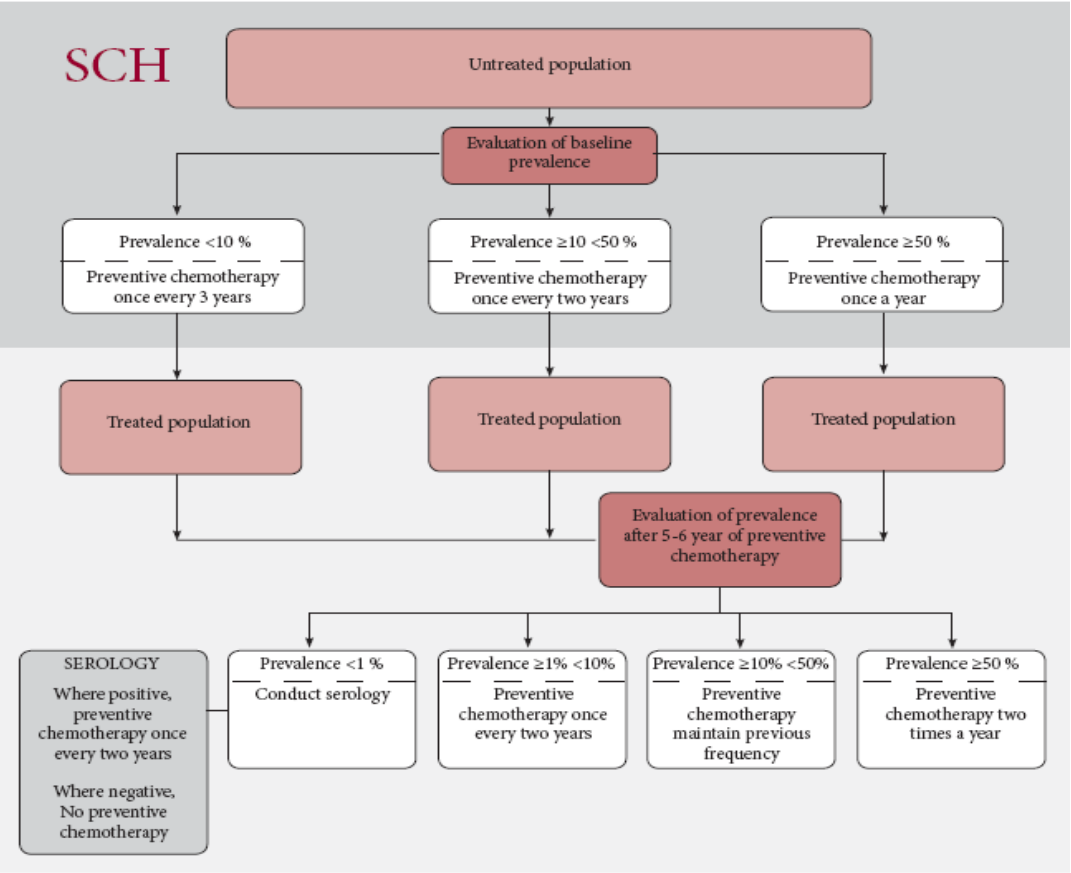
SCHISTOSOMIASIS

Schistosomiasis (SCH) is a parasitic disease acquired from skin contact with freshwater bodies where snails infected with the parasite are present. The cercarial stages of the parasite leave the snails, and swim in the water until they find an exposed person. The cercaria then penetrate the skin and migrate through the body as 'schistosomula' parasitic forms. They develop into adult male and female worms when they reach the venules of the intestines (intestinal schistosomiasis caused by *Schistosoma mansoni*) or bladder and genitals (urinary schistosomiasis caused by *S. haematobium*). It is important to note that in Africa where The Carter Center is working, SCH exists as these two different infections that have different (and often overlapping) geographical distributions, epidemiology, and disease patterns (morbidity). In both conditions, female worms lay thousands of eggs that exit the body in feces (in the intestinal form) or urine (in the urinary form). If the eggs gain access to fresh water, they hatch and release miracidiae, which swim in search of a specific type of snail (*S. mansoni* infects snails of the *Biomphalaria* species; *S. haematobium* infects *Bulinus* species). The miracidia penetrate and infect the snails, and transform and multiply, resulting in a single snail releasing thousands of cercaria, thus continuing the lifecycle.

Eggs deposited into human tissues by the adult female worms cause inflammation, organ damage, bleeding, and anemia. Although all age groups are infected, persons with the greatest number of adult worms have the greatest number of eggs in their tissues, as well as in their urine and feces. Adults most commonly suffer from liver fibrosis and esophageal bleeding (intestinal schistosomiasis) or bladder and cervical cancer (urinary schistosomiasis). School-aged children (ages 5 to 14) may have abdominal pain, anemia, and (in urinary schistosomiasis) bloody urine. They act as the main disseminators by contaminating water with excreta. Mass Drug Administration (MDA) with the safe and effective oral medicine praziquantel can significantly reduce schistosomiasis morbidity. Praziquantel kills the adult worms, reduces the number of eggs that accumulate in tissues and, as a result, reduces the disease (morbidity) associated with schistosomiasis. The Merck KGaA/World Health Organization (WHO) donation of praziquantel is given only for MDA in school-aged children, although adults and preschool-aged children would also benefit from treatment in endemic areas.

The Carter Center's SCH programs follow WHO guidelines for disease (morbidity) control (shown below). Note that the guidelines may call for praziquantel preventive chemotherapy once every 2 – 3 years, depending on parasite prevalence in a district. For this reason, treatment numbers in the same state can be very different from year-to-year, and training and logistics become much more complicated compared to annual or twice-per-year treatment. The guidelines are currently in the process of revision.

ANNEX 5: The Schistosomiasis/Soil-Transmitted Helminthiasis Control Program - *continued*

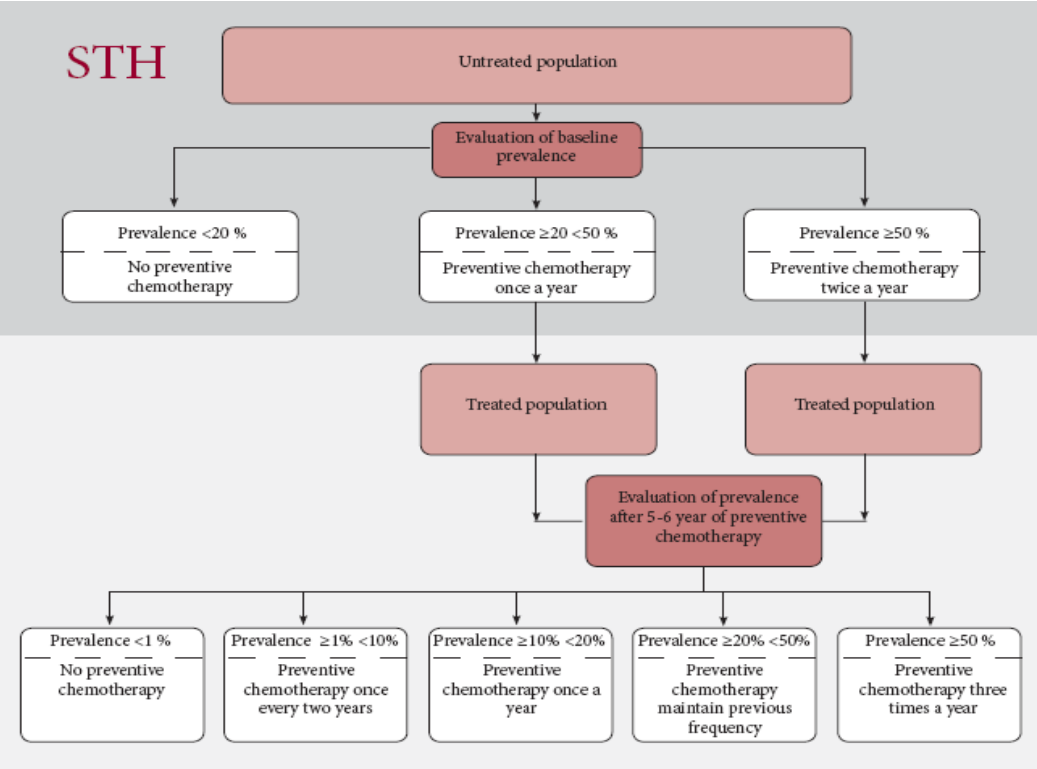


Transmission is unlikely to be interrupted by this paradigm of MDA targeted at school-aged children because: 1) transmission occurs in all age groups; 2) praziquantel does not kill the migrating schistosomula forms, thus single dose treatment in children in highly endemic areas is unlikely to be curative; and 3) until open defecation and urination (or reduction of release of raw sewage into fresh water) are halted through construction and use of sanitation systems, MDA will have little to no impact on infected snails (which live for many months) and infected water. In other words, persons treated are either not cured of their schistosomula (developing) infections, and/or they become reinfected when they reenter the contaminated water.

SOIL-TRANSMITTED HELMINTHS

Soil-Transmitted Helminthiasis (STH) is caused by a group of four different intestinal worms that infect humans: *Ascaris lumbricoides* (roundworm), *Trichuris trichiura* (whipworm), *Ancylostoma duodenale,* and *Necator americanus* (hookworms). STH are among the most common infections worldwide, and heavy infections lead to developmental delay, malnutrition, intestinal obstruction, and anemia (depending on the infecting species). As with SCH, school-aged children are usually the most heavily infected with these worms, with the exception of hookworms, which have their heaviest infections in adults.

ANNEX 5: The Schistosomiasis/Soil-Transmitted Helminthiasis Control Program - *continued*



Transmission of soil-transmitted helminths occurs through feces. Eggs from the adult females are passed into the environment in feces, where they become infective within days (hookworm and whipworm) or weeks (roundworm). Once in the environment, infective whipworm and roundworm eggs reach their next human host via human ingestion of fecally-contaminated food or water. Hookworm eggs hatch in soil and the resultant larvae infect humans by penetration of the skin (often entering via bare feet).

Once in the human, hookworm larvae migrate through the circulatory system until they reach the lungs. From there, they pass through the trachea and mouth where they are ingested, traveling then to the intestines. They mature, mate, and release eggs within 6-8 weeks. Whipworm and roundworm eggs hatch into larvae in the intestine and remain there through adulthood.

Heavy worm infections result in blood loss which can lead to anemia and hypoproteinemia. In children, this can lead to poor physical and developmental growth, stunting, and decreased mental acuity. In adults, hookworm-associated anemia reduces productivity and can be especially dangerous in reproductive-aged (menstruating) women. Pulmonary complications can occur due to migration of roundworm or hookworm larvae through the lungs and, in the case of ascaris, bowel obstructions can occasionally lead to death.

The current WHO guidelines for STH (see above) are in many ways similar to those of SCH in that they focus on providing treatment to school-aged children. STH MDA programs are for morbidity control; transmission will not be interrupted until open defecation is halted through deployment and the use of sanitary systems. Although STH treatments can be given (as with SCH) once every two years in a district, guidelines differ from SCH in that they commonly call for

ANNEX 5: The Schistosomiasis/Soil-Transmitted Helminthiasis Control Program - *continued*

MDA twice per year. As with SCH, the result is that STH treatment numbers in the same state can vary greatly from district to district and from year-to-year.

It is notable that the different species of worms have different sensitivities and cure rates from the MDA regimens provided. Albendazole is superior to mebendazole. Roundworm is most sensitive to treatment, while whipworm is least sensitive. The ivermectin/albendazole combinations given for LF improve whipworm cure rates.

The challenges for TCC Nigeria in implementing schistosomiasis and STH programs include: 1) complex WHO guidelines that result in different regimens tailored to district epidemiology (alternating year treatment schedules for schistosomiasis up to every third year compared with twice-per-year treatment programs for STH in some areas); 2) a focus on a Ministry of Education (school-based) approach rather than the traditional Ministry of Health (community-based) platform, which is more experienced at MDA activities; 3) a focus on teachers (in schools) rather than community distributors (house to house); 4) exclusion of potentially infected persons, including preschool children, unenrolled school-aged children (especially girls), and adults; 5) algorithms with thresholds statistically indistinguishable from one another; 6) mapping based on averages resulting in exclusion of communities that need interventions; 7) difficult calculations of coverage due to challenges with denominator determinations; 8) difficulty in justifying the closure of a longstanding distribution infrastructure that works well (community-based) to start a new approach (school-based); and 9) loss of high-quality STH control resulting from community-wide LF MDA with the most potent STH treatment (ivermectin and albendazole) when LF programs that pass Treatment Assessment Surveys (TAS) assessments cease treatment.

The written description of SCH/STH work under USAID's Act to End NTDs | East program, led by RTI International, focuses on "mainstreaming" the two diseases into the large health care delivery system and to abandon the vertical MDA approach to control. We believe it is likely that there will be less support in the near future for the TCC SCH/STH program. Accordingly, in Local Government Areas (LGAs) where the River Blindness (RB) or Lymphatic Filariasis (LF) platform does not exist, we are developing plans to transfer support of MDA fully to the Ministries of Health (MOH) and Education.

ANNEX 6: Publications by Year Authored or Coauthored by RBEP Personnel

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