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CARTER CENTER

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SUMMARY
2018 PROGRAM REVIEW
RIVER BLINDNESS ELIMINATION PROGRAMS
ETHIOPIA, NIGERIA, OEPA, SUDAN, AND UGANDA
MARCH 25-27, 2019
THE CARTER CENTER
ATLANTA, GA

OCTOBER 2019

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And to many others, our sincere gratitude.

*We appreciate the support of the donors listed here, whose funding was utilized in 2018 for the activities described in these proceedings.

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ACRONYMS

ACT	Artemisinin Combination Therapy
AJTMH	American Journal of Tropical Disease and Hygiene
APOC	African Program for Onchocerciasis Control
ATP	Annual Transmission Potential
ARVs	At Risk Villages
CDC	Centers for Disease Control and Prevention
CDD	Community Directed Distributors
CDHS	Community-Directed Health Supervisor
CDTI	Community-Directed Treatment with Ivermectin
CS	Community Supervisors
DEC	Diethylcarbamazine
DRC	Democratic Republic of Congo
EOEEAC	Ethiopia Onchocerciasis Elimination Expert Advisory Committee
EPHP	Elimination as a Public Health Problem
ELISA	Enzyme-linked immunosorbent assay
ESPEN	Expanded Special Project for Elimination of NTD's
FCT	Federal Capital Territory
FLHFS	Frontline Health Facilities
FMOH	Federal Ministry of Health
FTS	Filarial Test Strip
GSK	GlaxoSmithKline
HDA	Health Development Army
HE	Health Education
HEW	Health Extension Worker
IACO	InterAmerican Conference on Onchocerciasis
IHA	Indigenous Health Agent
IRB	Institutional Review Board
ITFDE	International Task Force for Disease Eradication
IVT	International Verification Team
KAP	Knowledge Attitude & Perceptions
kdr	Knockdown Resistance
KGaA	E-Merck
LCIF	Lions Clubs International Foundation
LF	Lymphatic Filariasis
LGA	Local Government Areas
LLIN	Long Lasting Insecticidal (bed) Net
MDA	Mass Drug Administration
MDP	Mectizan® Donation Program
MEC	Mectizan® Expert Committee

ACRONYMS (Continued)

Mectizan®	Ivermectin (Merck & Co., Inc., product name)
MITOSATH	Mission to Save the Helpless
MMDP	Morbidity Management and Disability Prevention
MOH	Ministry/Ministries of Health
MSD	Merck & Co., Inc.
NGDO	Non-Governmental Development Organization
NGO	Non-Governmental Organization
NOEC	The Nigerian Onchocerciasis Elimination Committee
NOTF	National Onchocerciasis Task Force
NTDs	Neglected Tropical Diseases
OEPA	Onchocerciasis Elimination Program for the Americas
OTS	Onchocerciasis Technical Subgroup/Subcommittee
PAHO	Pan American Health Organization
PCC	Program Coordinating Committee of OEPA
PCR	Polymerase Chain Reaction
PES	Post-Elimination Surveillance
PTS	Post-Treatment Surveillance
QGIS	Geographical Information System
RB	River Blindness
RBF	River Blindness Foundation
RBEP	River Blindness Elimination Program
RDT	Rapid Diagnostic Test
REMO	Rapid Epidemiological Mapping of Onchocerciasis
RLMF	Reaching the Last Mile Fund
RSS	Republic of South Sudan
RTI	Research Triangle Institute
SACAICET	Servicio Autónomo Centro Amazónico de Investigación y Control de Entermedades
SE/SS	South East/South South
SAE	Severe Adverse Events
SCH	Schistosomiasis
SIZ	Special Intervention Zone
SNNPR	Southern Nations, Nationalities and People's Region
STH	Soil Transmitted Helminths
SV	Sentinel Village
TAS	Treatment Assessment Survey
TCC	The Carter Center
TDA	Triple Drug Administration
TDR	Tropical Disease Research
UOEEAC	Ugandan Onchocerciasis Elimination Expert Advisory Committee

ACRONYMS

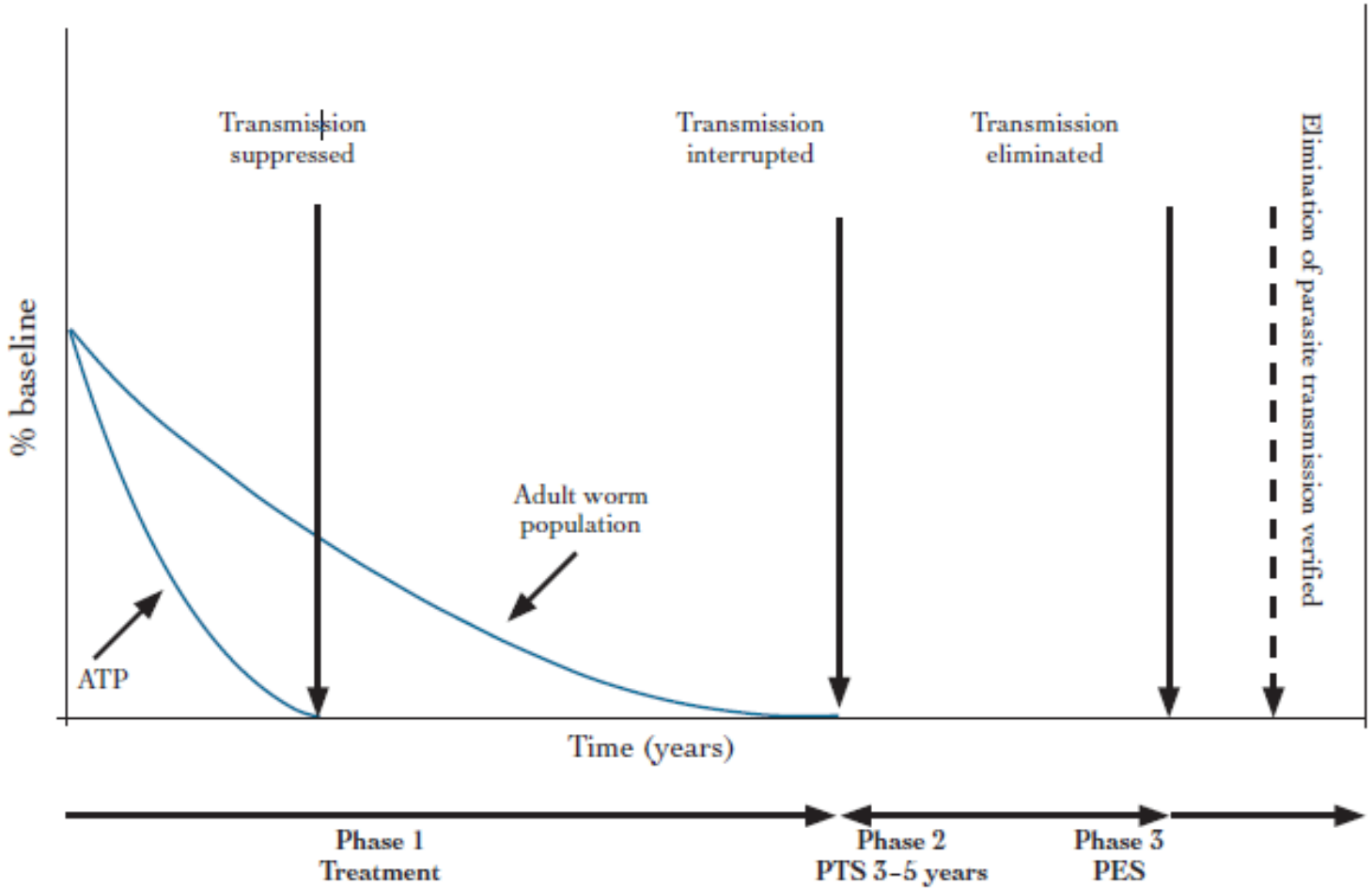
USAID	United States Agency for International Development
USF	University of Southern Florida
UTG	Ultimate Treatment Goal
WER	Weekly Epidemiological Record
WHO	World Health Organization
YFA	Yanomami Focus Area

Figure ES1

2018 River Blindness Elimination Program Review Participants

Figure ES2

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

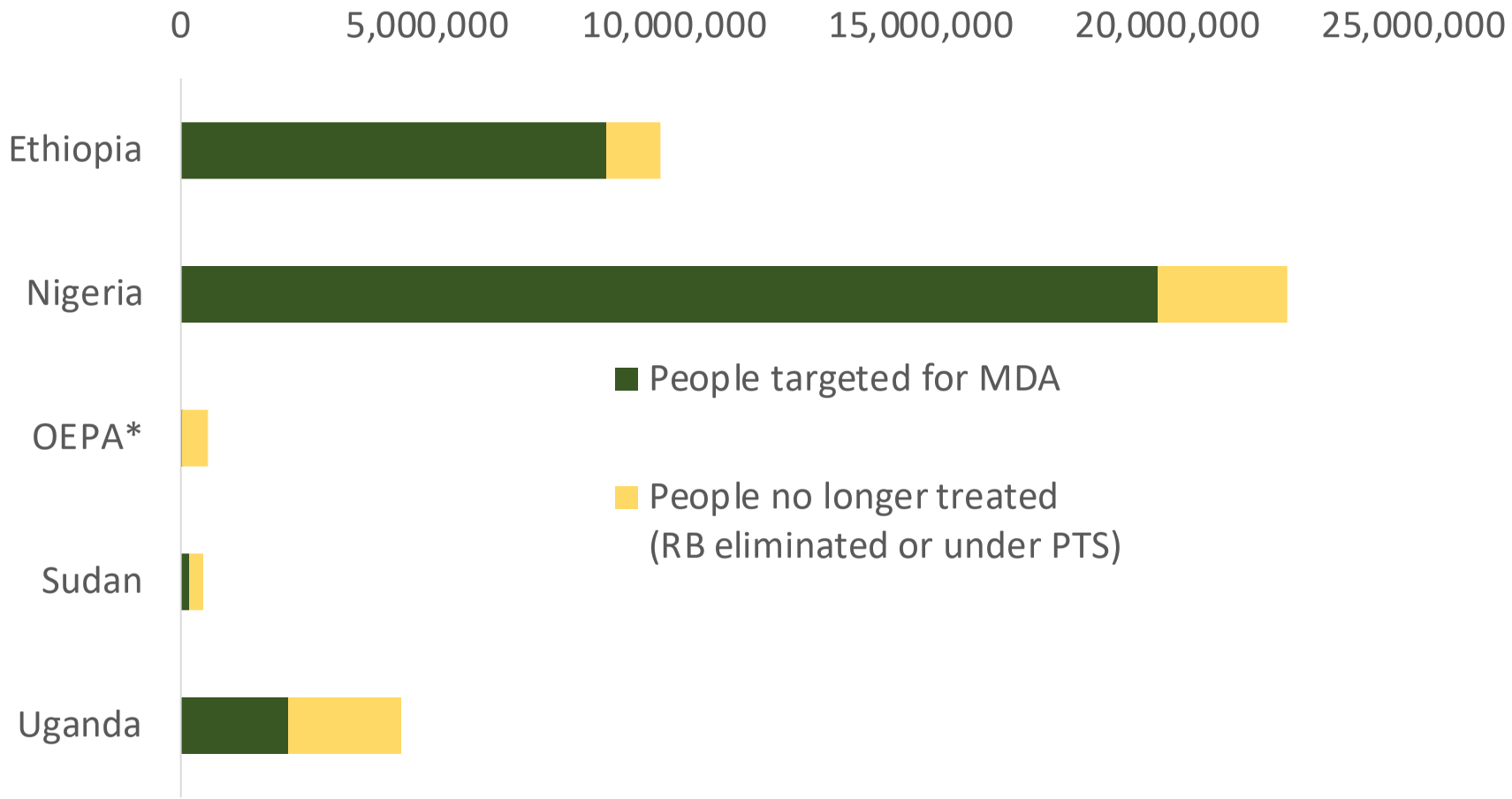


ATP, annual transmission potential; PES, post-elimination surveillance; PTS, post-treatment surveillance

*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 ES3

As a Result of Our RB Elimination Partnership, 6.8 Million People No Longer Need Mectizan® treatment in Carter-Center-assisted Areas in Nine Countries



*Representing Colombia, Ecuador, Guatemala, Mexico and Venezuela

Figure ES4

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

RIVER BLINDNESS		
Country	Populations NOT on MDA in 2018 (both eliminated and on PTS)	Stopped MDA in 2018
ETHIOPIA	1,100,000	
OEPA	538,517	
NIGERIA	2,618,861	
SUDAN	264,811	
UGANDA	2,298,715	311,844
TOTAL	**6,820,904**	**311,844**

Note: Uganda's figure excludes the eliminated Victoria focus (not TCC assisted, eliminated in the 1960s), population 2.7 million

LYMPHATIC FILARIASIS		
Country	Populations NOT on MDA in 2018 (both eliminated and on PTS)	Stopped MDA in 2018
ETHIOPIA	431,495	
NIGERIA	7,258,307	
TOTAL	**7,689,802**	

Figure ES5

2018 Mectizan® Mass Treatment Figures for Carter Center RBEP-Assisted Areas in Africa, Latin America (OEPA) and Sudan

2018 RBEP Mectizan® Treatment Figures

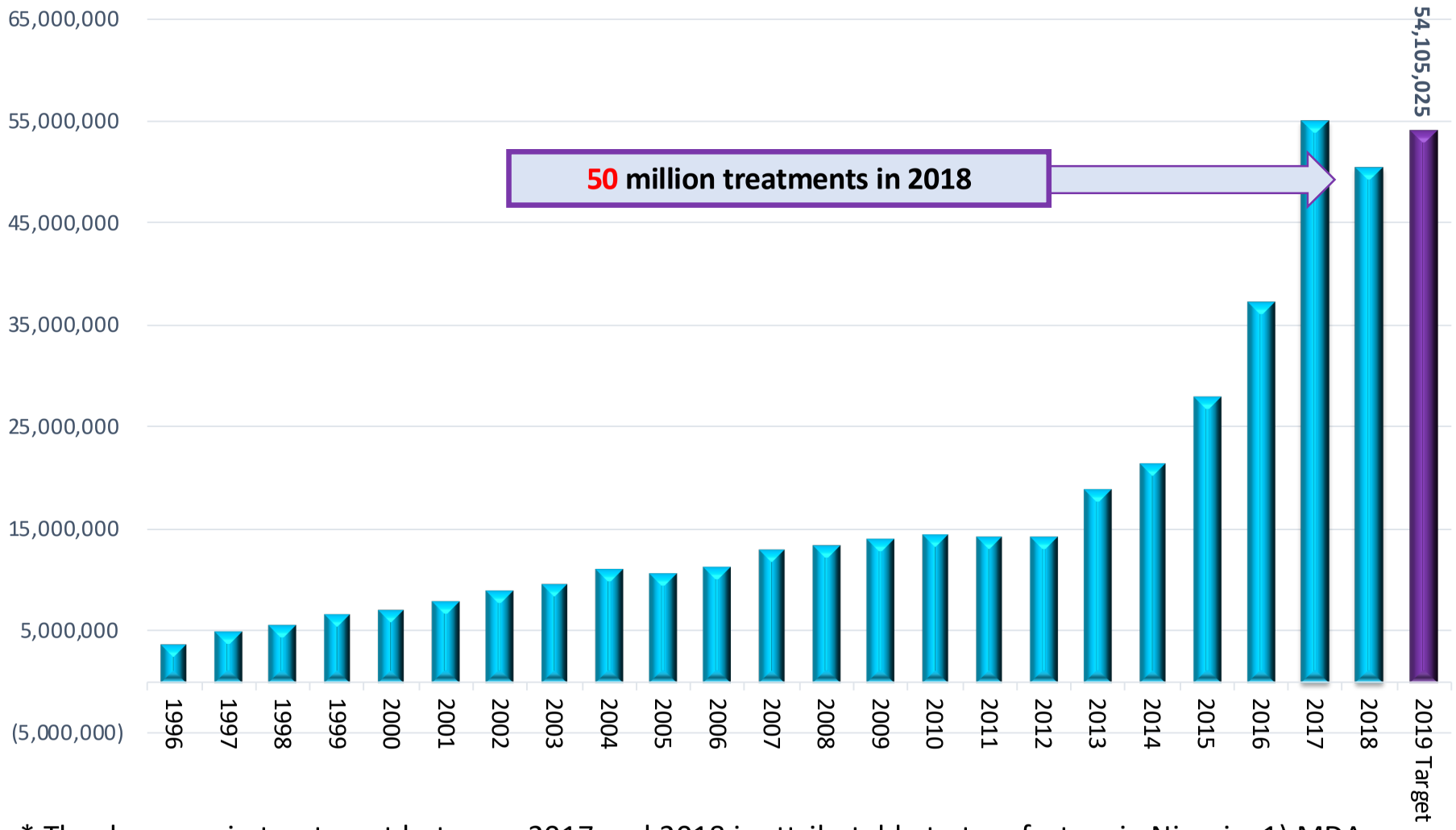
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	TOTAL	UTG	% UTG	% All RBEP
Nigeria																
Treatments	-	-	-	-	2,985	72,877	99,188	1,167,667	1,901,416	225,144	35,258	1,999,063	5,503,598	*6,572,636*	**84%**	**11%**
Villages treated	-	-	-	-	11	132	140	2,337	1,444	338	510	1,530	6,442	*5,636*	**114%**	**10%**
Nigeria 2x																
Treatments	-	-	-	-	8,765	1,569,614	2,354,856	2,878,048	3,841,452	444,208	2,857,052	9,200,707	23,154,702	*25,142,700*	**92%**	**46%**
Villages treated	-	-	-	-	16	2,358	3,816	5,270	3,507	381	1,387	13,308	15,022	*15,530*	**97%**	**22%**
Uganda 2x																
Treatments	-	-	-	78,884	866,219	863,470	44,965	-	-	1,113,032	709,535	108,932	3,785,037	*4,025,827*	**94%**	**8%**
Villages treated	-	-	-	259	2,090	1,454	60	-	-	2,356	1,377	130	3,863	*3,937*	**98%**	**6%**
OEPA 2x																
Treatments	-	-	-	-	-	19,811	-	-	-	-	19,578	-	39,389	*43,570*	**90%**	**0%**
Villages treated	-	-	-	-	-	-	-	-	-	-	-	-	-	*182*	**0%**	**0%**
OEPA 4x																
Treatments	-	-	3,773	-	-	4,336	-	-	3,065	-	4,428	-	15,602	*21,520*	**73%**	**0%**
Villages treated	-	-	-	-	-	-	-	-	-	-	-	-	-	*359*	**0%**	**0%**
Ethiopia 2x																
Treatments	-	-	143,440	241,627	-	4,265,031	4,538,507	-	-	-	2,300,105	6,278,512	17,767,222	*17,896,759*	**99%**	**35%**
Villages treated	-	-	-	1,475	-	22,325	25,671	-	-	-	-	33,871	41,671	*47,421*	**88%**	**62%**
Sudan																
Treatments	-	69,200	-	-	-	-	-	-	-	-	-	-	69,200	*71,700*	**97%**	**0%**
Villages treated	-	29	-	-	-	-	-	-	-	-	-	-	29	*29*	**100%**	**0%**
TOTALS																
Treatments	**-**	**69,200**	**147,213**	**320,511**	**877,969**	**6,795,139**	**7,037,516**	**4,045,715**	**5,745,933**	**1,782,384**	**5,925,956**	**17,587,214**	**50,334,750**	***53,774,712***	**94%**	
Villages treated	**-**	**29**	**-**	**1,734**	**2,117**	**26,269**	**29,687**	**7,607**	**4,951**	**3,075**	**3,274**	**48,839**	**67,027**	***73,094***	**92%**	

Cumulative RBEP-Assisted Treatments (1996 - 2018): 383,586,186

2018 Mass Treatments	50,334,750
2018 Passive Treatments	148,522
2018 TOTAL TREATMENTS	**50,483,272**

Figure ES6

RBEP-Assisted Programs: Mectizan® Treatments 1996 – 2018 and 2019 Target



* The decrease in treatment between 2017 and 2018 is attributable to two factors in Nigeria: 1) MDA was stopped in two states, and 2) the ongoing TCC assisted RB MDA programs had a Mectizan® shortage.

Figure ES7

Carter Center River Blindness Elimination Programs
Cumulative Treatments 1996-2018

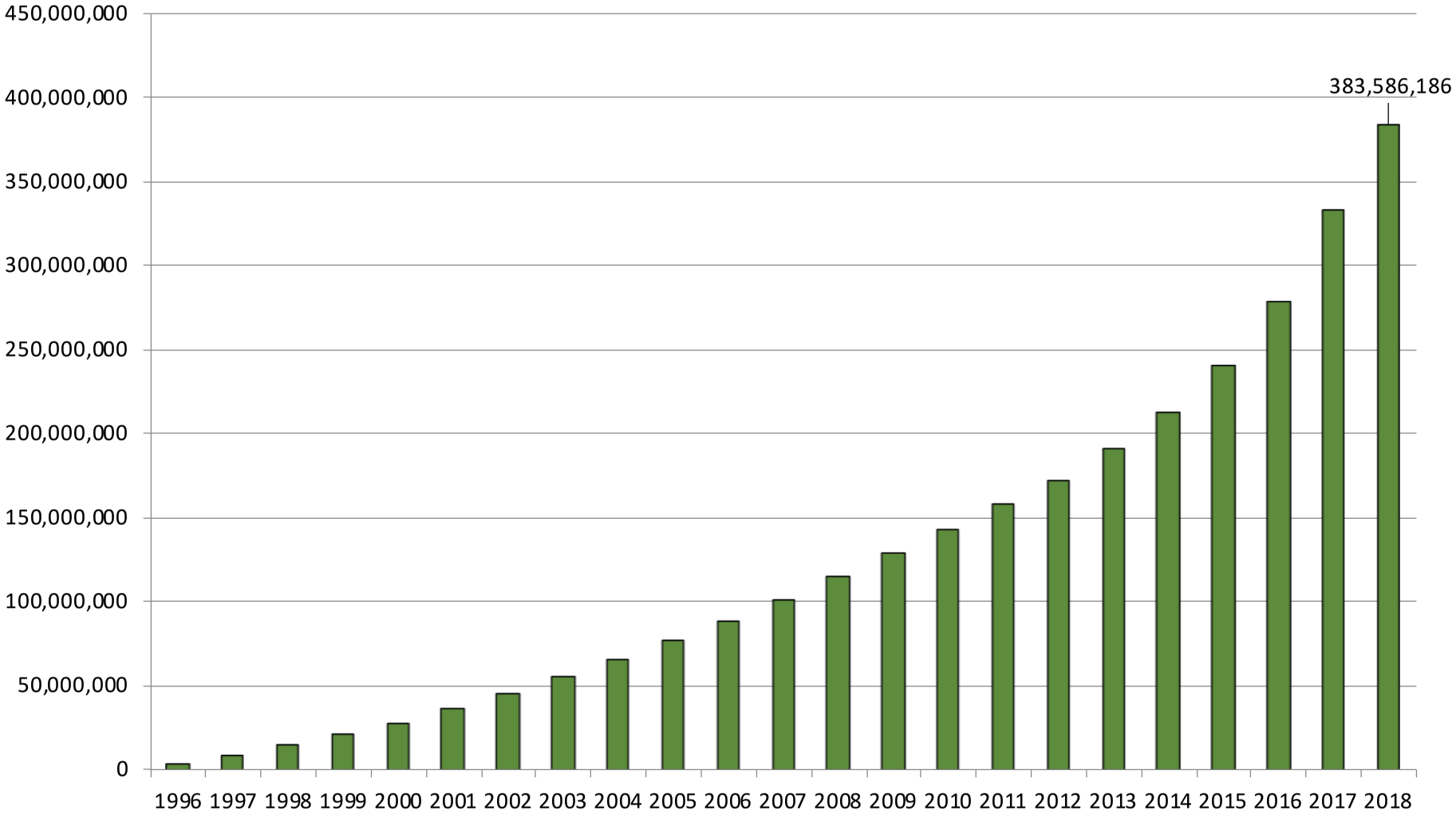


Figure ES8

Carter Center-Assisted Programs: 1996 – 2018 Mectizan® Treatments by Program

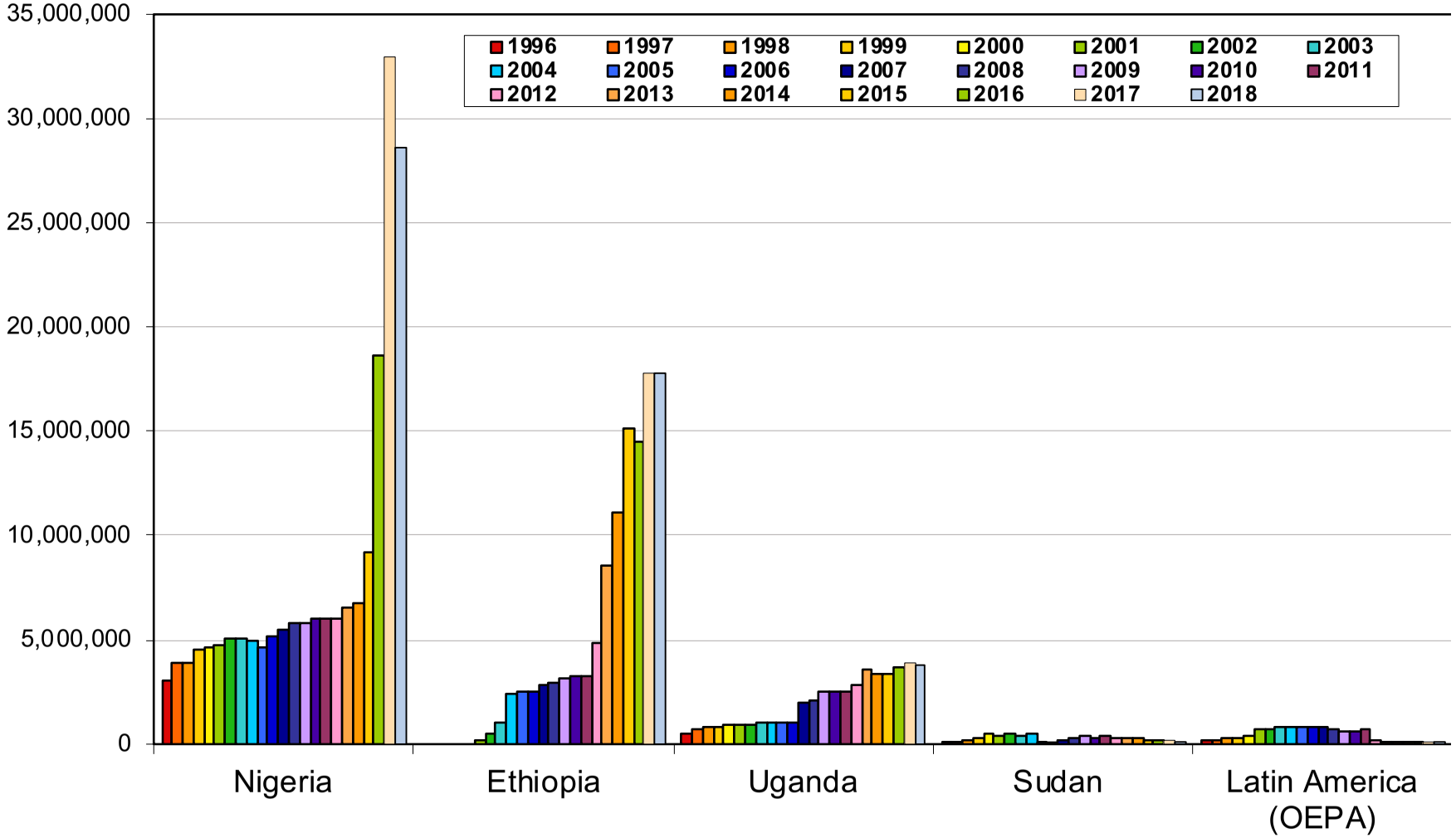
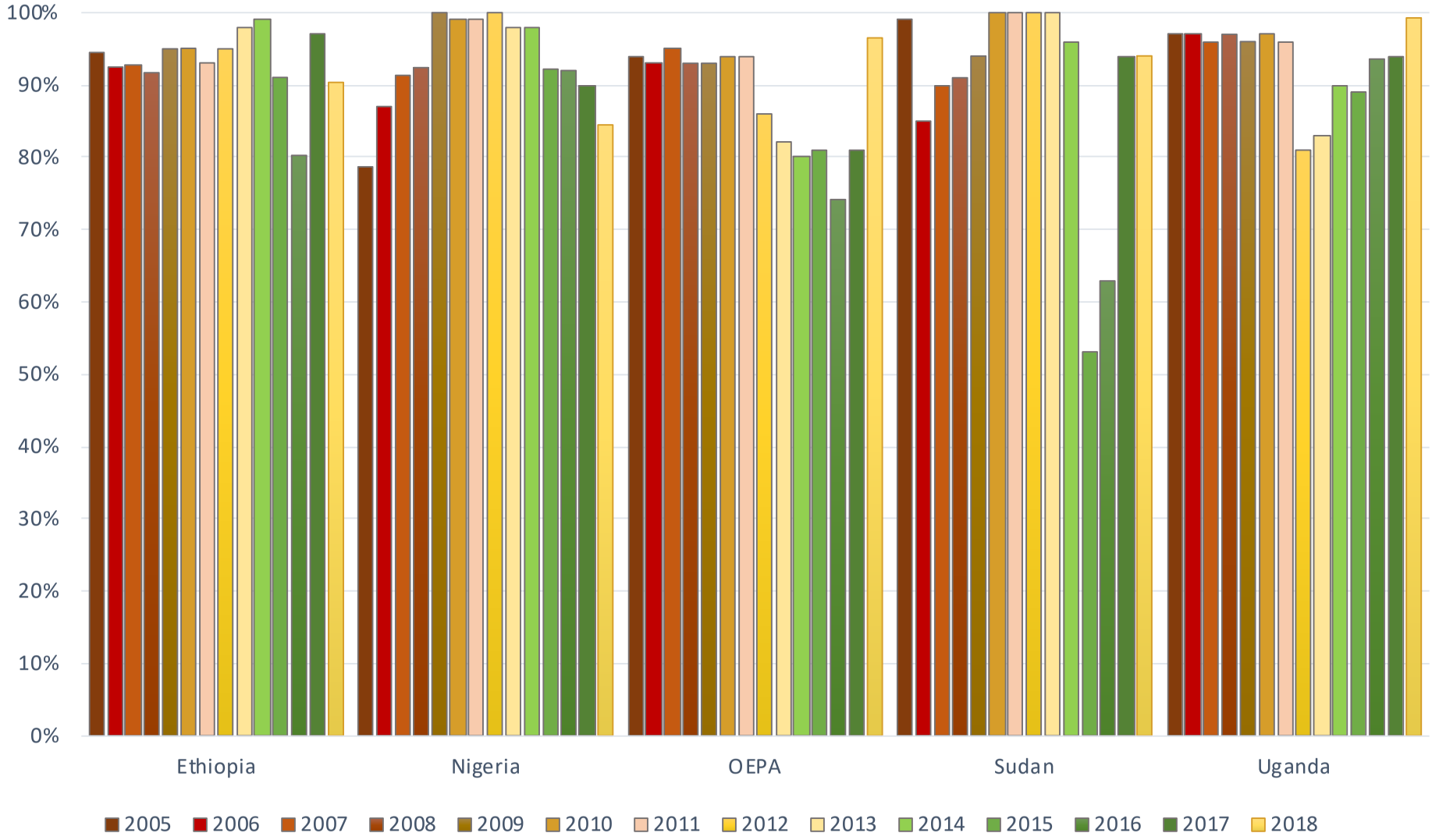


Figure ES9

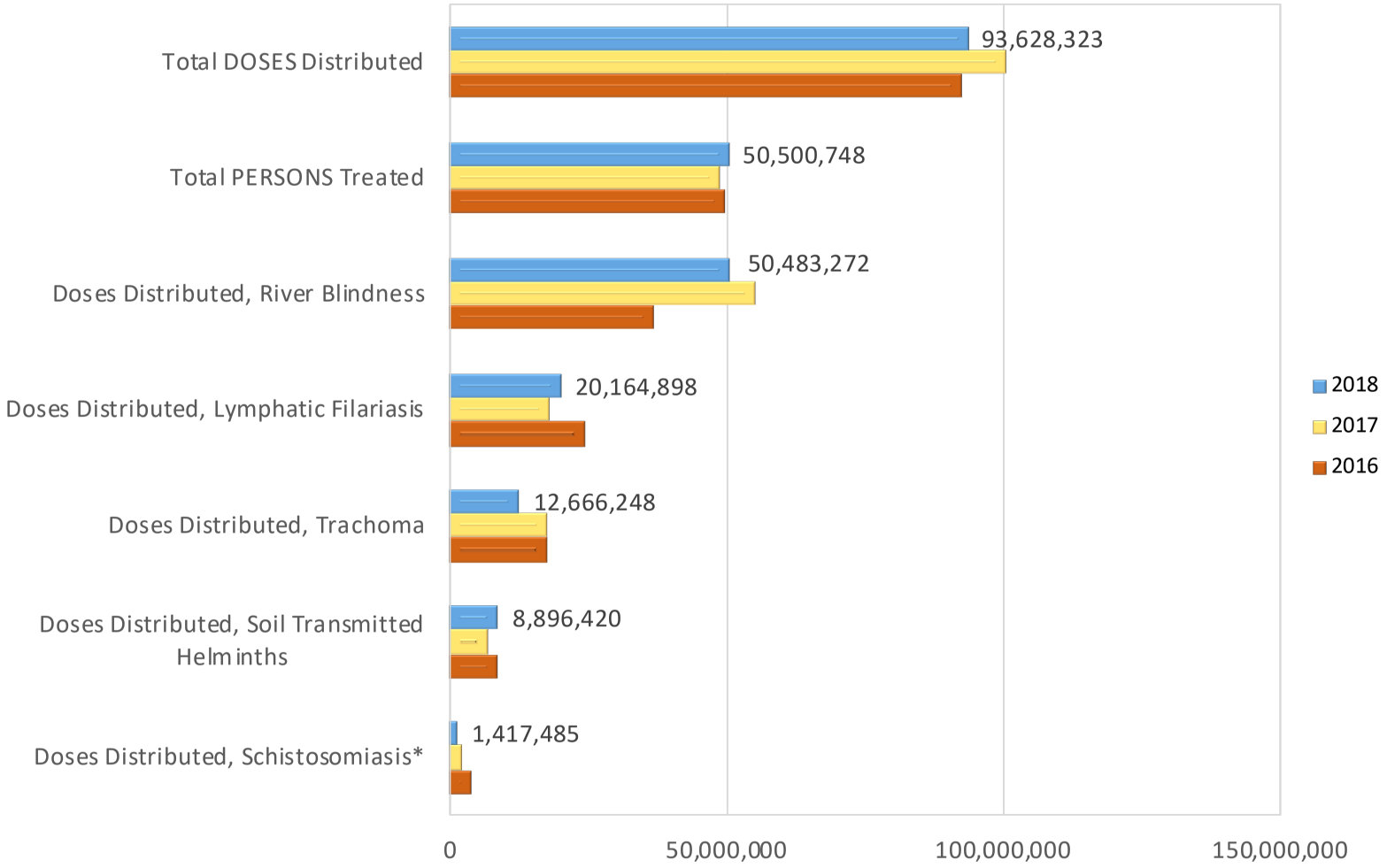
River Blindness Program: Reported Treatment Coverage (eligible population) by Project: UTG, UTG(2), or UTG(4) 2005 – 2018



The low 2018 coverage in Nigeria was due to Mectizan® shortage

Figure ES10

Carter Center-supported Treatment Doses, and Persons Treated, for Neglected Tropical Diseases, 2016 – 2018



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 2018 treatments was due to praziquantel shortage s in Nigeria

Figure ES11

Community-Directed Distributors (CDDs) Trained 2004 – 2018 and 2019 Total Targets

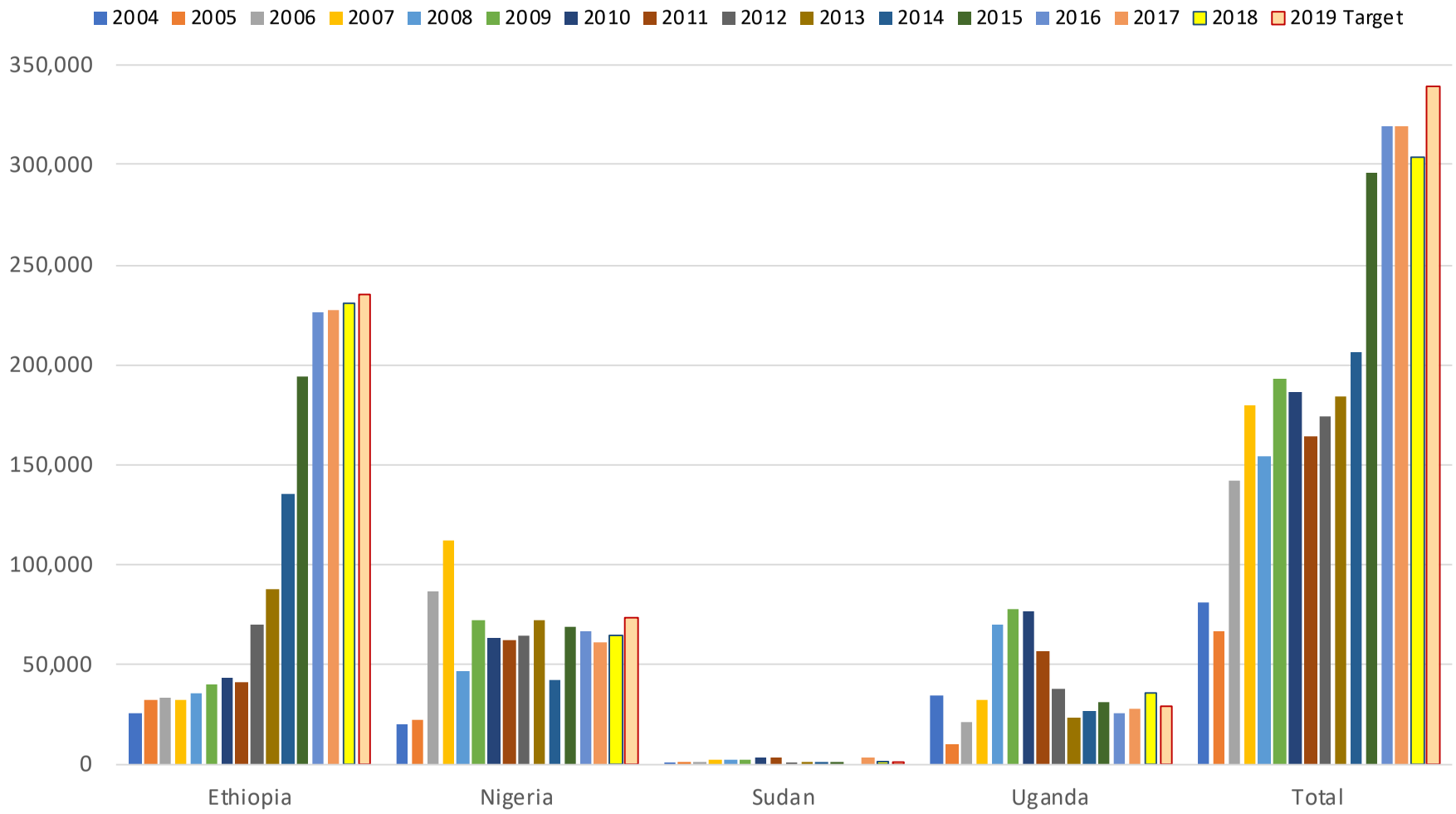
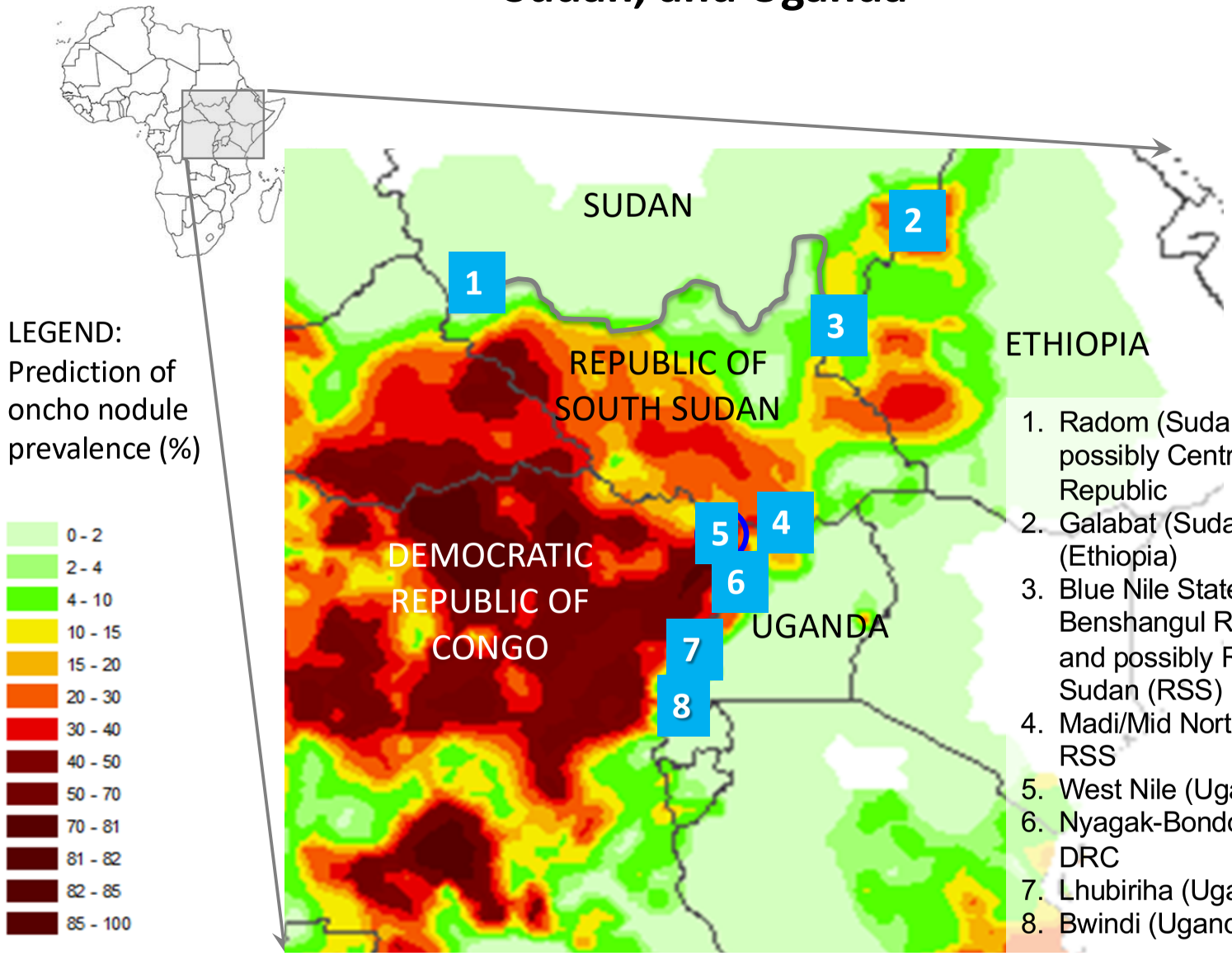


Figure ES12

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



Map source: APOC

Figure ES13

Nigeria: Carter Center Assisted River Blindness (RB), Lymphatic Filariasis (LF), Soil Transmitted Helminths (STH) and Schistosomiasis (SCH) Treatments 2012 – 2018 and 2019 Targets

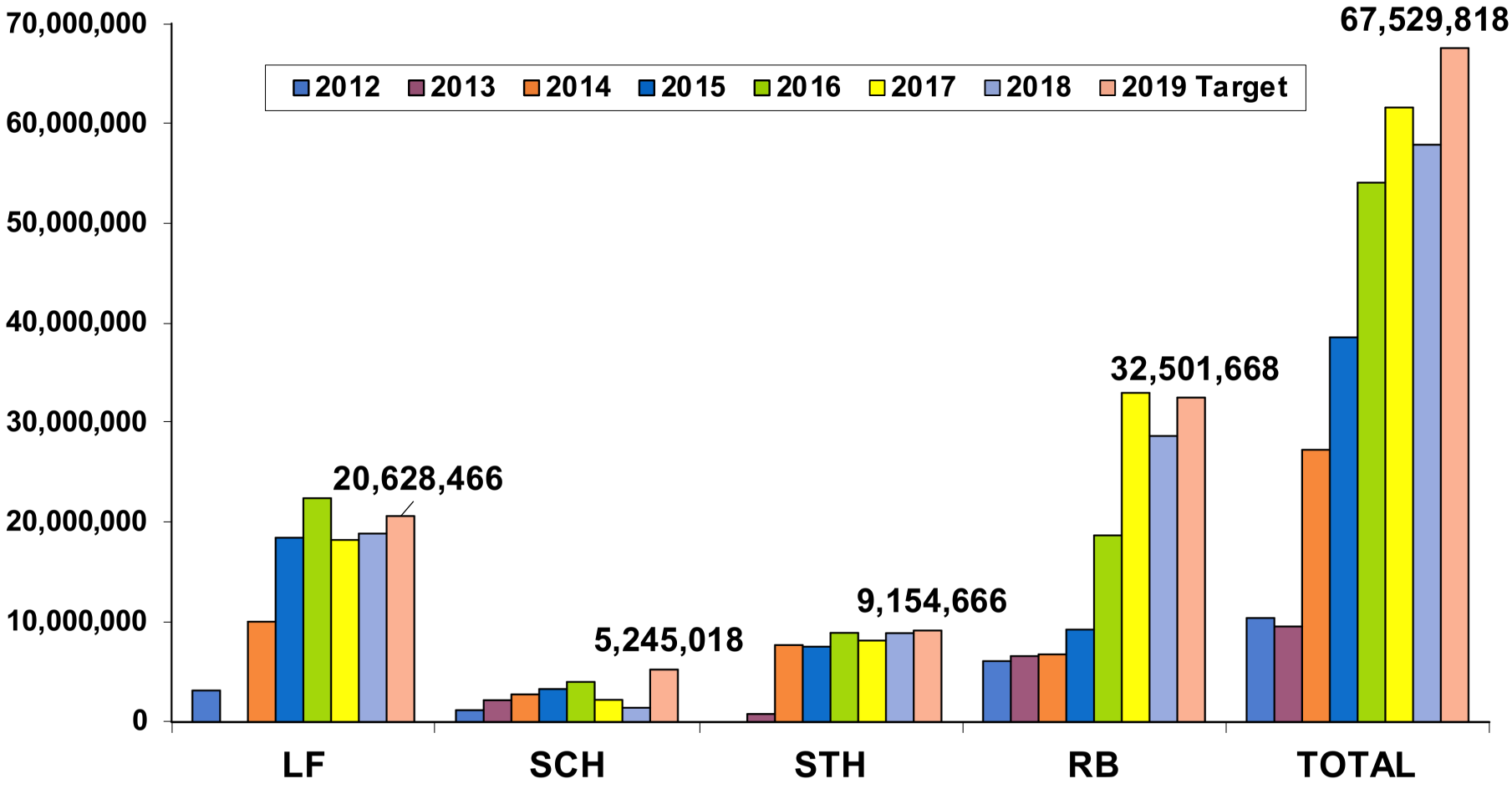
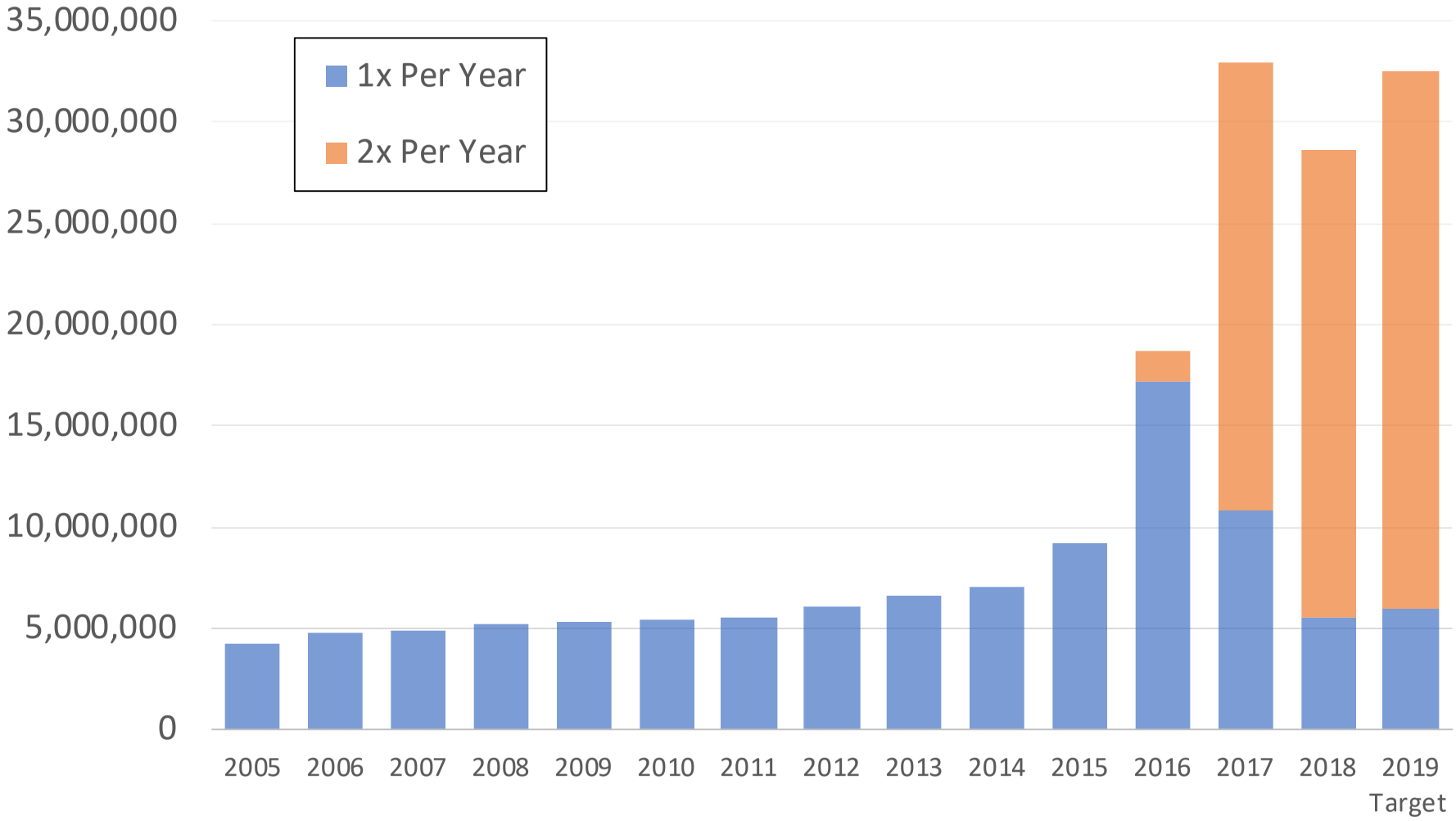


Figure ES14

Nigeria: Rapid Transition from Annual to Semiannual Mectizan® Treatments in RBEP-assisted Areas*



* The decrease in treatment between 2017 and 2018 is attributable to two factors: Plateau and Nasarawa states stopped MDA, and the program had a Mectizan® shortage due to an incorrect order.

Figure ES15

Status of Onchocerciasis Elimination in Nigeria (2017 & 2018)

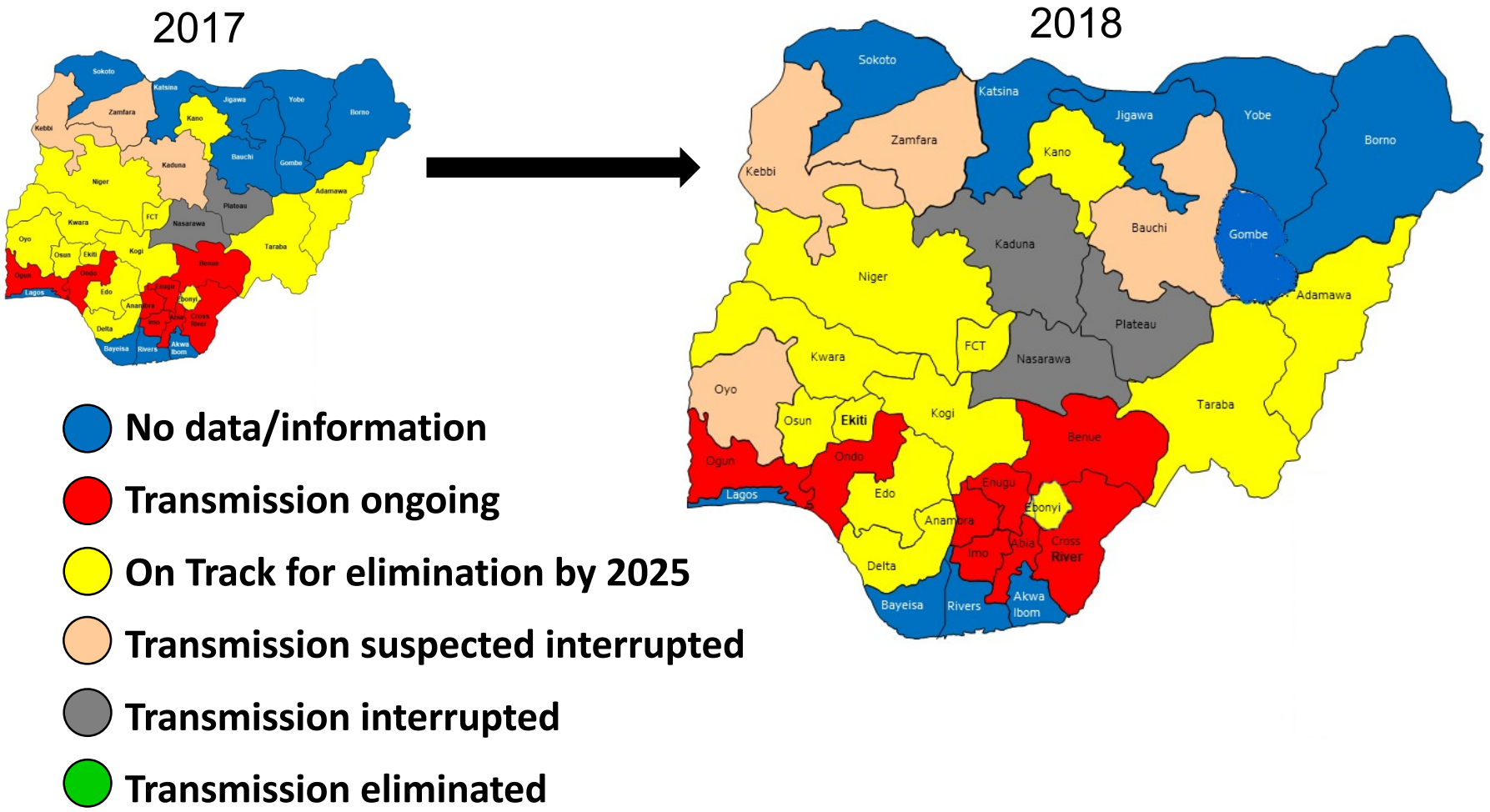


Figure ES16

1989-2018 History of Mectizan® Treatment in the Americas

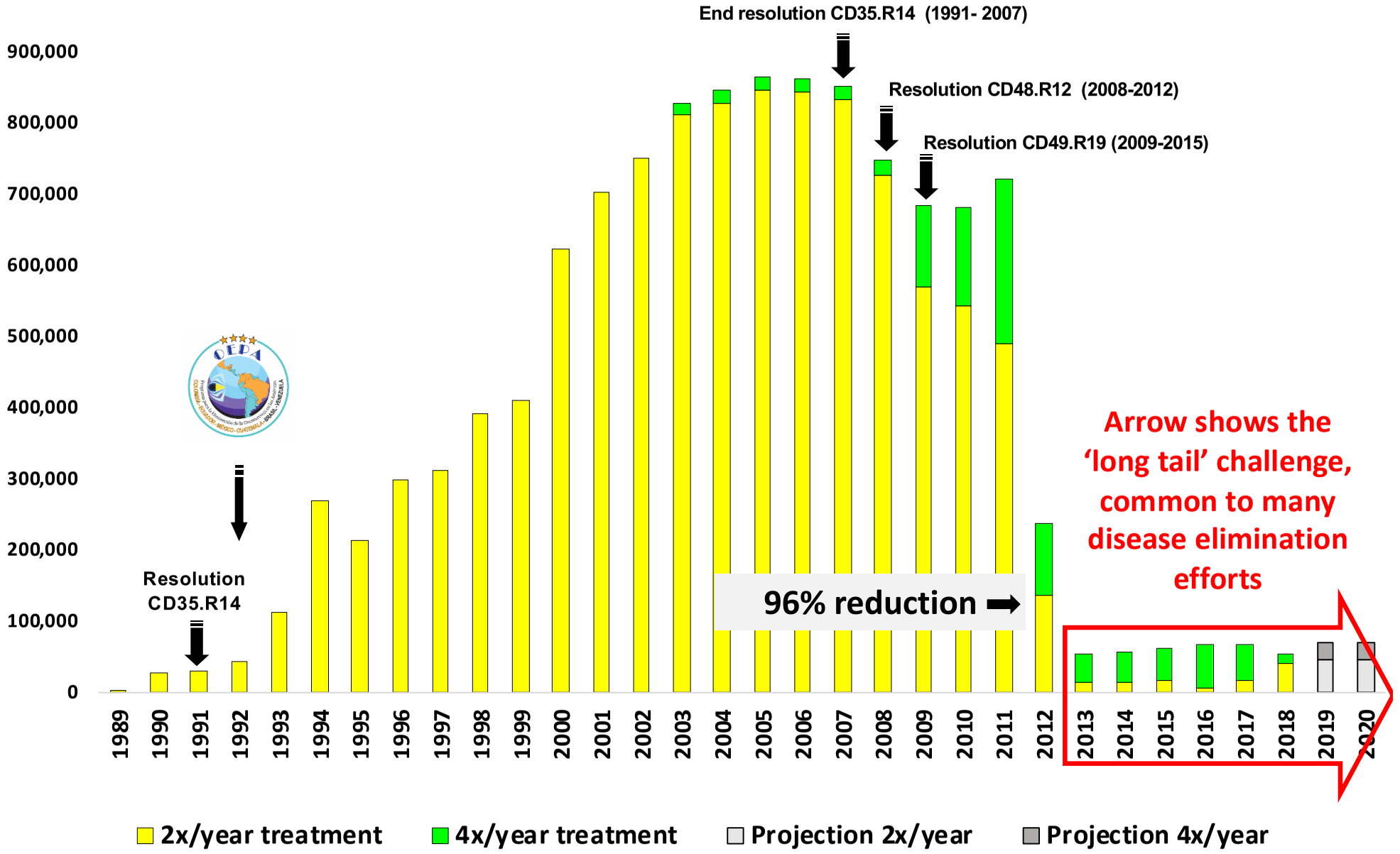


Figure ES17

2019 Onchocerciasis Transmission Status in the Americas, and Range of Endemicity in the Remaining Transmission Focus

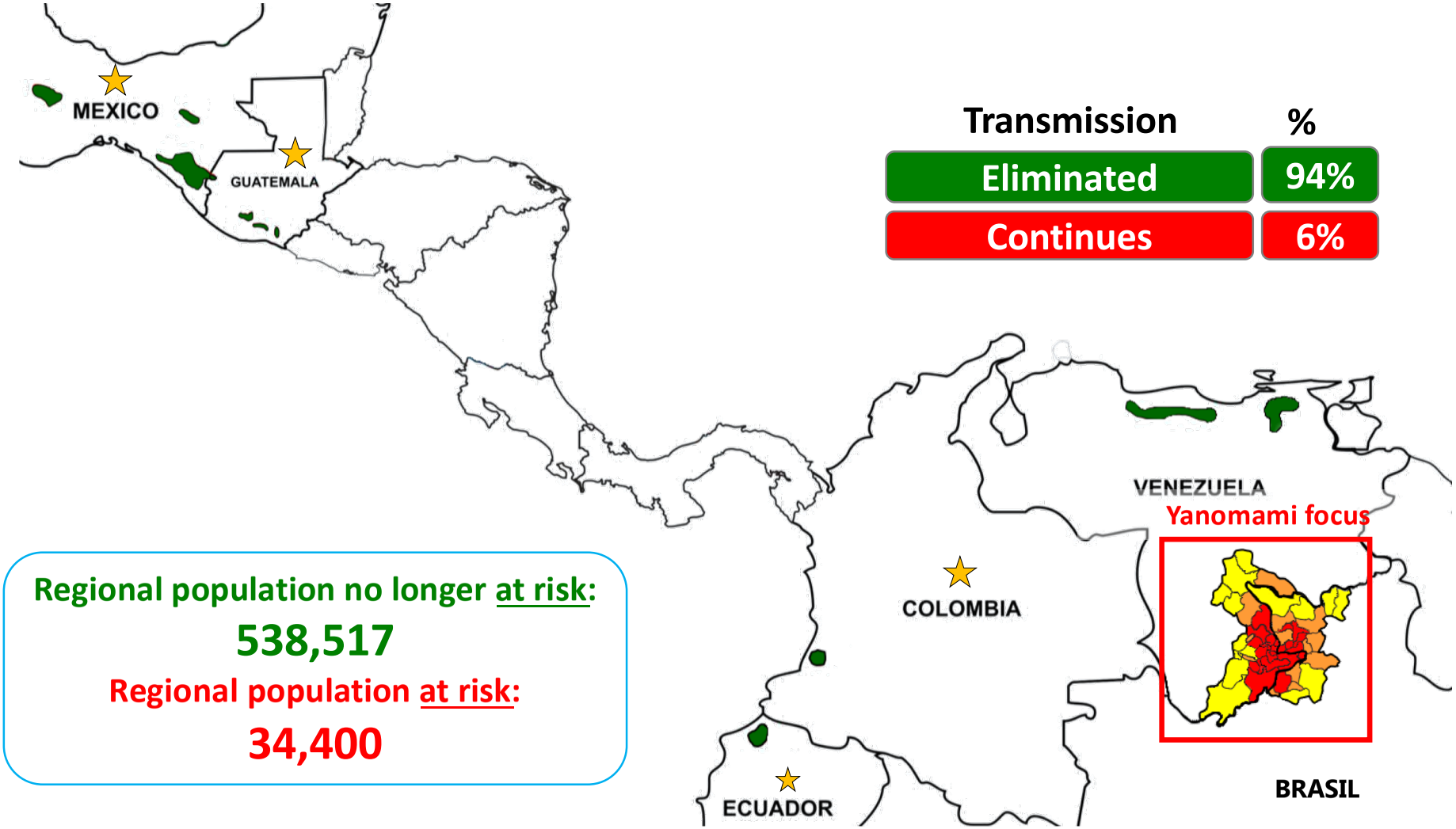
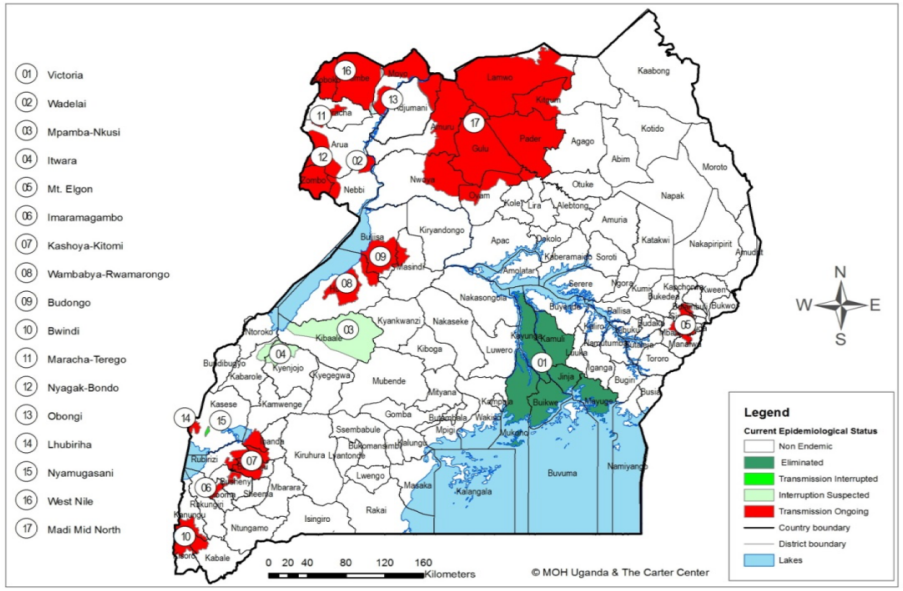


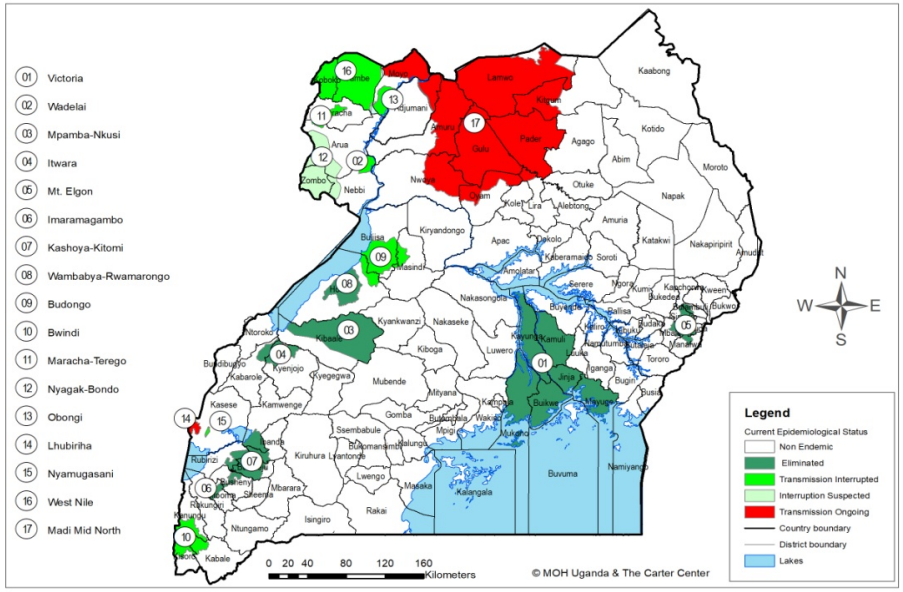
Figure ES18

Uganda: Eleven Years of Progress in Eliminating Onchocerciasis Transmission

2007



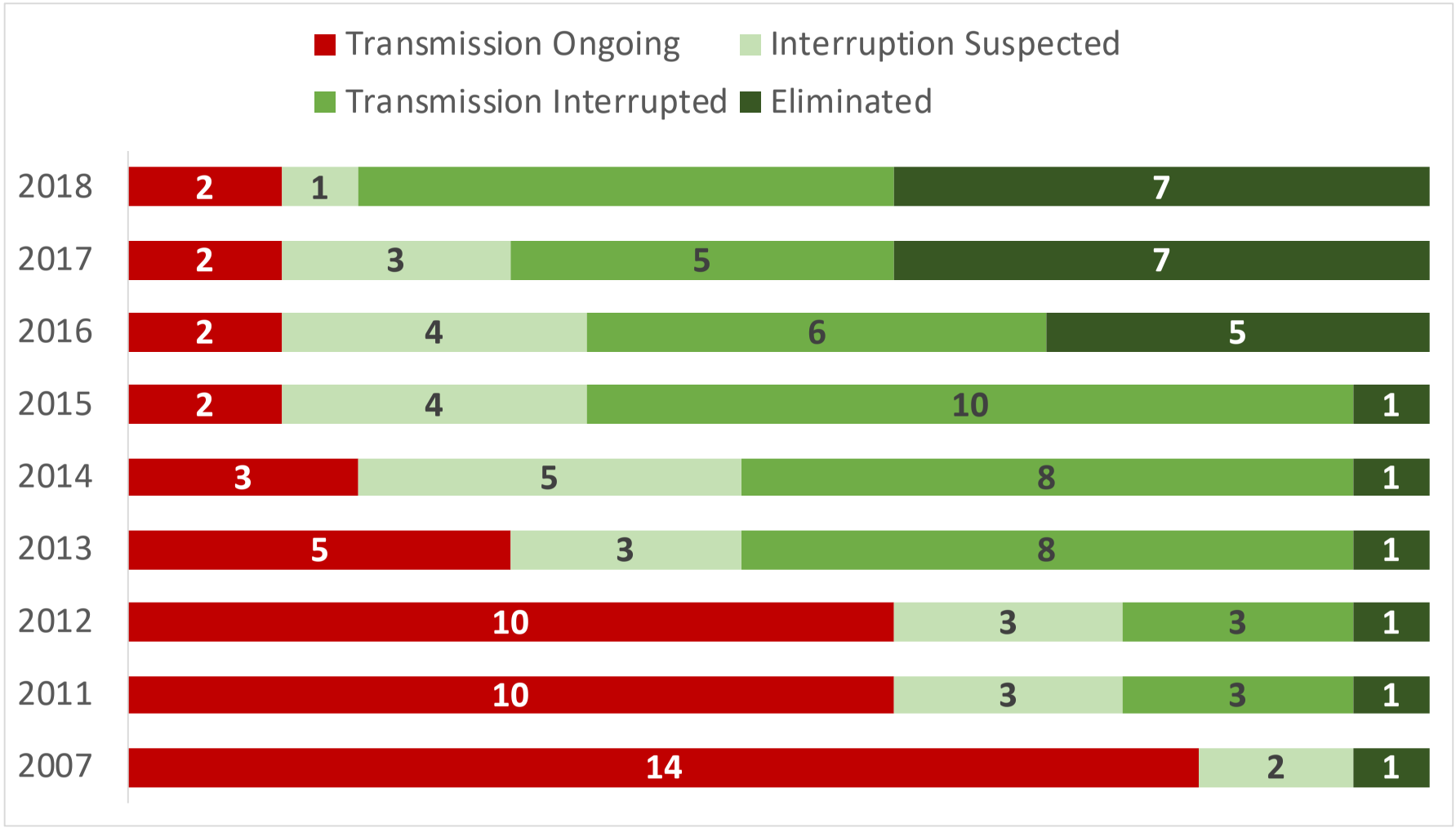
2018



Red = Foci with ongoing transmission

Figure ES19

Uganda Progress in Eliminating Onchocerciasis Transmission (Change in Endemic Status in Foci) 2007-2018



ABSTRACT

The Carter Center (TCC) River Blindness Elimination Program (RBEP) held its 23rd Annual Review, March 25-27, 2019 at its Atlanta headquarters (meeting photo, Figure ES1). The Review focused on the 2018 RBEP achievements, challenges, and operational research, and provided recommendations for 2019 activities in each RBEP-assisted country. The meeting was attended by Carter Center headquarters and field staff, ministry of health officials of countries assisted by RBEP, and key partners and donors.

The goal of the RBEP is to assist ministries of health (MOHs) in 6 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.), given twice-per-year, and spaced by four to six months. 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 transmission, and six foci in Uganda followed. The approach to RB elimination is defined by WHO guidelines, which provide three milestones (shown by the vertical lines in Figure ES2): 1) transmission suppressed; 2) transmission interrupted and MDA halted; and 3) three to five years of Post Treatment Surveillance (PTS) completed and transmission declared eliminated.

As a result of our RB elimination partnership, 6.8 million people no longer need Mectizan treatment in Carter Center-assisted areas in eight countries (Figures ES3 and ES4).

The 2018 Review continued to highlight challenges in cross-border transmission areas that we have termed 'Special Intervention Zones' (SIZs).

In 2018, The Carter Center assisted in a total of 50,483,272 mass ivermectin treatments for river blindness (onchocerciasis) in six countries, 94% of the 2018 treatment target (Figures ES5 and ES6). A goal of 62 million treatments has been set for 2019 (Figure ES6).

RBEP's cumulative treatments since 1996 have now reached 384 million (Figure ES7). Figures ES8 and ES9 show our assisted annual 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 ≥85% coverage.

RBEP is an integrated program and during the Review, treatment numbers were reported for 2018 MDA results for several other TCC Neglected Tropical Diseases (NTDs) efforts in addition to river blindness. In fact, RB treatments represented were only about 54% of the 94 million MDA treatments for NTDs assisted by The Carter Center in 2018 (see Annex 1-2 for a background on all these diseases and a program achievement timeline). Figure ES10 shows the last three years of treatments by disease, and the estimated number of persons treated for RB, lymphatic filariasis with ivermectin and albendazole (donated by GlaxoSmithKline-GSK) in Ethiopia and Nigeria (20,164,898 treatments, 94% of the target), schistosomiasis with praziquantel (donated by Merck KGaA, Germany) and soil-transmitted helminthiasis with mebendazole (donated by Johnson & Johnson) or albendazole (GSK) in Nigeria (1,417,485 and

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

8,894,524 treatments, for 35% and 79% of the targets, respectively). The decrease in schistosomiasis (SCH) treatments was due to rotating treatments based on WHO guidelines, in addition to serious delays in 2018 of the praziquantel supply.

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 330,161 CDDs were trained in 2018, all of whom were trained and mentored by MOH personnel working in affected districts assisted by TCC (Figure ES11).

EXECUTIVE SUMMARY OF THE 23rd PROGRAM REVIEW

Dr. Frank Richards, Director of The Carter Center's River Blindness, Lymphatic Filariasis, and Schistosomiasis Programs, co-chaired the meeting with three RBEP Country Representatives: Dr. Emmanuel Miri (Nigeria), Dr. Mauricio Sauerbrey (Director, Onchocerciasis Elimination Program for the Americas-OEPA), and Dr. Zerihun Tadesse (Ethiopia). In addition to Carter Center field and headquarters staff, attendees included representatives from: Bill & Melinda Gates Foundation; Centers for Disease Control and Prevention (CDC); DigitalGlobe; Emory University; the WHO Expanded Special Project for Elimination of NTDs (ESPEN); Health Development International; Imo State University; Ithaca College; IZUMI Foundation; Kuwait Fund; Lions Clubs International Foundation; Liverpool John Moores University; LUI Che Woo Prize; Ministries of Health of Brazil, Ethiopia, Nigeria, Sudan, and Uganda; University Medical Center Rotterdam; SACAICET; Mectizan Donation Program; RTI International; Sightsavers; The END Fund; Task Force for Global Health; University of Notre Dame; University of South Florida; and the United States Agency for International Development (USAID). Key findings and country reports follow. (See Annexes 3–8 for lists of participants, contacts, program publications and the Review agenda).

Binationally coordinated 'Special Intervention Zones' (SIZs) for cross-border onchocerciasis transmission areas have become an important focus for all RBEP country offices. 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 and in Africa. The 'final' inch to achieving regional elimination in the Americas is the challenging Yanomami Area that straddles the border between Brazil and Venezuela. In Africa, the SIZs currently addressed are: 1) the Radom focus of Sudan that extends into Republic of South Sudan (RSS) and possibly Central Africa Republic; 2) the Galabat (Sudan) and Metema (Ethiopia) transmission zones where a coordinated cross-border stop-MDA took place in 2018; 3) at least three potential Blue Nile State (Sudan) cross-border foci that are likely shared with Benshangul region of Ethiopia, and in the case of Khor Yabus, also with Maban county in RSS; 4) the Madi-MidNorth focus of Uganda, which extends into RSS; and four Ugandan foci that extend into Democratic Republic of Congo (DRC) 5) West Nile, 6) Nyagak-Bondo, 7) Lhubiriha and 8) Bwindi (See Figure ES12 for a map of some of these areas in East Africa). All RBEP international SIZs in the Americas and Africa require considerable diplomatic and programmatic work to intensify interventions. We also consider internal borders to, in some cases, be SIZs. For example, in Nigeria, there are important state cross-border transmission zones between 1) Edo State (Carter Center-supported) and Ondo State (supported by an NGO called 'Mission to Save the Helpless-MITOSATH') and 2) Plateau/Nasarawa States (Carter Center-supported) with the Federal Capital Territory (FCT) and Kaduna, Benue, Bauchi and Taraba States (all supported by other NGOs).

Ethiopia and Sudan

Ethiopia is now in its third year of conducting primarily twice-per-year treatments for river blindness to aggressively pursue its policy of onchocerciasis elimination by 2020. In 2018, Ethiopia delivered a total of 17,767,222 Mectizan treatments, roughly equal to treatments in 2017. The TCC-assisted LF program provided 809,783 annual treatments with Mectizan and albendazole. A total of 230,266 community drug distributors were trained, about 3,737 more than in 2017 (ES11). Ethiopia's RBEP is aiming for 26 million treatments in 2019. The Carter Center's work in Ethiopia is based on a longstanding partnership with the Federal Ministry of Health, Lions Clubs, the Lions Clubs' SightFirst Program, the END Fund and other donors.

Sudan aims to give about 71,700 treatments in 2019 in their Radom focus, security permitting.

Nigeria
Thanks to NTD funding from USAID's ENVISION project, led by RTI International, and funding from Margaret A. Cargill Foundation, IZUMI Foundation, and other generous donors, the program assisted 57.8 million treatments for river blindness, LF, SCH, and STH in nine states of Nigeria in 2018 (Figure ES13).

RBEP assisted in 28,658,600 Mectizan treatments for river blindness in 2018, a 14 percent decrease from 2017, due in part to the halting of 2.2 million annual treatments among eligible persons at risk in Plateau and Nasarawa after their successful interruption of transmission of river blindness, and in part to insufficient ivermectin supply to our other seven assisted states. Plateau and Nasarawa states have also stopped MDA for LF among 7.2 million persons at risk, so our LF treatment also focuses on those same seven southern states we assist, where 18,873,034 treatments were assisted in 2018. Our LF target in 2019 is 22 million treatments. The NTD programs in Nigeria were supported in large part by the USAID's ENVISION project led by RTI International and will have renewed support from those partners in 2019 under Act to END NTDs | East.

The Carter Center assisted in 1,417,485 praziquantel treatments for schistosomiasis in four of the nine assisted states in Nigeria in 2018, a 35% decrease because the program rotates treatments based on WHO guidelines, but also due to serious delays in praziquantel supply. Praziquantel is donated to The Carter Center through the World Health Organization by Merck KGaA, Germany. The IZUMI Foundation also supports this program. Our target in 2019 is 5.2 million treatments (a 24% increase). Treatments in 2018 for STH were 8,894,524, and the 2019 target is 9 million treatments (a 2% increase). The medicines used for STH treatment are donated by GSK (albendazole) or Johnson & Johnson (mebendazole).

Uganda
In 2007, Uganda declared a goal of river blindness transmission elimination from all its 17 transmission zones (foci). The program continued to make progress in 2018. The Ugandan Onchocerciasis Elimination Expert Advisory Committee (UOEEAC) meeting recommended that two foci (Budongo and Bwindi) be reclassified as having interrupted transmission and MDA among a total population of 312,304 people persons in those foci be stopped in 2019. Another focus (Nyagak-Bondo) is suspected to have interrupted transmission but requires additional assessments in 2019. Two foci (Lhubiriha and Madi-MidNorth) have active transmission. Uganda administered a total of 3.7 million Mectizan treatments in 2018, all under the twice-per-year strategy. For 2019, the target is for 3.6 million treatments, most of which will take place in the large Madi-MidNorth focus that encompasses 11 districts, many of which border with South Sudan. Uganda also has important cross-border foci shared with the Democratic Republic of the Congo. Currently, the MOH’s onchocerciasis elimination program is supported by The Carter Center, USAID’s ENVISION project led by RTI International, and Sightsavers.

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/WHO, and other partners. The OEPA initiative has stopped treatments in 94 percent 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 ES16 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 ES17),

The remaining active transmission zone is an SIZ populated by about 34,000 indigenous, migratory people (the Yanomami) residing in the Amazon rainforest in an area bordering Brazil and Venezuela. The challenge with the Yanomami area lies in the remoteness of its population, the lack of high-level coordination between Brazil and Venezuela, and a deteriorating political situation in Venezuela. In 2018 OEPA assisted Brazil and Venezuela in about 55,000 Mectizan treatments. Given the political, humanitarian and health crises of Venezuela, OEPA supported Venezuelan teams to provide vaccinations, malaria treatments, and other health services.

The countries and Carter Center staff are trying to creatively solve the problems of extreme isolation and difficult access to this area, and in Venezuela 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 67,000 treatments are planned in the Yanomami Area in 2019. The OEPA program receives financial support from USAID and the Carlos Slim Foundation.

2019 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 River Blindness Elimination Program (TCC/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 entering into post treatment surveillance (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/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 'Special Intervention Zones' (SIZs) and the needed collaboration on both sides to stop transmission.
- Monitoring the impact of interventions using sensitive tools.

TCC/RBEP encourages the concerned Ministries of Health and local authorities to evaluate and treat cross-border foci in a coordinated manner. Promote the concept of SIZs where concerted efforts towards elimination are conducted on both sides of an international or internal border.

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

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

The Carter Center field offices should conduct treatment coverage surveys, in consultation with HQ.

At the 2019 RBEP review 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 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 headquarters informed on the process.

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

The Carter Center website should house key public domain documents from National Onchocerciasis Elimination Committees (NOECs) of Ethiopia, Nigeria, and Uganda.

TCC/RBEP will maintain laboratories for OV16 serology, entomology, and parasitology (including O-150 PCR testing in vectors and skin snips), with technical support by Dr. Thomas Unnasch and his team at University of South Florida (USF). In consultation with USF, field 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. TCC will use as our principle OV16 test the 'OEPA' OV16 ELISA until further data deems that test to be unacceptable.

Cautiously review, internally and with national onchocerciasis elimination committees in countries we assist, the frequent changes in recommendations being produced by the WHO Onchocerciasis Technical Subgroup (OTS), particularly as these relate to mapping of onchocerciasis hypoendemic areas. These recommendations are causing considerable confusion for the programs.

Through national mechanisms, TCC/RBEP offices should monitor government, ESPEN, and other partners' financial contributions for elimination efforts in RBEP-assisted areas.

Carter Center program staff must complete or renew the Emory 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.

The Carter Center's River Blindness (RB), Lymphatic Filariasis (LF), Schistosomiasis (SCH) and Soil-Transmitted Helminths (STH) Programs propose to assist ministries of health to provide **98,772,575** treatments for NTDs in 2019.

2019 Treatment and Training Objectives:
UTG = Ultimate Treatment Goal
UTG2 = Twice-per-year Treatment Goal
UTG4 = Four-times-per-year Treatment Goal

River Blindness	
Annual (UTG)	6,054,383
Semiannual (UTG2)	56,240,683
Quarterly (UTG4)	13,945
Total RB Treatments	**62,309,011**

Lymphatic Filariasis	
Annual (UTG)	22,063,880
Total LF Treatments	**22,063,880**

Schistosomiasis	
Annual (UTG)	5,245,018
Total SCH Treatments	**5,245,018**

Soil-Transmitted Helminths	
Annual (UTG)	6,088,968
Semiannual (UTG2)	2,673,738
Total STH Treatments	**9,154,666**

Training Objectives	
CDDs	338,805
CSs	95,421

ONCHOCERCIASIS ELIMINATION PROGRAM FOR THE AMERICAS (OEPA)

Summary: The Onchocerciasis Elimination Program for the Americas (OEPA) celebrated its 25th anniversary of operations in 2018 (Figures O1 and ES16). OEPA is a Carter Center-led program that serves as the vanguard of the regional initiative working to eliminate transmission of onchocerciasis from the Americas. The OEPA strategy is based on mass drug administration (MDA) of Mectizan® twice or four times per year, reaching a target of ≥85% coverage of the population eligible for treatment. Ninety-four percent of Mectizan treatments in the Region of the Americas have been successfully halted, and the cross-border focus between Venezuela and Brazil, called the Yanomami Focus Area (YFA), is now the only remaining active transmission zone (Figure ES17). An important development in 2018 was that the Brazilian Program decided to end its quarterly MDA treatment approach given failure to reach the required 85% coverage in 2017 under that strategy; in 2018 all treatments in Brazil were on the 2x/year regimen. Venezuela continued with quarterly distribution in some areas but continued to fail to reach the 85% goal in 2018. A highlight in 2018 was the preparation of the first binational map of the Yanomami focus area produced in QGIS-based workshops involving technical staff from OEPA and the Brazilian and Venezuelan programs. This success was published in the annual OEPA report in the WHO Weekly Epidemiological Record (Figures O2 – O3). Additional OEPA successes related to: new remote sensing data that identified more unknown and potentially endemic villages in Venezuela, continued recruitment and training of Indigenous Health Agents to assist in Mectizan delivery, and the 'More than Mectizan' mantra of the YFA teams who delivered other health care interventions during their MDA activities.

Background: The OEPA initiative was launched by the River Blindness Foundation (RBF) in 1993 in response to the 1991 Resolution XIV of the 35th PAHO Assembly that called for the elimination of onchocerciasis morbidity from the Americas by the year 2007. With the closure of the RBF in 1996, The Carter Center assumed administrative responsibilities for OEPA. In 2001, the WHO established a set of guidelines to assist onchocerciasis programs to determine whether interruption of transmission had occurred and when MDA with Mectizan® could be safely stopped. These guidelines were revised in 2016 (See Executive Summary and Figure ES2). Once all transmission zones (foci) in a country reach the elimination stage, final country verification can be requested from an independent international verification team (IVT) working under the auspices of the WHO. In 2008, PAHO renewed the call to eliminate onchocerciasis (Resolution CD48.R12) throughout the region. A 2009 PAHO Resolution (CD49.R19), called for the elimination or control of 12 neglected tropical diseases (NTDs) in the Americas, includes onchocerciasis as an elimination target. Thereafter four countries successfully completed the IVT process: Colombia (WHO verified in 2013), Ecuador (2014), Mexico (2015) and Guatemala (2016). These are the only countries in the world so far to receive WHO verification of onchocerciasis transmission elimination. A 2016 PAHO Resolution (CD55.R9) on NTDs called for elimination of onchocerciasis from Venezuela and Brazil by 2022.

In addition to The Carter Center, the OEPA coalition includes ministries of health (MOHs) of the six currently or formerly endemic countries in the Americas (Brazil, Colombia, Ecuador, Guatemala, Mexico, and Venezuela), the Pan American Health Organization/WHO (PAHO/WHO), the United States Agency for International Development (USAID), the Carlos Slim Foundation, the Lions Clubs International Foundation (LCIF) and local Lions Clubs, the Bill & Melinda Gates Foundation, Merck and the Mectizan® Donation Program (MDP), the U.S. Centers for Disease Control and Prevention (CDC), and several U.S. and Latin American universities. A Program Coordinating Committee (PCC) serves as the steering body for OEPA. Technical and

financial assistance to the countries flows through the OEPA office, which is based in Guatemala City, Guatemala.

The Yanomami Focus Area (YFA): The YFA is the remaining active onchocerciasis transmission zone in the Americas and the only area in the Americas that was under ivermectin MDA treatment for onchocerciasis in 2018. Being a cross border focus shared by Brazil and Venezuela (Figures O2 – 4), the YFA is considered a 'Special Intervention Zone' (SIZ), and political considerations often hamper holistic approaches to stopping transmission here.

The YFA is comprised of the South focus of Venezuela and the Amazonas focus of Brazil. The YFA is named after the approximately 34,000 nomadic indigenous Yanomami people (16,926 in Venezuela and 17,474 in Brazil) who live in onchocerciasis endemic communities scattered throughout approximately 168,000 square kilometers of Amazon rainforest along the border between those two countries (Figure ES17). The people reside in 637 very small (usually under 75 persons) villages (called "shabonos" or "malocas"): 367 in Venezuela and 270 in Brazil. MDA treatments are scheduled either twice or four times-per-year. The goal is to obtain at least 85% treatment coverage in each treatment round. This ambitious plan is tackled on each side of the border by the staff of both the Venezuelan and Brazilian Onchocerciasis Programs. They have varying degrees of success depending on villages' accessibility, MDA frequency, availability of areal transport, weather conditions, and government support with permits and helicopter flights. The endemicity breakdown in the YFA is shown in Figure O4. The treatment regimens in operation in 2018 are shown in Figure O5.

The challenges for the treatment programs are multiple. There are no roads in the area and the isolated, hard-to-access villages are reached by boat, foot, fixed-wing small aircraft, or helicopter. Given the Yanomami people have a high degree of mobility, communities often are (permanently or temporarily) empty when the program staff visits. There is conflict between Yanomami communities or with armed illegal gold miners. In Venezuela there have been disease outbreaks of measles, diphtheria, and malaria. There are no diplomatic relations between Venezuela and Brazil and therefore an adverse political environment and lack of binational coordination. Despite these challenges, onchocerciasis transmission suppression is believed to have taken place (based on the numbers of rounds delivered with good coverage) in over 60% of communities (Figure O6).

Treatments in the YFA in 2018:

2018 treatments provided in the YFA that were reported at the March 2019 Program Review are shown in table Figure O7. For the YFA as a whole, a total of 54,991 Mectizan treatments were delivered in 2018 (39,389 in the twice-per-year scheme [90% UTG2 coverage] and 15,602 in the four-times-per-year scheme in Venezuela [73% UTG4 coverage]). As noted above Brazil abandoned the four-times-per-year scheme at the end of 2017 in an ultimately successful bid to reach $\geq$85% coverage in all villages using the twice-per-year strategy in 2018. Overall in the YFA the twice-per-year MDA scheme reached a coverage of 91% in the first six months, and 90% in the second (note Venezuela's second round coverage was 84%. In contrast, coverage in the four-times-per-year approach in Venezuela never reached the $\geq$85% goal: 70% during the first quarter, 81% during the second, 57% during the third, and 82% during the fourth.

Other activities in the YFA:

The Venezuela South focus team has continued in its efforts to rehabilitate old landing strips that have fallen into disrepair due to jungle overgrowth. An inspiring video was shown at the Review of this effort that readers are encouraged to watch: https://tinyurl.com/y3awwuyd. The Venezuelan program seeks to fulfill its goal to recover and maintain 14 airstrips and to construct two new strips, including one in the Siapa river valley (see arrow in Figure O3).

Unregistered and untreated endemic Venezuelan villages have been a major challenge for over a decade: Figure O8 shows that 137 villages with a population of nearly 6,000 have been discovered piecemeal since 2008. It should be noted however that in 2018 only 12 new endemic villages were added to the Venezuelan treatment list, with 326 persons. This is the smallest addition of persons (representing only a 1.9% increase of the overall population at risk) to the Venezuelan program since 2011. In 2018 DigitalGlobe (DG) was contracted to use their high-resolution (30-50 cm) satellite data to seek unknown villages in the Siapa valley, Chalbaud, and Hashimu. In November 2018, DG sent 63 images and coordinates of potential communities to be compared with the known community inventory of the Venezuelan Program. These will be analyzed by the program in 2019.

A village scoring system has been developed and is being refined to prioritize Venezuelan villages targeted for four-times-per-year treatment (with the objective of reducing their numbers). Currently about 48% of Venezuelan villages are targeted for four-times-per-year. The 'score' is derived from a number of programmatic variables in addition to geographic features: baseline endemicity (hyper-,meso-,hypoendemic), year when Mectizan treatment began, the number of rounds with *any* treatment coverage, the number of rounds with >85% treatment coverage, and the number of *consecutive* rounds of >85% coverage, the efficiency of the vector (there are three main species in the YFA) in the area, and accessibility. Those with the lowest score are progressing very well and could be candidates to revert to the 2x/year approach.

Both programs are recruiting and using Yanomami residents as Indigenous Health Agents (IHAs) to participate in treatment and supportive activities (Figure O9). In Venezuela the onchocerciasis program has 180 IHAs (of whom only 2 are women). This is compared to a staff of 20 onchocerciasis supervisors and 143 paid staff (lab technicians, translators, carriers, guides). In Brazil there are 145 IHAs (7 of whom are women), but by law they may not administer treatments. These IHAs participate as in activities such as treatment assistance, transporting materials, registering people for treatment, serving as guides/communicators, and measuring and weighing community members. The impact of the 2013 launching of the IHA initiative in the Venezuelan Komitarope sector (Alto Ocamo Parima Area) shows considerable contribution of IHAs to increasing coverage in the 24 communities of the sector (Figure O10). Another IHA project involves the production of 'sketch maps' that describe distances between communities in terms of walking time rather than kilometers (Figure O11).

"More than Mectizan": The extreme economic and political crisis in Venezuela has resulted in hyperinflation, critical shortages of food, medicine and fuel, and diminished health services. Outbreaks of malaria, measles, diphtheria, and tuberculosis are occurring, and these conditions are spilling into neighboring countries (including Brazil) due to the massive emigration of Venezuelans. Some of the only aid to Yanomami people experiencing these outbreaks came thanks to the Venezuelan program that benefits from RBEP/OEPA support. Onchocerciasis program teams secure flights and take along physicians and nurses, and their medicines, vaccinations and equipment. Over 410 cases of malaria have been diagnosed by malaria point-of-care rapid diagnostic tests and treated with artemisinin combination therapy (ACTs) by the

onchocerciasis team. The team has also treated diarrhea and pneumonia and provided thousands of vaccinations.

Publications pertaining to the OEPA Regional Initiative: In addition to the aforementioned WHO WER report on onchocerciasis in the Americas, one book and three peer reviewed journal papers appeared in 2018.

- R. Guderian et al. Historia de la Oncocercosis, 'Ceguera de los Ríos' en el Ecuador. Desde su descubrimiento hasta su eliminación. Editorial Universitaria, Quito-Ecuador, 2018, pp. 290
- S. Nicholls et al. Elimination of onchocerciasis from Colombia: first proof of concept of river blindness elimination in the world. *Parasites & Vectors* 2018; 11:237.
- A. Guevara et al. Elimination of onchocerciasis in Ecuador: findings of post-treatment surveillance. *Parasites & Vectors* 2018; 11:265.
- M. Sauerbrey et al. Progress toward elimination of onchocerciasis in the Americas. *International Health* 2018; 10: i71–i78.

The Cost of the Regional Initiative: The cumulative cost (1991 – 2018) of the program has been US$176,937,881: 39% of this money has been provided by the six country programs, 33% is the in-kind value of the Mectizan donation by Merck, and 28% has been provided through donors to the Carter Center's OEPA program. Figure O12 is an interesting graphic showing an important pattern often observed in the end game of a transmission interruption/eradication program. The yellow line shows the 94% decrease in treatments for onchocerciasis in the region that can be considered a proxy for decreases in cases. The decrease in donation value of Mectizan follows a similar 90% reduction but is not shown in the figure. Government investments in the programs (green line) have also decreased since 2014 as four of the six countries have been verified as having eliminated onchocerciasis. To maintain the program in the final two countries the OEPA (international) investment is rising (blue line) and exceeded government contributions for the first time in 2016. With the crossover of the blue and green lines, the overall costs of the regional program now exceed government contributions.

The 28th Annual InterAmerican Conference on Onchocerciasis (IACO'18) in Guatemala:

The theme of the 28th InterAmerican Conference on Onchocerciasis (IACO) was "Walking with the Yanomami on cross-border health paths to reach the 2022 goal." Held November 7 - 8, 2018 in Antigua Guatemala, 45 partners of The Carter Center's Onchocerciasis Elimination Program for the Americas (OEPA) reviewed progress towards eliminating onchocerciasis from the Western hemisphere (Figure O13). Onchocerciasis now affects just 6% of the population initially at risk in the Americas, all of whom are indigenous people (the Yanomami indigenous) living in the areas bordering Brazil and Venezuela.

The Brazil and Venezuela programs reported their ever-increasing array of innovative approaches to accelerate the end game of elimination including: 1) the community score system, 2) creating the binational GIS map, 3) using satellite imagery to detect villages that are not yet registered with the health system, 4) using sketch maps generated in consultation with the Yanomami people, 5) increasing involvement of indigenous health workers, 6) recovering aircraft landing strips deep in the jungle to allow health teams better access to communities, 7) the 'More

than Mectizan' approach and 8) providing doxycycline treatment to accelerate elimination in certain settings [Editors' note: doxycycline will be the topic of the 2019 OEPA WHO WER report].

IACO also included post-elimination surveillance presentations for each of the four WHO-verified eliminated countries (Colombia, Ecuador, Guatemala and Mexico), and for the two eliminated foci in northern Venezuela.

This year's IACO was honored by the presence of a distinguished delegation of Lions Clubs International representatives from Brazil and the formerly endemic countries of Colombia, Mexico and Guatemala (Figure O14). The Lions Clubs International Foundation has been a valued Carter Center partner in the effort to eliminate River Blindness in the Americas since 1999.

2019 RECOMMENDATIONS FOR THE ONCHOCERCIASIS ELIMINATION PROGRAM FOR THE AMERICAS (OEPA)

By the end of 2019, identify any remaining communities in the South Venezuela Focus of the Yanomami Area not yet known in the Venezuelan health system. Consider another project with DigitalGlobe if the program deems it necessary. Make progress in the epidemiological assessment and treatment of all recently identified Yanomami communities. Activities should include: 1) active search of new communities by the health teams during field treatment distribution and continued remote sensing studies, if available, to identify all suspected villages; 2) a confirmatory 'fly-over' or site visit of all newly identified villages to confirm they are inhabited; 3) all new inhabited villages should then have an epidemiological assessment; and 4) if the village is confirmed to be onchocerciasis endemic, Mectizan treatment (preferably four times-per-year) should be started immediately.

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

In Venezuela, focus implementation of treatment in villages prioritized by their scoring system. High priority for 4x-per-year treatment is being given to communities based on how they 'score' on a series of programmatically-determined factors, including: year when treatment began, the number of rounds with any treatment coverage, the number of rounds with >85% treatment coverage, the number of consecutive rounds of >85% coverage, baseline endemicity, the efficiency of the vector in the area, and accessibility. This scoring system will also allow the reevaluation of those communities that could revert to the 2x/year approach.

OEPA should encourage Brazil to continue their development of a specialized scoring system similar to that of Venezuela, adapted to the data that they maintain at the village level. It is uncertain if Brazil will return to a 4x-per-year treatment schedule at this time.

Promote the highest level of political support from Venezuela accordingly with what the current adverse political situation allows, and Brazil celebrate IACO 2019 in Brasilia, so the new health authorities become acquainted with the regional initiative. All these actions in favor of the elimination of onchocerciasis from the Yanomami Area.

Complete the recovery and maintenance of 14 airstrips and complete construction of an airstrip in the Siapa river valley.

Launch programmatic activities in the Siapa river valley in Venezuela.

Identify candidates and train Yanomami residents as Indigenous Health Agents (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, etc.).

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.

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

Seek medical commodities (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.

Invite all six OEPA country representatives to IACO regardless of verification of elimination status.

Encourage the Lions Clubs International Foundation to maintain support to a Lions representative from each of the six countries to attend IACO.

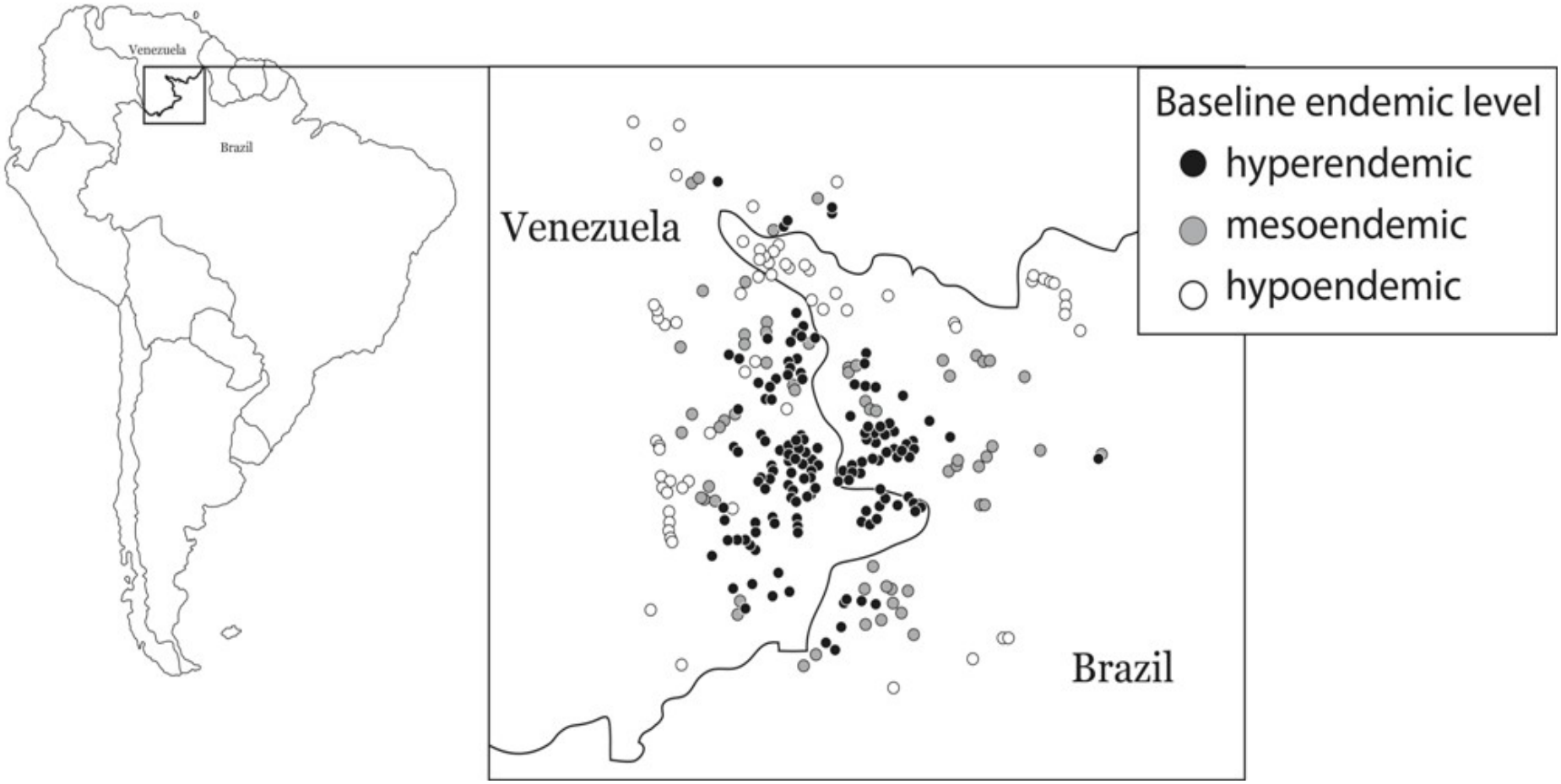
OEPA 2019 Treatment Targets	
Semiannual (UTG2)	45,934
Quarterly (UTG4) VZ Only	22,248
Total Treatments	68,182

Figure O1

25 years of the Onchocerciasis Elimination Program for the Americas!

Figure O2

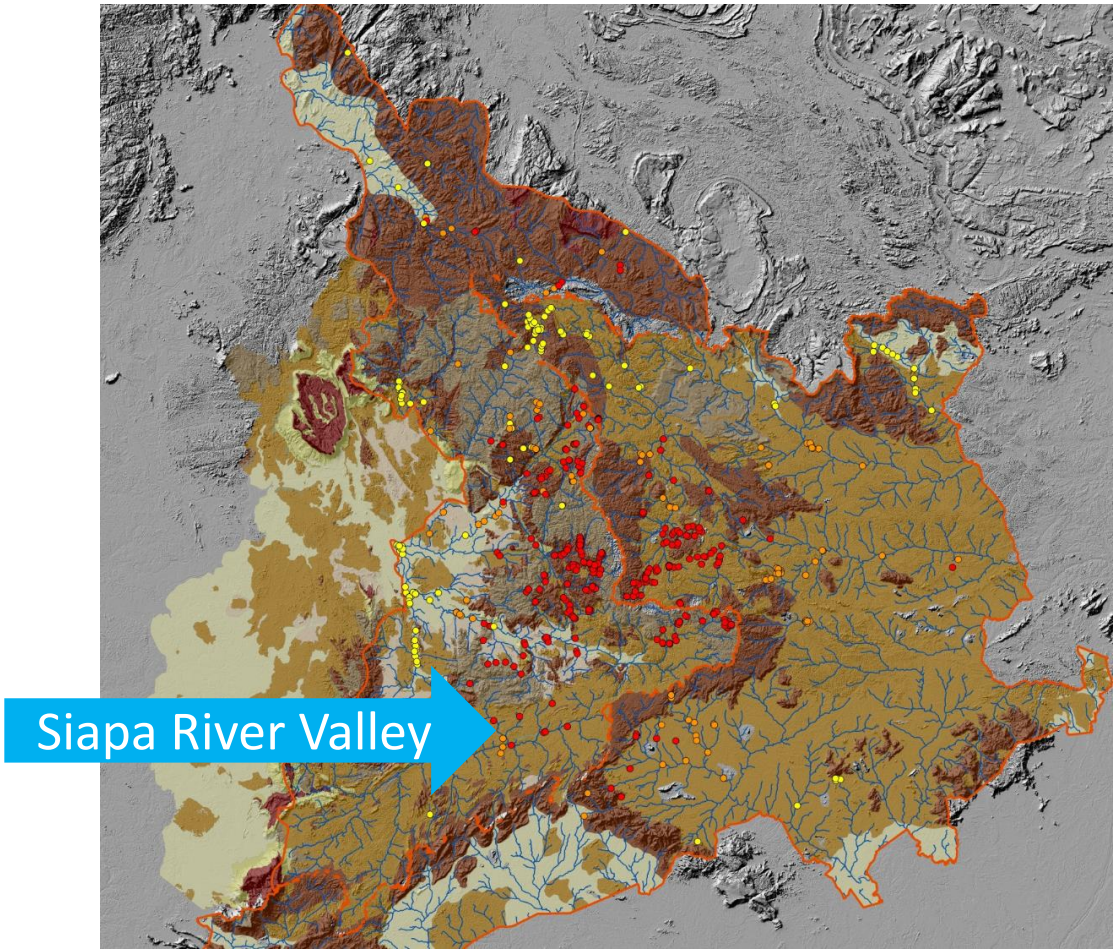
Map of Communities in the Cross-border Yanomami Focus Area, by Pre-MDA Endemicity Levels



Source: WHO. Progress towards eliminating onchocerciasis in the WHO Region of the Americas: advances in mapping the Yanomami focus area. *Wkly Epidemiol Rec.* 2018. 93, 541–552.

Figure O3

Elevation Profile of Onchocerciasis and Transmission in the YFA shows Hypendemicity in Mountainous Regions



Hyperendemic
Mesoendemic
Hypoendemic
Mountain
Plateau
Valley
Hill
Peneplain
Plains

Source: Binational Mapping Group, IACO 2018

Figure O4

The Yanomami Focus Area (YFA) in 2018

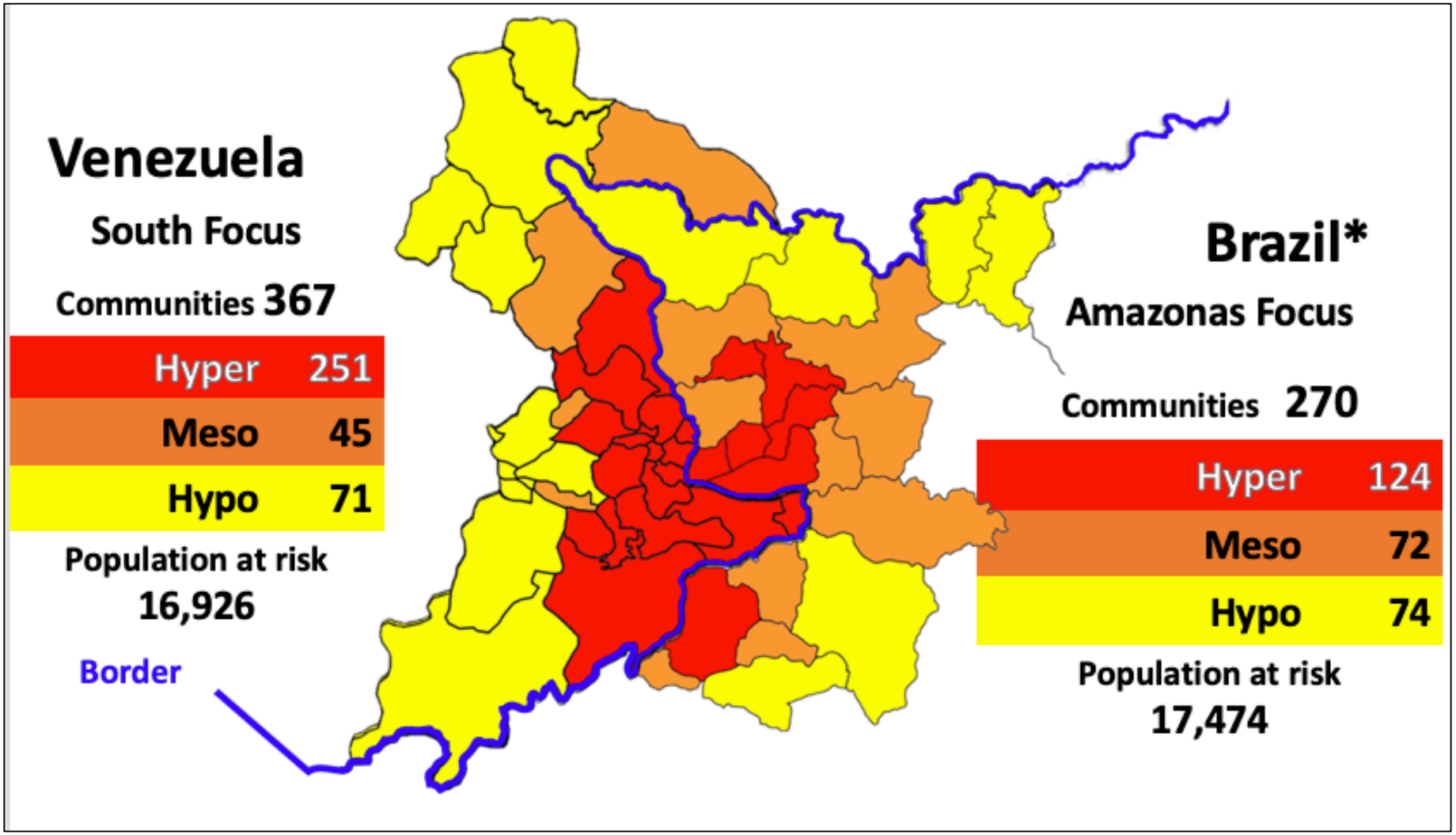


Figure O5

Yanomami Focus Area 2018: Populations and Mectizan® Treatment Approaches, by Country

Country	Focus	Treatment Approach	Communities	Population at Risk	Population Eligible for Treatment
Venezuela	South	2x/Year	189	9,916	8,598
		4x/Year	178	7,010	5,912
		Total Focus	*367*	*16,926*	*14,510*
Brazil	Amazonas	2x/Year	270	17,474	13,945
	TOTAL		**637**	**34,400**	**28,455**

Figure O6

RB Transmission Status in the Yanomami Focus Area 1995 - 2018

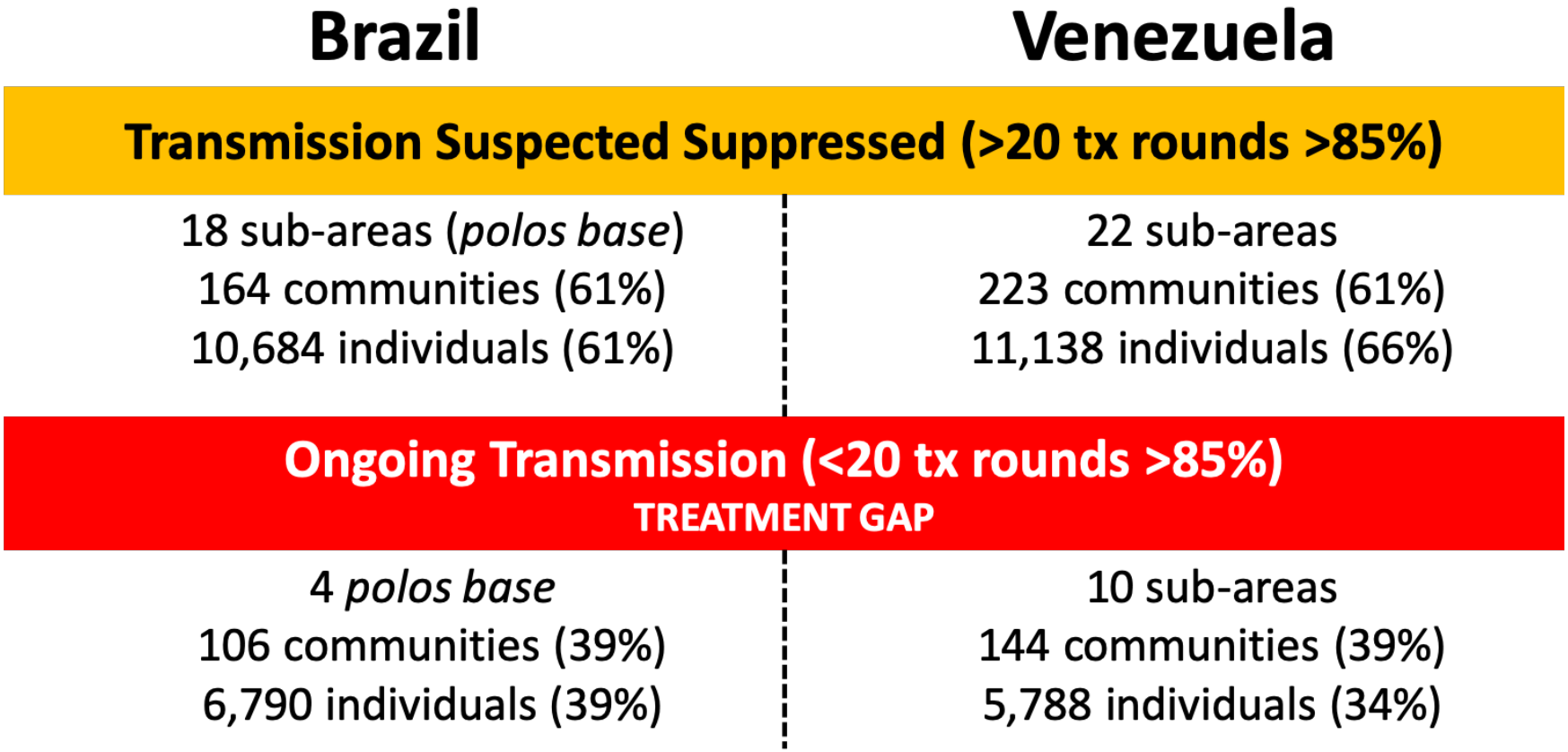


Figure O7

2018 Yanomami Focus Area Treatment Report

Twice-Per-Year

Focus	Communities				Pop @ risk 2x/year	Eligible for Tx	Treated 1st Rd	Cov 1st Rd	Treated 2nd Rd	Cov 2nd Rd	UTG2	Treated UTG2	Cov UTG2
	Total	Hyper	Meso	Hypo				%		%			%
Amazonas-BRA*	262	123	66	73	16,088	13,086	11,741	90%	12,286	94%	26,172	24,027	92%
South-VEN	187	102	15	70	9,948	8,699	8,070	93%	7,292	84%	17,398	15,362	88%
TOTAL	449	225	81	143	26,036	21,785	19,811	91%	19,578	90%	43,570	39,389	90%

Four-Times-Per-Year

Focus	Communities			Pop. at risk 4x/year	Eligible for tx	Tx 1st Rd	Cov 1st Rd	Tx 2nd Rd	Cov 2nd Rd	Tx 3rd Rd	Cov 3rd Rd	Tx 4th Rd	Cov 4th Rd	UTG4	Tx UTG4	Cov UTG4
	Total	Hyper	Meso				%		%		%		%			%
South-VEN	166	138	28	6,431	5,380	3,773	70%	4,336	81%	3,065	57%	4,428	82%	21,520	15,602	73%

Figure O8

Endemic Communities Discovered in the South Focus of Venezuela 2008 - 2018

Year	UHS* (new) Communities	Population
2008	15	578
2009	3	304
2010	9	282
2011	7	232
2012	16	728
2013	12	548
2014	11	553
2015	27	954
2016	11	400
2017	14	946
2018	12	326
Total	**137**	**5,851**

Source: Venezuelan South Focus Program

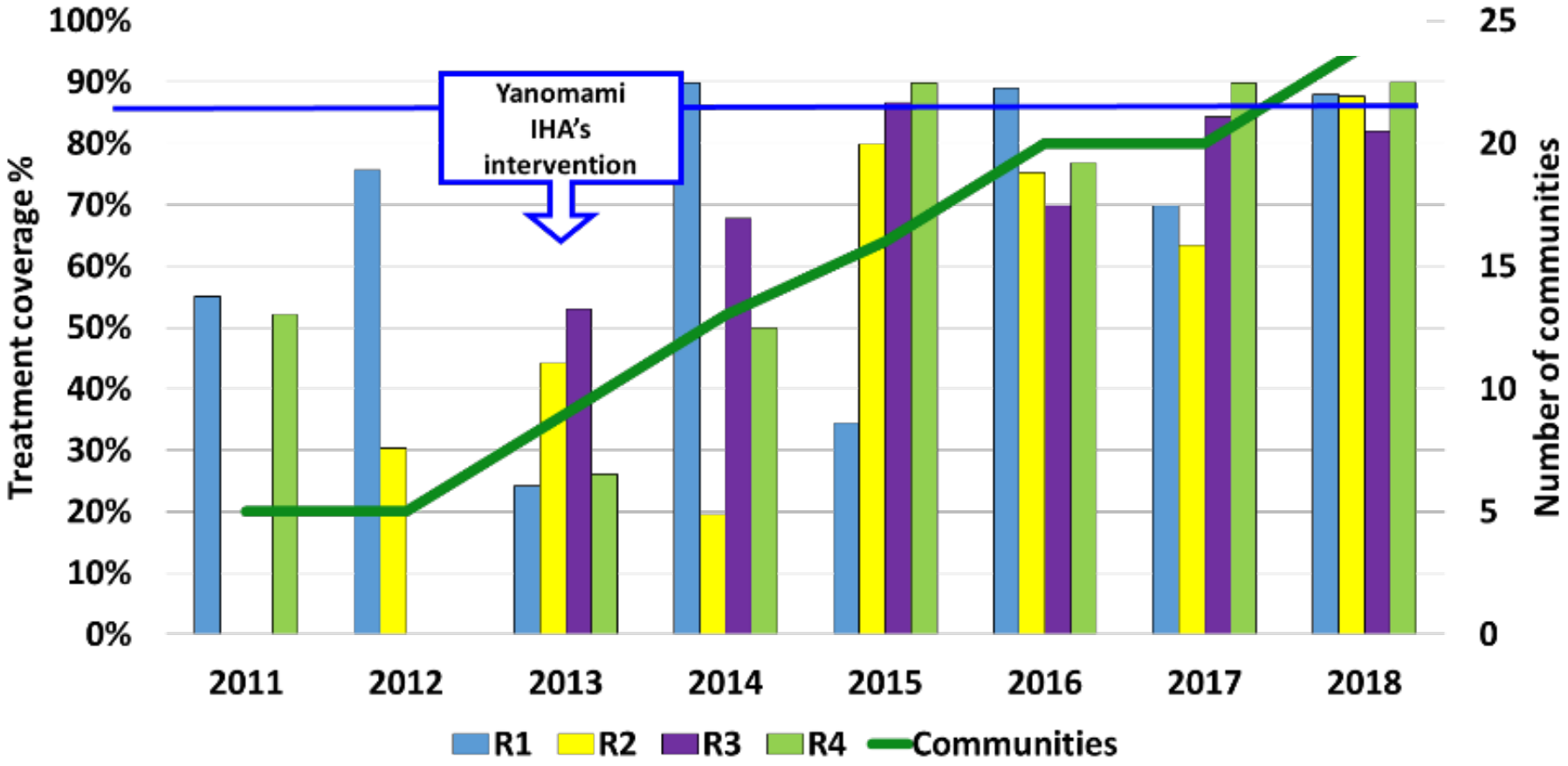
***UHS**: Unknown by Health System

Figure O9

Indigenous Agents Conduct Health Education in Brazil (left) and Treatment in Venezuela (right)

Figure O10

Treatment Coverage and Number of Communities in the Komitarope Sector, Alto Ocamo Parima Area, Venezuela South Focus



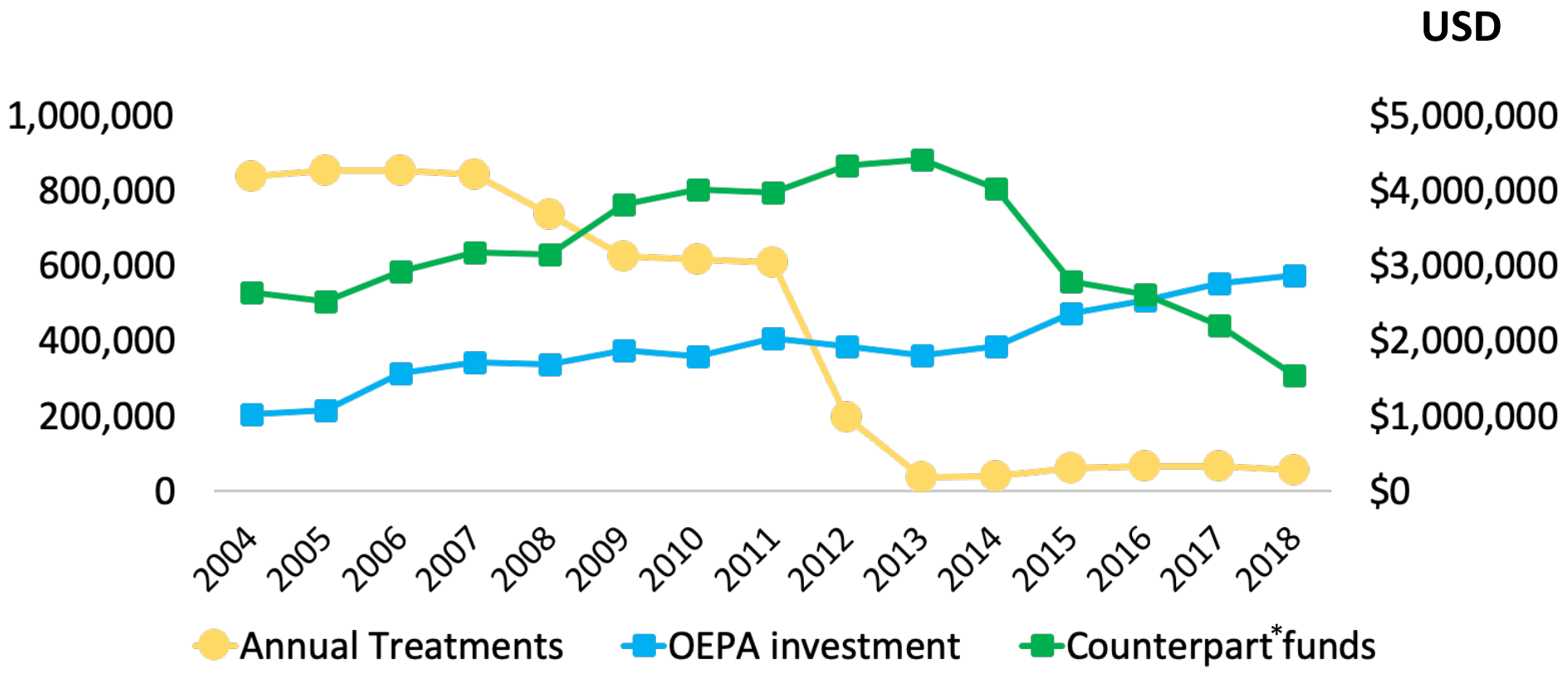
IHA = Indigenous Health Agent

Figure O11

Example of a Yanomami Sketch Map

Figure O12

Mectizan Treatments vs Funding for Onchocerciasis Elimination in the Americas, 2004 - 2018



*This refers to domestic funding by the six endemic countries: Brazil, Colombia, Ecuador, Guatemala, Mexico and Venezuela

Figure O13

IACO 2018 in Antigua Guatemala

Figure O14

Lions at IACO 2018

The Carter Center and OEPA staff are joined by Lions Clubs representatives and their spouses at IACO (left to right: Madelle Hatch; Dr. Ricardo Gurgel and Vania Gurgel, Brazil; Dr. Frank Richards; (the now late) Kay Cabrera Coello and Dr. Florencio Cabrera Coello, Mexico; Dr. Libardo Bastidas Passos, Colombia; Craig Withers; Dr. Angel Soto and Telma Soto, Guatemala; and Dr. Dean Sienko)

UGANDA

Summary: Since Uganda declared elimination of onchocerciasis transmission as a goal in 2007, the country has classified 14 of its 17 river blindness foci as either 'transmission interrupted', or 'transmission eliminated' (Figures U1 and ES18). In 2018, two foci (Budongo and Bwindi) were newly classified as having interrupted transmission. This translates into about 2.2 million treatments for onchocerciasis no longer being required in Uganda.

Transmission interruption is suspected in one focus (Nyagak-Bondo), but this focus forms a Special Intervention Zone (SIZ) with an adjacent area of the Democratic Republic of the Congo (DRC) where transmission is still ongoing. Transmission is active in two foci, the small Lhubiliha focus bordering DRC, and the large Madi-MidNorth focus bordering the Republic of South Sudan (RSS). Both these foci also have potential cross-border transmission and therefore are considered SIZs. For the last three years, since 2016, the 11 districts comprising the Madi-MidNorth focus have attained the desired treatment coverage of at least 90% of the UTG.

Figure U1 shows the current status of onchocerciasis endemicity in Uganda. Figure U2 shows that 1,192,022 people are no longer at risk for oncho (e.g., they are living in areas where the disease has been eliminated and PTS has been successfully completed. Another 1,106,693 reside in areas where MDA has stopped, but PTS is not completed.

Background: Onchocerciasis was initially endemic in 17 transmission zones (foci), in 38 of the 112 districts in Uganda (Figure U1). The first Ugandan focus to successfully eliminate the disease was Victoria, where DDT was used to treat its river systems in the 1970s. Onchocerciasis control using annual mass treatment with Mectizan® began in 1989 in three districts with support from Sightsavers. The original Ministry of Health (MOH) control program based on ivermectin MDA received financial support from The River Blindness Foundation (RBF), GTZ/Bernhard Nocht Institute for Tropical Medicine, Hamburg, AVSI, Christoffelblindenmission (CBM), and Sightsavers. In 1996, The Carter Center (TCC) assumed the activities of RBF. In 1997, the African Program for Onchocerciasis Control (APOC) began supporting some Ugandan efforts and introduced the community-directed treatment with ivermectin (CDTI) approach. APOC also supported successful vector elimination efforts in two foci (Itwara and Mpamba-Nkusi) that used ground larviciding with temephos (Abate®) together with annual Mectizan distribution. In 2006, The Lions-Carter Center partnership helped launch semi-annual treatments (every six months) in a demonstration project designed to eliminate onchocerciasis from the Wadelai focus. This initiative was funded by the Mectizan Donation Program. Wadelai showed that twice-per-year treatment could be successfully provided by the CDTI approach**.**

The Uganda Ministry of Health announced a nationwide elimination policy in 2007 based on a 'flexible' strategy of twice-per-year treatment (where necessary and feasible) vector elimination/control using ground-based larviciding. The flexible elimination policy, which aimed for nationwide elimination of onchocerciasis by the year 2020, was immediately applauded and supported technically and financially by the Lions-Carter Center partnership (with special support from Mr. John Moores) and Sightsavers. Since 2007, The Carter Center has supported technical services, vector elimination/control activities and CDTI activities.

Currently, onchocerciasis elimination in Uganda is supported by The Carter Center, the United States Agency for International Development (USAID) ENVISION project led by RTI International, and Sightsavers, under the coordination of the Ministry of Health. The Carter

Center River Blindness Elimination Program (RBEP) provides technical assistance in all foci in Uganda regardless of its primary CDTI partners (and in the now 36 onchocerciasis endemic districts[1]), and in the cross-border SIZs.

The Lions Clubs International Foundation (LCIF) SightFirst program provided financial support through 2016, but the Ugandan Lions Clubs remain active participants and advocates for the national river blindness elimination activities, including engaging and mobilizing members of parliament, district and other relevant government officials. The Carter Center's Country Representative in Uganda, Ms. Peace Habomugisha, is a Lions Club member.

Uganda Laboratory Activity: In support of the elimination effort, The Carter Center has continued to fund equipment and reagent supplies for the MOH laboratory that offers diagnostic support to the elimination program. The laboratory is located at the MOH Vector Control Division in Kampala and provides polymerase chain reaction (PCR) testing for black flies and skin snips, and serologic enzyme-linked immunosorbent assay (ELISA) testing for OV16 IgG4 antibodies. Technical backup and reference lab support is provided by Prof. Thomas Unnasch's laboratory at the University of South Florida in Tampa, Florida. Prof. Unnasch is also the chair of the Ugandan Onchocerciasis Elimination Expert Advisory Committee (UOEEAC). In 2018, the lab analyzed 16,686 blood spots for OV 16 antibodies, about 15.5% (n=2,233) more than what was analyzed (n=14,453) in 2017. The lab also analyzed 11,436 *Simulium* flies by PCR compared to 1,483 analyzed in 2017.

Ugandan Onchocerciasis Elimination Expert Advisory Committee (UOEEAC): To ensure that the elimination decisions are supported with the best scientific and technical advice, in 2008 the Uganda MOH established the UOEEAC to: 1) review programmatic activity reports from each elimination-targeted focus in Uganda annually; 2) advise the MOH on focus-specific monitoring and evaluation activities and recommend halting of interventions when appropriate in accord with international and national guidelines; and 3) make any other recommendations to the MOH on activities needed to reach the national 2020 elimination goal. In addition to MOH and institutional representatives, the UOEEAC includes several members-at-large who are recognized for their international expertise in onchocerciasis. Mr. David Oguttu (MOH), National Coordinator for the onchocerciasis elimination program and Ms. Peace Habomugisha (The Carter Center country representative) serve as committee co-secretaries. The World Health Organization (WHO) Uganda representative attends these meetings as an observer, to avoid any conflict of interest since WHO will coordinate the future international verification team visit.

At its eleventh meeting, the UOEEAC recommended reclassification of two foci (Budongo and Bwindi) to "transmission interrupted". This means that 524,426 MDA treatments in these foci will halt in 2019 (292,804 in Budongo and 231,622 in Bwindi). Another focus (Nyagak-Bondo) remained under "suspected interruption" of onchocerciasis due to the potential for cross-border transmission per the UOEEAC decision, and the focus remains under mass treatment with ivermectin twice yearly. Interventions cannot be halted until the RB transmission status across the border in DRC is determined. UOEEAC recommended that the Ministry of Health work alongside DRC MOH personnel to conduct joint cross-border SIZ assessments. The DRC will

[1]36 oncho endemic districts: Kabale, Kanungu, Kasese, Kisoro, Rubirizi, Buhweju, Kamwenge, Ibanda, and Mitooma (in southwest Uganda); Buliisa, Hoima, Kabarole, Kibale, Kyenjojo, and Masindi (in western Uganda); Adjumani, Arua, Koboko, Maracha, Moyo, Nebbi, Yumbe, and Zombo (in the West Nile region bordering the Democratic Republic of the Congo); Amuru, Gulu, Kitgum, Lamwo, Lira, Nwoya, Oyam, Omoro and Pader districts (in the Mid North focus); and Bududa, Manafwa, Mbale, and Sironko (in the Mount Elgon focus in the east, bordering Kenya).

launch its own national advisory committee for onchocerciasis elimination in 2019 that will hopefully take up the issue of cross-border transmission.

Treatments: The Uganda RBEP assisted 3,785,037 MDA treatments including 148,512 passive treatments in clinics, totaling 3,933,549 treatments (Figure U3). All MDA treatments were delivered on a semiannual basis. The program achieved 94% of the 2018 MDA treatment target of 4,025,827. The Carter Center assisted 3,655,720 treatments in Bwindi, Lhubiliha, Madi/Mid-North and Nyagak-Bondo foci, while Sightsavers assisted 277,829 in the Budongo focus (Figures U3 and U4). The Uganda RBEP reached 98% of the 3,937 villages targeted for treatment. The kinship/neighborhood-based CDTI approach in northern Uganda (called the "Rwot Kweri" system) allowed all 11 districts in Madi/Mid-North to exceed the minimum treatment coverage of 90% of the eligible population (Figure U5).

Training and Health Education: Uganda trained or retrained 35,172 Community-Directed Distributors (CDDs) and 9,055 Community-Directed Health Supervisors (CDHSs) in 2018. Of those trained in 2018, 46% of the CDDs and 33% of the CDHSs were female. The current ratio of CDDs to population served is 1 CDD to 80 persons served, and the supervisor-to-CDD ratio was 1:5.

Integration: The RBEP-assisted CDTI program actively co-implements with the national lymphatic filariasis MDA treatments with ivermectin and albendazole in districts with both onchocerciasis and LF. This is especially important since according to WHO guidelines, onchocerciasis PTS cannot begin until LF MDA is halted.

2019 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, UGANDA

In 2019 stop MDA in Bwindi and Budongo foci, inform communities as to the reasons for stopping MDA, and launch Post Treatment Surveillance.

Conduct serological and entomological assessments in selected river systems in Madi-Mid North focus in order verify results obtained in sentinel sites.

Report Madi-MidNorth results by district with specific recommendations development by district, rather than by the entire focus.

Conduct treatment coverage surveys in consultation with HQ.

Continue Post-Treatment Surveillance in Bwindi, Budongo and Nyamugasani foci.

Maracha-Terego onchocerciasis focus was declared transmission interrupted in 2012 but PTS has not begun due to ongoing LF MDA. Encourage Maracha District to obtain high coverage with LF MDA so that it can pass TAS, thus allowing for stop LF MDA so that PTS for oncho to commence.

Continue integrating RB and LF activities where applicable.

When conditions are secure and there is successful control of Ebola in DRC, assist the Uganda Ministry of Health (MOH) in launching cross-border activities between Lhubiriha focus in Uganda, and adjacent areas in DRC (Health Zones of Beni, Kamango, Mutwanga, and Oicha).

Assess Nyagak-Bondo focus in Uganda as well as the adjacent area of Ituri (south) around Omi and Mi river systems in order to declare transmission interruption in the cross-border onchocerciasis focus.

Provide financial and administrative support for the 2019 Uganda Onchocerciasis Elimination Expert Advisory Committee (UOEEAC) meeting.

Support the Uganda MOH in its joint cross-border activities with DRC and RSS in Special Intervention Zones (SIZ) and provide a report that includes number of treatment rounds, numbers of treatments, and coverage in DRC and RSS border areas at the 2019 UOEEAC and Program Review. The Uganda MOH should promote promote twice-per-year treatment in border areas with DRC and RSS where RB transmission is ongoing.

Publish the post elimination surveillance report on Victoria Focus in a peer reviewed journal.

Complete the analysis of the 2016 Knowledge Attitude and Perceptions (KAP) survey conducted in three PTS foci (Kashoya-Kitomi, Mt. Elgon, and Imaramagambo). In consultation with Atlanta Headquarters, conduct a new study to determine what the former RB CDDs in these foci are doing now that onchocerciasis interventions have been halted.

Launch “slash and clear” activities on River Acii and River Esia once the Ministry of Health has formally accepted that vector control strategy for use in its program.

Carry out final evaluation for Obongi focus after Post-Treatment Surveillance period.

2019 Treatment and Training Objectives:

River Blindness	
Semiannual (UTG2)	3,606,442
Training Objectives	
CDDs	29,274
CSs	8,644

Figure U1

Uganda's Progress Towards Elimination of Onchocerciasis 2018

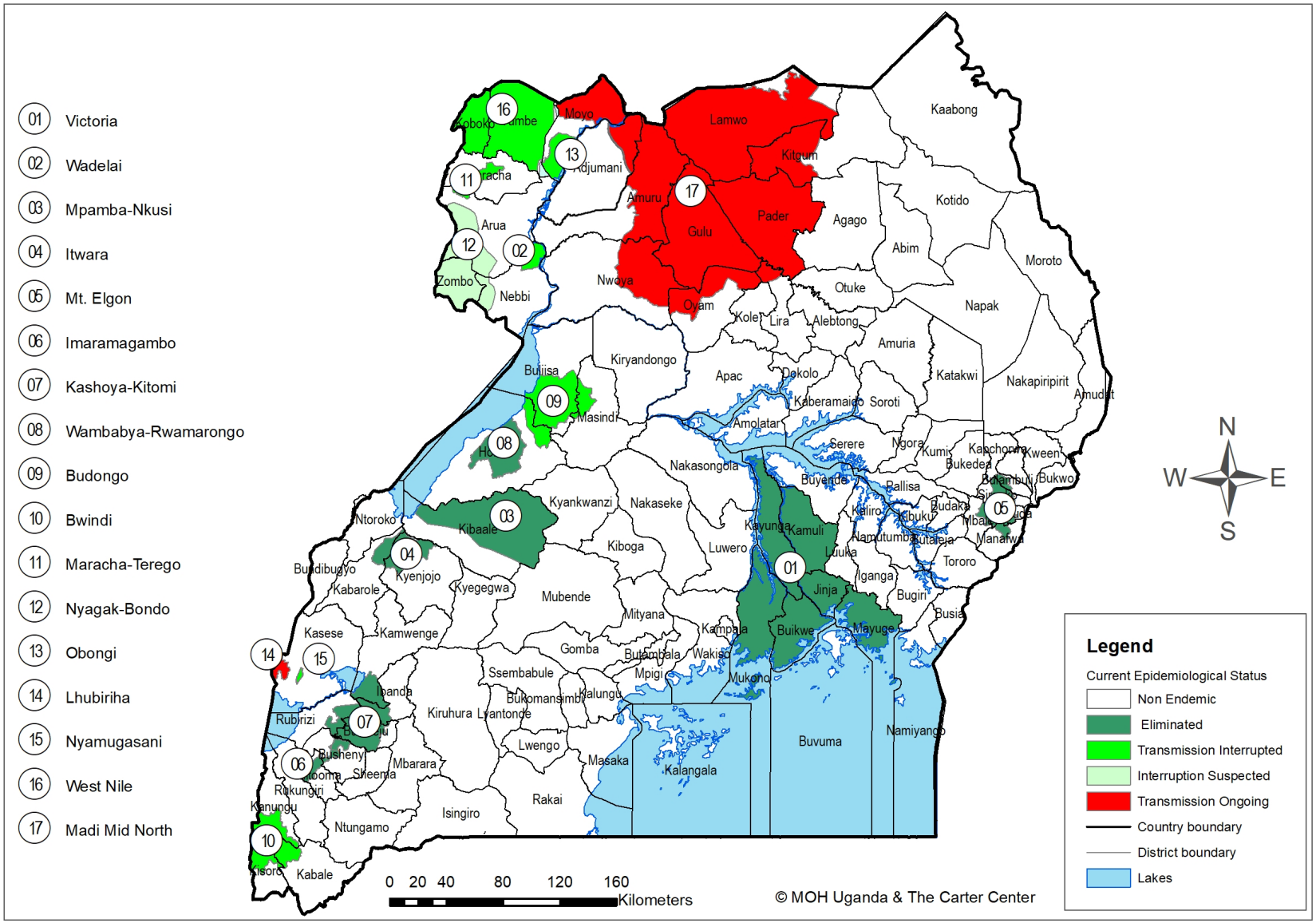


Figure U2

Foci Under Transmission Eliminated or Transmission Interrupted: Treatments Stopped (2011-2018)

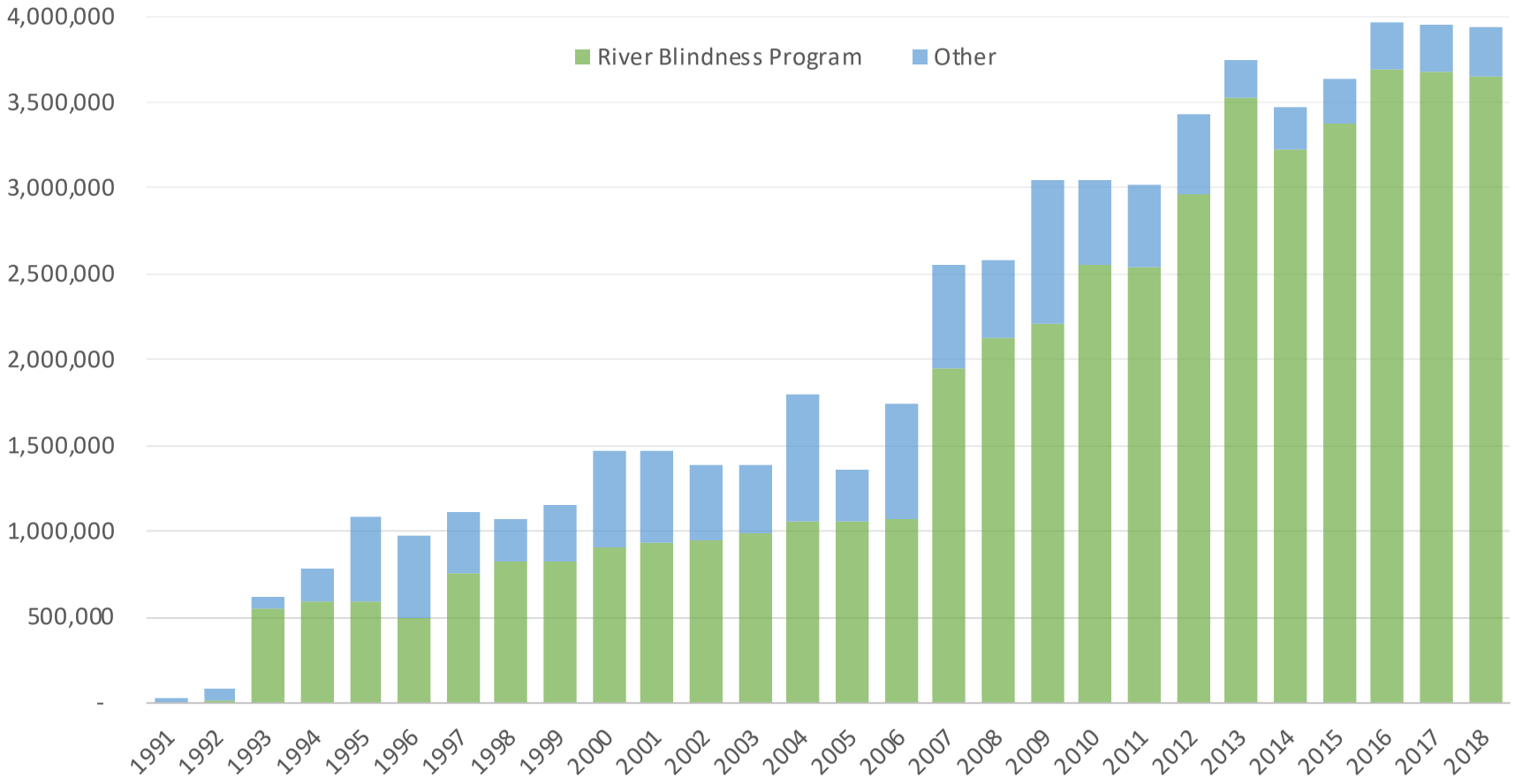
Focus	District	Transmission Interrupted	Total Popn (time of interruption)	UTG1	UTG2	Projected Popn	Treatments Stopped	Comms	PTS Status
Itwara	Kabarole	2011	31,763	26,999		39,636	33,691	49	PES
	Kyenjojo	2011	66,085	56,172		82,465	70,095	83	PES
Mt. Elgon	Manafwa	2011	40,604	33,698	67,396	48,955	83,224	98	PES
	Mbale	2011	50,253	40,781	81,562	60,589	103,001	131	PES
	Sironko	2011	76,375	64,396	128,792	92,083	156,542	179	PES
	Bududa	2011	161,630	139,656	279,312	194,873	331,284	412	PES
Mpamba-Nkusi	Kibale	2012	194,045	160,062	320,124	229,446	390,058	330	PES
Imaramagambo	Bushenyi	2012	112,633	95,738		123,196	104,716	212	PES
Kashoya-Kitomi	Buhweju	2013	60,255	49,512	99,024	67,818	115,290	97	PES
	Rubirizi	2013	77,250	63,676	127,352	86,946	147,807	170	PES
	Ibanda	2013	26,144	21,805	43,610	29,425	50,023	60	PES
	Kamwenge	2013	45,626	37,173	74,346	51,352	87,299	58	PES
Wambabya-Rwamarongo	Hoima	2013	75,733	62,654	125,308	85,238	144,905	70	PES
Sub Total			*1,018,396*	*852,322*	*1,346,826*	*1,192,022*	*1,817,935*	*1,949*	*PES*
Wadelai	Nebbi	2010	17,979	14,727	29,454	23,713	40,311	34	PTS
Maracha-Terego	Maracha-Terego	2012	120,121	108,098		205,371	174,565	307	No PTS
Obongi / Moyo	Moyo	2014	37,539	30,848		42,250	35,913	61	PTS
Nyamugasani	Kasese	2015	11,368	10,237		12,422	10,559	7	PTS
West Nile	Yumbe	2017	313,192	266,213		322,588	274,200	284	PTS
	Koboko	2017	182,568	155,183		188,046	159,839	394	PTS
Budongo	Masindi	2018	55,621	45,465	90,930	55,621	90,930	60	PTS
	Buliisa	2018	35,408	30,607	61,214	35,408	61,214	54	PTS
	Hoima	2018	84,994	70,330	140,660	84,994	140,660	70	PTS
Bwindi	Rubanda	2018	33,767	28,393	56,786	33,767	56,786	59	PTS
	Kanungu	2018	59,286	51,059	102,118	59,286	102,118	107	PTS
	Kisoro	2018	49,228	36,359	72,718	43,228	72,718	47	PTS
Sub Total			*995,071*	*847,519*	*29,454*	*1,106,693*	*1,219,813*	*1,484*	
Total			**2,013,467**	**1,699,841**	**1,900,706**	**2,298,715**	**3,037,747**	**3,433**	

Eliminated | Transmission interrupted

Note: There is no PTS in Maracha-Terego foci due to co-endemicity with LF

Figure U3

Uganda: Carter Center-Assisted Treatments and Total Mectizan® RB Treatments Provided, 1991-2018



*Treatments in 1992-1995 assisted by River Blindness Foundation.

Figure U4

Uganda - Transmission Interruption Suspected: Semiannual Treatments 2018

Focus	District	Transmission Suspected	Total Popn	UTG1	UTG2 RD1/RD2	Popn Treated		Popn Treated Cumulative	% TX Coverage UTG1		% TX Coverage UTG2 RD1/RD2	Active Villages UTG	LF Endemicity
						Rd1	Rd2		Rd1	Rd2			
Bwindi	Rubanda	2013	33,767	28,393	56,786	26,691	27,284	53,975	94.0	96.1	95.0	59	No LF
	Kanungu	2013	59,286	51,059	102,118	48,878	49,241	98,119	95.7	96.4	96.1	107	No LF
	Kisoro	2013	43,228	36,359	72,718	33,216	34,852	68,068	91.4	95.9	93.6	47	No LF
Nyagak-Bondo	Nebbi	2014	132,853	113,597	227,194	103,846	110,478	214,324	91.4	97.3	94.3	169	No LF
	Zombo	2014	259,661	214,414	428,829	195,057	202,331	397,388	91.0	94.4	92.7	742	No LF
	Arua	2014	187,992	160,783	321,566	145,026	155,242	300,268	90.2	96.6	93.4	325	LF
Budongo* *(Supported by TCC (vector) & Sightsavers (CDTI)*	Hoima	2014	84,994	70,330	140,660	64,028	64,028	128,056	91.0	91.0	91.0	70	No LF
	Buliisa	2014	35,408	30,607	61,214	29,839	30,065	59,904	97.5	98.2	97.9	54	No LF
	Masindi	2014	55,621	45,465	90,930	44,965	44,904	89,869	98.9	98.8	98.8	60	No LF
Total			**892,809**	**751,007**	**1,502,015**	**691,546**	**718,425**	**1,409,971**	**92.1**	**95.7**	**93.9**	**1,633**	

Note: Bwindi and Budongo foci qualified for Transmission Interrupted Status at the 2018 UOEEAC, MDA will be halted in 2019 .

Figure U5

Uganda: Transmission Ongoing- Semiannual Treatments 2018

Focus	District	Total Population	UTG1 2018	(UTG2) 2018 RD1/RD2	Popn Treated Cumulative 2018		Popn Treated Cumulative RD1/RD2	% TX Coverage UTG1 2018		% TX Coverage UTG2 2018 RD1/RD2	Active Villages UTG 2018	LF Endemicity
					Rd1	Rd2		Rd1	Rd2			
Lubiriha	Kasese	132,585	114,272	228,544	107,366	110,679	218,045	94.0	96.9	95.4	129	No LF
Madi Mid North	Adjumani	27,980	23,540	47,080	22,403	23,139	45,542	95.2	98.3	96.7	43	No LF
	Moyo	92,538	80,488	160,976	73,916	77,040	150,956	91.8	95.7	93.8	166	No LF
	Gulu	132,575	116,552	233,104	106,442	110,943	217,385	91.3	95.2	93.3	83	LF
	Omoro	171,517	146,947	293,894	134,193	139,747	273,940	91.3	95.1	93.2	149	LF
	Amuru	226,102	189,270	378,540	172,980	182,454	355,434	91.4	96.4	93.9	67	LF
	Pader	194,516	163,727	327,454	152,585	158,007	310,592	93.2	96.5	94.9	617	No LF
	Kitgum	99,600	84,608	169,216	77,922	81,262	159,184	92.1	96.0	94.1	236	LF
	Lamwo	146,483	124,555	249,110	113,323	120,083	233,406	91.0	96.4	93.7	427	LF
	Lira	75,303	63,217	126,435	58,946	60,422	119,368	93.2	95.6	94.4	224	No LF
	Oyam	24,557	21,038	42,075	19,938	20,696	40,634	94.8	98.4	96.6	35	No LF
	Nwoya	157,302	133,692	267,384	121,978	128,602	250,580	91.2	96.2	93.7	54	No LF
Total		**1,481,058**	**1,261,906**	**2,523,812**	**1,161,992**	**1,213,074**	**2,375,066**	**92.1**	**96.1**	**94.1**	**2,230**	

SUDAN

Summary: In 2018 Sudan and Ethiopia jointly declared a stop ivermectin MDA decision in the cross-border onchocerciasis transmission zone (focus) located between Gedarif State and North Gondar zone of Amhara Region, Ethiopia. Together with Ethiopia about 1.2 million treatments were stopped. A three to five-year post treatment surveillance (PTS) period began in accordance with World Health Organization guidelines. There are, however, other potential cross-border transmission areas on the eastern border of Sudan with Ethiopia. The Sudan program should collaborate with Ethiopia in order to map the border area if the security situation allows. If new endemic areas are found, the two programs should try to collaborate in a coordinated effort to eliminate onchocerciasis there. The Carter Center Peace program is investigating approaches to develop a project to bring peace and security in areas where the RBEP would wish to assess or augment programs.

In recent years, the RBEP has provided only technical support to Sudan, since all financial support has been provided by the Sudan government (an example for the rest of Africa to emulate)!

Background: The Republic of Sudan was the first African country to declare a nationwide onchocerciasis elimination policy, in December 2006. At that time, four river blindness foci were known in Sudan: Abu Hamad (River Nile state), Galabat (Gedaref state), Radom (South Darfur state), and Khor Yabus (Blue Nile state) (Figure S1). In moving from a control to elimination strategy, Mectizan® treatments were increased in 2007 from annual to semiannual in order to accelerate elimination in the isolated desert focus of Abu Hamad in the River Nile state. Successful interruption of transmission was declared in Abu Hamad in 2012 when semi-annual treatment with Mectizan ceased. A three-year PTS was successfully completed in 2015. In October 2015, the FMOH declared transmission in Abu Hamad focus to have been eliminated. Abu Hamad was the first published African focus eliminated under WHO Geneva guidelines (Zarroug et al, 2016).

Semiannual treatment was launched in Galabat in the Gedaref State in 2007 and continued until 2014. In 2015, assessments indicated that transmission had been interrupted and MDA could stop. However, Sudan agreed to continue annual Mectizan treatments because the cross-border sub-focus in Metema (in Ethiopia) had not satisfied all WHO guidelines for stopping MDA. The Sudan FMOH elected to reduce treatment frequency from semi-annual to annual (Figure S2). In 2017, Metema successfully fulfilled the WHO requirements and MDA will be halted in a coordinated fashion on both sides of the border in 2019.

The presence of onchocerciasis in Khor Yabus in Blue Nile state was originally described over 20 years ago, but the current status is unknown due to ongoing conflict there; there is no MDA program there. Khor Yabus borders Ethiopia and RSS and there is need to assess all sides of the border to determine if transmission is active. It is important to note that there are major population displacements due to the conflict. There are also other potential RB cross-border foci between the Geissan District of Sudan (also in Blue Nile state) adjacent to Assosa and Kemashi zones of Benshangul Gumuz region of Ethiopia and Wad Elmahi district (Blue Nile state) adjacent to Guba district of Metekel Zone in Ethiopia (Figure ES12).

The long lasting civil conflict in South Darfur rendered treatments in the Radom focus difficult. Recent improvement in security has resulted in some treatment expansion in recent years (Figure S2). The southwest and northeast boundaries of the focus have not yet been determined, and it could extend into South Sudan and the Central African Republic (Figure

ES12). In addition, it is hosting about 23,000 south Sudanese, most of whom are from Raja and West Bahr Ghazel State, areas known for their blinding strain of river blindness.

Treatments: The Sudan program provided a total of 69,200 treatments in 2018 in one round in Radom focus (Figure S2). The UTG in Radom, is still unknown. Currently, we are aware that there are at least 23,000 refugees from RSS that were treated in 2018 and should be treated during 2019. There is also a possibility of more indigenous communities requiring treatment, but mapping must be completed.

Training and Health Education: During 2017, the program trained a total of 1,441 Community-directed distributors. Most were male and the ratio of CDDs:population in Radom was about 1:500.

2019 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.

Galabat Focus in Gedaref State

Publish in a peer reviewed journal the experience of binational collaboration in the stop MDA decision in Galabat and Metema (Ethiopia).

Radom

If the Peace Program at The Carter Center or Sudan government is able to secure a stable peace where increased activities in the field are feasible in Radom, seek funds to launch an enhanced MDA program. This should involve detailed discussions with Headquarters. Given recent developments in Sudan this initiative has been postponed until political stability has been achieved.

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

If the security situation in Blue Nile allows, evaluate the status of onchocerciasis transmission in Khor Yabus, Wad Elmahi and Geissan districts of Blue Nile state. These surveys should be done in coordination with similar surveys in corresponding areas across the border in Ethiopia where RBEP assists.

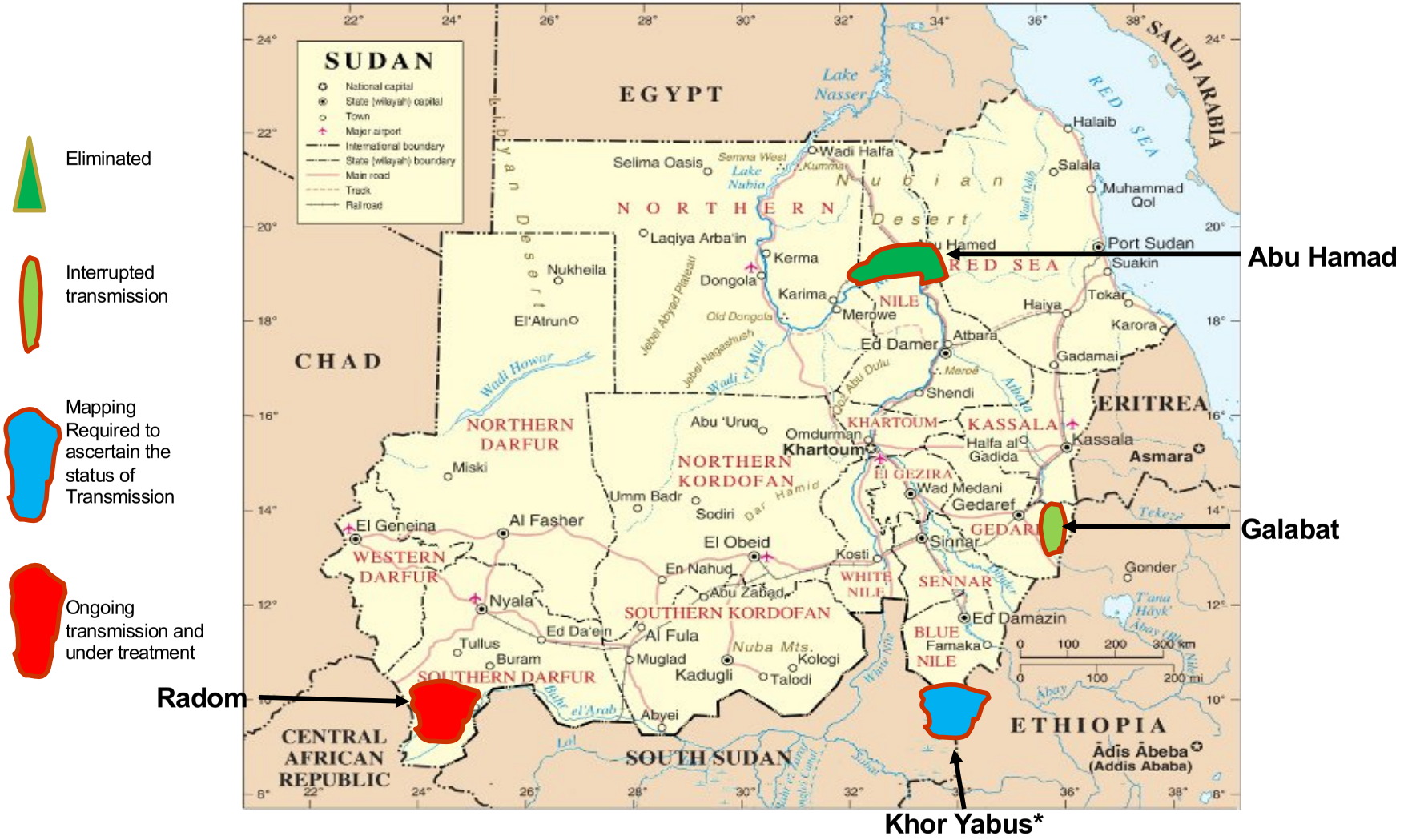
If these areas are shown to be endemic for onchocerciasis, then it is recommended that TCC/RBEP work to determine if an enhanced MDA program is feasible in Blue Nile state. In addition to twice-per-year MDA the program should determine whether a SIZ is needed between Sudan, Ethiopia and South Sudan. This decision should involve discussions with HQ.

2019 Treatment and Training Objectives:

River Blindness	
Semiannual (UTG2)	71,700
Training Objectives	
CDDs	692

Figure S1

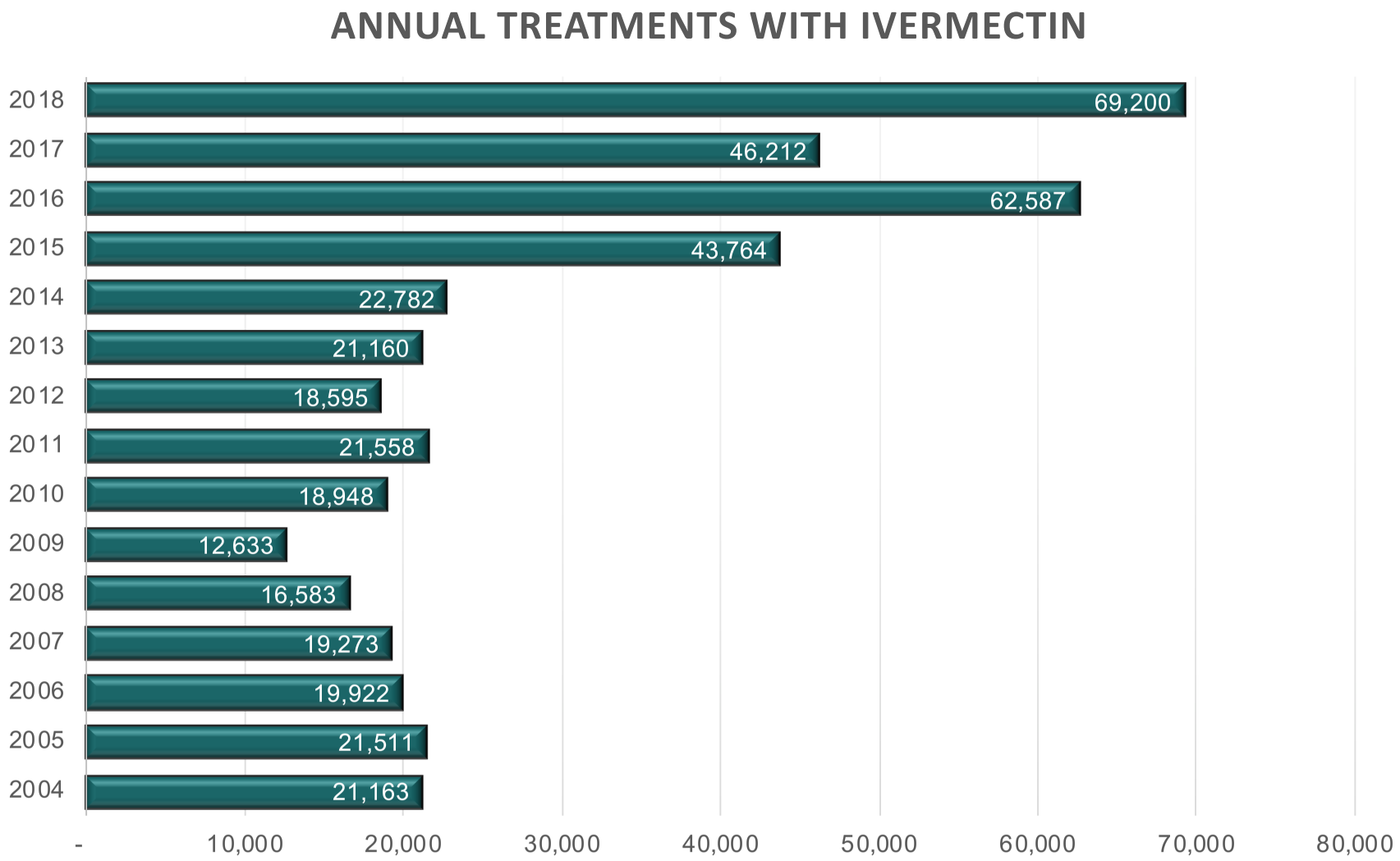
Map of Sudan Onchocerciasis Program Areas



**Note: In addition to Khor Yabus, potential transmission areas to be assessed in Blue Nile include Wad Elmahi and Geissan Districts. These multiple potential cross border foci with Ethiopia and South Sudan need to have their actual status determined which requires peace and security be established.*

Figure S2

Radom Mectizan® Treatments 2018



NIGERIA

Summary: The River Blindness Elimination Program (RBEP) in Nigeria seeks to interrupt transmission of onchocerciasis in the nine states it assists (Abia, Anambra, Delta, Ebonyi, Edo, Enugu, Imo, Nasarawa, and Plateau) (Figure N1) by 2025, in accord with the Federal Ministry of Health's (FMOH) plan for onchocerciasis elimination. The RBEP in Nigeria is headquartered in Jos, Plateau state, with supporting sub-offices in Benin City, Enugu, Lagos, and Owerri.

In 2018, 28,658,300 Mectizan® mass treatments (with health education) for onchocerciasis were distributed (Figures N2 – N3) in seven of those nine states with assistance from The Carter Center (TCC). Transmission of RB in Plateau and Nasarawa states was interrupted in 2018. TCC assisted in approximately 38% of all RB treatments in Nigeria in 2018 (Figure N4). Twice-per-year treatments for onchocerciasis numbered 23,154,702 in the six TCC-assisted states that the FMOH has determined require accelerated efforts to eliminate RB.

The RBEP in Nigeria is an integrated NTD program working also against lymphatic filariasis, schistosomiasis and intestinal worms (soil-transmitted helminthiasis-STH). For lymphatic filariasis (LF), Plateau and Nasarawa states stopped MDA at the end of 2012 (Figure N5). TCC is assisting these states to maintain good coverage with long lasting insecticidal bed nets (LLIN) to prevent reintroduction of the LF parasite and simultaneously fight malaria. Plateau and Nasarawa now must complete Morbidity Management and Disability Prevention requirements before they will reach Elimination as a Public Health Problem (EPHP) status. TCC did not assist any LF treatments in Nigeria in 2013. The seven southern RBEP-assisted states launched their LF programs in 2014, and quickly scaled up treatments (Figures N5 - N6). TCC's LF program supported 18,873,034 LF treatments in 2018.

In 2018, TCC assisted in providing 1,417,485 praziquantel treatments to school-aged children for schistosomiasis (SCH) (Figure N7), just 35% of our treatment target due to a praziquantel shortages in Nigeria. Praziquantel arrived too late for most programs to meet their treatment targets. In contrast, drug supply of mebendazole and albendazole was sufficient in 2018 for TCC to meet its targets for treating school-aged children for soil-transmitted helminths (STH); the 8,894,524 treatments assisted was an 18% increase over 2017 (Figures N8 - N10). It should be noted that both STH and SCH treatment objectives vary by year based on WHO guidelines for treatment schedules based on prevalence surveys.

The 2018 activities in Nigeria are thanks in large part to TCC's partnership with USAID's ENVISION project, led by RTI International, along with other key partners, such as the Margaret A. Cargill Foundation, the Izumi Foundation, and many generous individual donors. In addition to the FMOH, we acknowledge The Task Force for Global Health and the World Health Organization. Our programs would not be possible without donated products from many different partners: MSD, also known as Merck & Co., Inc., Kenilworth, N.J. USA for Mectizan (ivermectin); Merck KGaA, Darmstadt, Germany (E-Merck) for praziquantel; GSK for albendazole; Johnson & Johnson for mebendazole; and Clarke Cares Foundation/Clarke Mosquito Control for LLIN.

River Blindness in Nigeria

***Background on River Blindness*:** Nigeria is home to about 24% of the global population at risk for onchocerciasis, making it the most endemic country in the world. The country's onchocerciasis program is the largest Mectizan® distribution program globally. In 2013, the Federal Ministry of Health (FMOH) of Nigeria released a master plan for neglected tropical

diseases (NTDs) that articulated a national policy of onchocerciasis elimination. The FMOH also established its Nigeria National Onchocerciasis Elimination Committee (NOEC) in 2015, whose meetings are supported by The Carter Center. Based on assessments done in 2017, a major milestone was reached when the NOEC recommended MDA for RB be stopped in Plateau and Nasarawa states in 2018. Plateau and Nasarawa are the first two Nigerian states to interrupt RB transmission and stop MDA in according with WHO Geneva guidelines. The two states demonstrated, with tests of over 6,000 children and more than 18,000 black flies, that the infection was no longer present, and Mectizan treatment could be stopped after up to 26 years of annual therapy in some areas.

Treatments: In 2018, the TCC-assisted RBEP program in Nigeria provided 28,658,300 Mectizan® treatments along with health education (Figures N2 and N3), achieving 90% of the treatment target. This is a 13% decrease from 2018 treatments, primarily due to the withdrawal of treatments in Plateau and Nasarawa.

In accordance with NOEC guidelines that call for twice-per-year treatment in states 'not on track' to reach interruption of transmission by 2022 (including 5 TCC-assisted states: Enugu, Anambra, Imo, Abia, and parts of Edo), the majority of treatments in 2018 (23,154,702) were semiannual. These are the so-called 'red states' in the NOEC RB stratification of Nigeria states (ES12). No severe adverse events (SAEs) were reported following Mectizan® treatments in RBEP-assisted SE/SS states in Nigeria in 2018. The program conducts close monitoring for adverse reactions because of the presence of *Loa loa* in this part of Nigeria. A TCC study conducted in over 10,000 persons resident in the southern states in 2016 showed no very high-density *Loa* infections, which is the only risk factor for central nervous system related SAEs (Emukah et al 2018).

RB training, health education, and financial contributions are discussed in the Integrated Programs sections below.

The Integrated LF, SCH, and STH Programs in Nigeria

Background: The RBEP is an integrated program in Nigeria, where we pioneered the concept of using the RB mass treatment logistical system as a platform for launching of LF elimination and SCH control activities, sharing costs and infrastructure across several programs (Hopkins 2001, Dean 2003). The integrated RB program began in 1999 with urinary schistosomiasis interventions, expanding to include LF in 2000, trachoma in 2001, malaria in 2003, and STH in 2014. Background information on LF, SCH and STH is provided in Annexes 7 and 8. Our studies on integration showed that it offered broader services with lower costs and higher efficiency among disease programs that use similar community-based strategies. The Carter Center also pioneered 'triple drug administration' (TDA) – simultaneous administration of ivermectin, albendazole, and praziquantel – demonstrating that TDA is safe, feasible, and gave enormous savings (40%) compared with giving two separate treatment rounds (ivermectin and albendazole separated from praziquantel) (Evans et al. 2011, Eigege et al. 2013).

Training and Health Education: There were 72,361 health personnel and volunteers involved in drug distribution in TCC-assisted states for the various programs in 2018: 8,310 community supervisors and 64,051 CDDs. The ratio of CDDs to persons served decreased in 2018 to an average 421 to 1 but remained well above the target in Nigeria of one CDD per 250 persons. The primary reason for this is heightened denominators due to expansion of MDA to urban areas, where distribution often occurs via health workers, not CDDs. The ratio will improve as the program finetunes this calculation by separating out the urban population from its

denominator and focusing on population-to-CDD ratios only in rural areas. In 2018, one community supervisor managed about six CDDs (an improvement from 2017, and nearing the target of five), and 51% of community supervisors were female.

Lymphatic Filariasis: The goal of the LF program is to achieve the national and WHO goal to eliminate LF as a public health problem with MDA, health education, distribution and use of LLIN, and MMDP. However, TCC is also interested in gathering additional evidence to demonstrate elimination of LF transmission. Entomological surveys showing no LF infection, and expanded surveys beyond the child-based TAS surveys have shown no LF antigen in the adult population (Noland, in preparation).

The TCC LF program in Plateau and Nasarawa was the first to be launched in Nigeria, in 2000 and has been well documented. Early mapping and MDA launching and scale up was published by Eigege et al. (2003) and Richards et al. (2011). When the program began, LF was widespread in Plateau and Nasarawa states, and mass treatment and health education was required in all cities and villages in the 30 LGAs of the two states. MDA started in 2000 and achieved scale in 2003. In 2008, a survey for LF prevalence demonstrated that 10 of the 30 LGAs had achieved the elimination threshold (based on LF antigenemia prevalence) and MDA could be stopped (King et al. 2012). In subsequent surveys conducted in 2012 (Eigege et al. 2017) using the newly released WHO Transmission Assessment Survey (TAS) methodology, it was determined that MDA for LF could be stopped throughout both states, and approximately 4 million treatments were halted at the end of 2012. Entomological assessments demonstrated that transmission was halted when LLIN were distributed (Eigege et al. 2013). All 30 LGAs entered a period of post-treatment surveillance (PTS), beginning in 2013. In 2014 and 2016, PTS TAS-2 and TAS-3 surveys confirmed that LF antigen levels remained negative after LF MDA stopped. Plateau and Nasarawa are the first two Nigerian states to stop MDA for LF and demonstrate no recrudescence of infection.

In the seven TCC-assisted states in the SE/SS, annual LF MDA was launched in 2014 with support from USAID's ENVISION project, led by RTI International. To manage this transition, and in keeping with the integration approach, the program began in LGAs with an existing river blindness program (Figure N4), then expanded rapidly into LGAs without river blindness. In 2018 there were 18,873,034 treatments with ivermectin and albendazole. This expansion is remarkable, particularly because the area is challenged by the presence of *Loa loa*. Current WHO recommendations for LF MDA in *Loa loa* areas avoids the use of Mectizan® due to its associated risk of SAEs. The TCC-assisted program therefore began in ivermectin-naïve areas by following the WHO strategy for twice-per-year MDA with albendazole alone, together with LLINs. However, the Carter Center, in partnership with the Federal and local governments of Nigeria, conducted a large *Loa loa* survey in 2016 (using the 'LoaScope') and determined that high density infections with *Loa loa* were not detectable in ivermectin-naïve RBEP assisted areas, as noted above in the RB section (Emukah *et al., AJTMH,* 2018). After our results were reviewed by the FMOH, NOEC and the Mectizan Expert Committee (MEC), we were given approval by the FMOH and the MEC to use Mectizan in MDA in the southern states. Thus, after two years of albendazole-alone monotherapy MDA, the program switched to annual treatment with ivermectin and albendazole in 2017 with considerable savings of time and money.

Fighting Malaria and Lymphatic Filariasis with LLINs: In Nigeria, LF is transmitted by the same mosquitoes that transmit malaria (*Anopheles gambiae* sl and *Anopheles funestus*). LLINs, one of the most important prevention tools for malaria, have been shown to also be useful as an adjunct to MDA in the LF elimination program. As noted above, Eigege et al. (2013) demonstrated in an entomological longitudinal study that LLINs were synergistic with MDA in

halting transmission of LF. Accordingly, TCC continues to support the FMOH policy of integrated malaria LF field operations in Nigeria. Between 2009 and 2013, all nine TCC-supported states received LLINs as part of the nationwide mass distribution of nets that aimed to provide two nets to every household. TCC has assisted with the distribution of 11.6 million LLINs in Nigeria since 2004.

Schistosomiasis (SCH) Control and Soil-Transmitted Helminthiasis (STH) Control: The SCH program was launched in Plateau and Nasarawa states in 1999 with a focus on urinary SCH (*Schistosoma haematobium* infections) (see Annex 8). The program initially remained limited for several reasons, most importantly the lack of donated praziquantel (Richards at al. 2006, Gutman et al 2008, Gutman et al 2009). With the advent in 2008 of large praziquantel donations through the World Health Organization (WHO) by Merck KGaA (E-Merck), Germany, and with support from USAID's ENVISION project, led by RTI International, and the Izumi Foundation, the SCH program expanded in scope to also include intestinal schistosomiasis (*S. mansoni* infections) as well as in breadth, with new praziquantel distribution in the seven states of the SS/SE.

In 2018, we assisted in providing 1,417,485 praziquantel treatments (Figure N7). SCH treatment figures normally vacillate from year to year in adherence to the WHO recommendations (more can be found on this topic in Annex 8). However, in 2018, the reason for the fluctuation was the very late arrival of praziquantel, which resulted in insufficient treatments; we were only able to reach 35% of our target of 4.1 million.

In 2018, we assisted 8,894,524 treatments for soil-transmitted helminths, achieving 79% of the target for the year. Of these treatments, 2,734,470 were given in areas targeted for twice-per-year treatments.

Both SCH and STH have complicated WHO treatment guidelines (Annex 8), which have been a challenge to implement. Between the two diseases there are five potential treatment frequencies, and the treatment frequency can change when prevalence is evaluated after 5 or so years of treatment. Coupling this with RB (annual or semiannual) and LF treatments (annual), the integrated MDA program is extremely complicated to implement in the 168 LGAs TCC assists. The design of health education, training, budgeting, and logistics/drug supply must be tailor-made for each LGA, all of which could change for a given LGA from year to year.

As Plateau and Nasarawa States are not treating for LF and RB due to elimination and interruption of transmission, respectively, the two states are in the process of transitioning completely to school-based SCH/STH treatment, which means new collaboration with both the Ministry of Health and the Ministry of Education. It is important to study this transition and implications that the school-based (versus community-based) programs might have; i.e. they might be unable to reach children not in school (particularly girls, who are less likely to be enrolled), as well as preschool children, all of whom could be more easily reached in community-based programs.

In 2013, the FMOH and The Carter Center, with support from USAID/RTI ENVISION funding, mapped the prevalence of SCH and STH in Plateau and Nasarawa states by conducting urine and stool surveys among 11,000 school children. An impact evaluation was conducted 2018 in the same schools that participated in the 2013 survey; 9,660 children participated. Both studies looked at both SCH/STH prevalence and intensity of infection. While data analysis is still underway, we have preliminary results. Compared to 2013, schistosomiasis prevalence

dropped from 15% to 7% in Nasarawa and from 11% to 6% in Plateau. Infection with soil-transmitted helminths dropped from 15% to 11% in Nasarawa but was flat at 8% in Plateau. Several LGAs saw statistically significant changes in schistosomiasis infection, but only one did for STH. The 2018 survey identified poor latrine coverage, with less than half of the 202 surveyed schools having a latrine. Once the results are finalized, some LGAs will likely see adjustments in their treatment regimen based on WHO guidelines.

2019 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, NIGERIA

Overarching for the three programs:

As soon as possible, meet with FMOH NTD drug supply personnel to submit a supplementary 2019 drug application for TCC-assisted areas, as the order already submitted for our LGAs are insufficient for 2019 treatment targets.

Complete the feasibility assessments for rolling treatment coverage surveys, in close consultation with Headquarters. The final outcome should be one dedicated team per state serving to rapidly and continually assess the entire state.

Whenever possible, include LF, RB, SCH, and STH (as appropriate) sentinel villages in any population-based survey activities being conducted (in these SVs' states or LGAs). This would help us to conduct serial monitoring of SVs.

Continue providing awards in each state to the best CDD, FLHFS, village leader and community supervisor.

The ratio of CDDs: 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 community supervisor:5 CDDs and 1 community supervisor per village. When calculating population served per CDD, remove urban populations from the equation since these are typically served directly by health workers.

Conduct (in consultation with Headquarters) a quantitative CDD attrition study (see Kaplan-Meier survival methodology) and attempt to determine causes of CDD attrition. Develop with Headquarters a common definition of 'CDD attrition.' Explore the relationship of increasingly complicated registers and roll up forms to CDD attrition rates.

Improve community mobilization so that more communities support their CDDs.

Report results at the next Program Review on the success of the Carter Center-developed household rollup forms being used in the SE/SS by CDDs to help them more accurately tally data from the CDD treatment registers prior to submission to frontline health facilities.

Lymphatic Filariasis/Malaria:

The program in Plateau and Nasarawa should undertake 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 do at least the required level of MMDP work to prepare the dossier supporting the two states' claim to have 'eliminated LF as a public health problem.' Launch in close consultation with Headquarters Morbidity Management and Disability Prevention (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 referral systems. Seek Izumi support for this work.

In the SS/SE states, continue to focus only on MDA for the time being; only support MMDP work only in states that have stopped MDA by passing TAS-1. It is important to note that USAID/RTI Act to End NTDs | East does not support MMDP work.

Publish in a peer reviewed journal the Greg Noland-led studies that demonstrate elimination of transmission of LF was accomplished in Plateau and Nasarawa states.

Complete the analysis of specimens (Wb123 and OV16) from the research funded by Task Force for Global Health.

Continue entomological collections in LF sentinel villages in Plateau and Nasarawa, but store (rather than dissect) specimens for later molecular testing for kdr genes. Seek a collaborator to undertake lab evaluations of the collections.

Conduct pre-TAS in 19 LGAs in Anambra, Ebonyi and Imo with FTS. Where these LGAs are oncho-endemic, also collect blood spots for OV16 to determine onchocerciasis transmission status (see below in Onchocerciasis section). Conduct subsequent TAS1 where pre-TAS indicates and conduct additional pre-TAS in collaboration with the FMOH as LGAs become eligible.

Onchocerciasis:

A major effort should be made in 2019 to identify the next TCC-assisted states ready to propose to NOEC for stop MDA surveys. To help us assess onchocerciasis transmission status and maximize resources, take a DBS for OV16 ELISA in the 19 LF pre-TAS LGAs.

Publish the results from the 2017 Plateau and Nasarawa Stop MDA studies in a peer reviewed journal.

Publish the hypoendemic onchocerciasis mapping data (from the 2016 *Loa loa* study) that used OV16 RDTs.

Provide results from entomological surveillance in areas bordering Plateau and Nasarawa, such as Benue state and Bauchi. Collect flies and preserve vector flies in Plateau and Nasarawa at selected cross border sites.

Provide entomological lab support for halting MDA for RB in Kebbi and, Zamfara states (states assisted by Sightsavers), if specimens are provided. Offer technical support to other states for stop MDA assessments, in consultation with Headquarters.

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).

Expand twice-per-year treatment (obtaining good coverage in all rounds) in SE/SS assisted areas, wherever drugs are being made available by FMOH.

Consider providing support to MITOSATH for treatment in the Edo-Ondo SIZ, so that it is occurring with good coverage on both sides of the border.

Conduct a reclassification survey in Edo, Delta and Ebonyi using OV16 prevalence to determine whether these states will receive a new status on the NOEC map.

Present to NOEC, for implementation decisions, the survey results from the assessment of RBEP-assisted ivermectin-naïve local government areas in SE/SS that are not yet slated for ivermectin treatment either for RB or LF.

In consultation with Headquarters, calibrate black fly collection by traps with nearby collections by human attractants so that ATP calculations are possible.

Provide financial and administrative support for the 2019 NOEC meetings.

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

The written description of SCH/STH work under the new USAID/RTI Act to End NTDs | East focuses on "mainstreaming" the two diseases. We are awaiting indicators and detailed guidance to clarify the meaning of "mainstreaming." Headquarters will seek to determine if this means future pressure to reduce external funding to the SCH/STH program.

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.

A priority activity should be to, reassess SCH/STH prevalence in LGAs where the RB or LF platform does not exist, and consider options for either stopping MDA (if WHO guidelines and the FMOH permit) or to 'mainstream' MDA such that national funds will begin to support the program.

Complete SCH/STH mid-term assessment for impact for IZUMI.

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

Reanalyze data available from Plateau and Nasarawa studies comparing three treatment approaches to reach out of school (but school aged) children and girls: a) teacher MDA, b) CDD MDA and c) combination MDA (teacher and CDD). Consider publishing existing data or collecting additional data if necessary, to publish.

2019 Treatment and Training Objectives:

River Blindness	
Annual (UTG)	5,982,683
Semiannual (UTG2)	26,518,985
Total RB Treatments	**32,501,668**

Lymphatic Filariasis	
Annual (UTG)	20,628,466

Schistosomiasis	
Annual (UTG)	5,245,018

Soil-Transmitted Helminths	
Annual (UTG)	6,480,928
Semiannual (UTG2)	2,673,738
Total STH Treatments	**9,154,666**

Training Objectives	
CDDs	73,248
CSs	9,577
Teachers	15,591
FLHFS	6,930

Figure N1

Nigeria: Carter Center-Assisted States

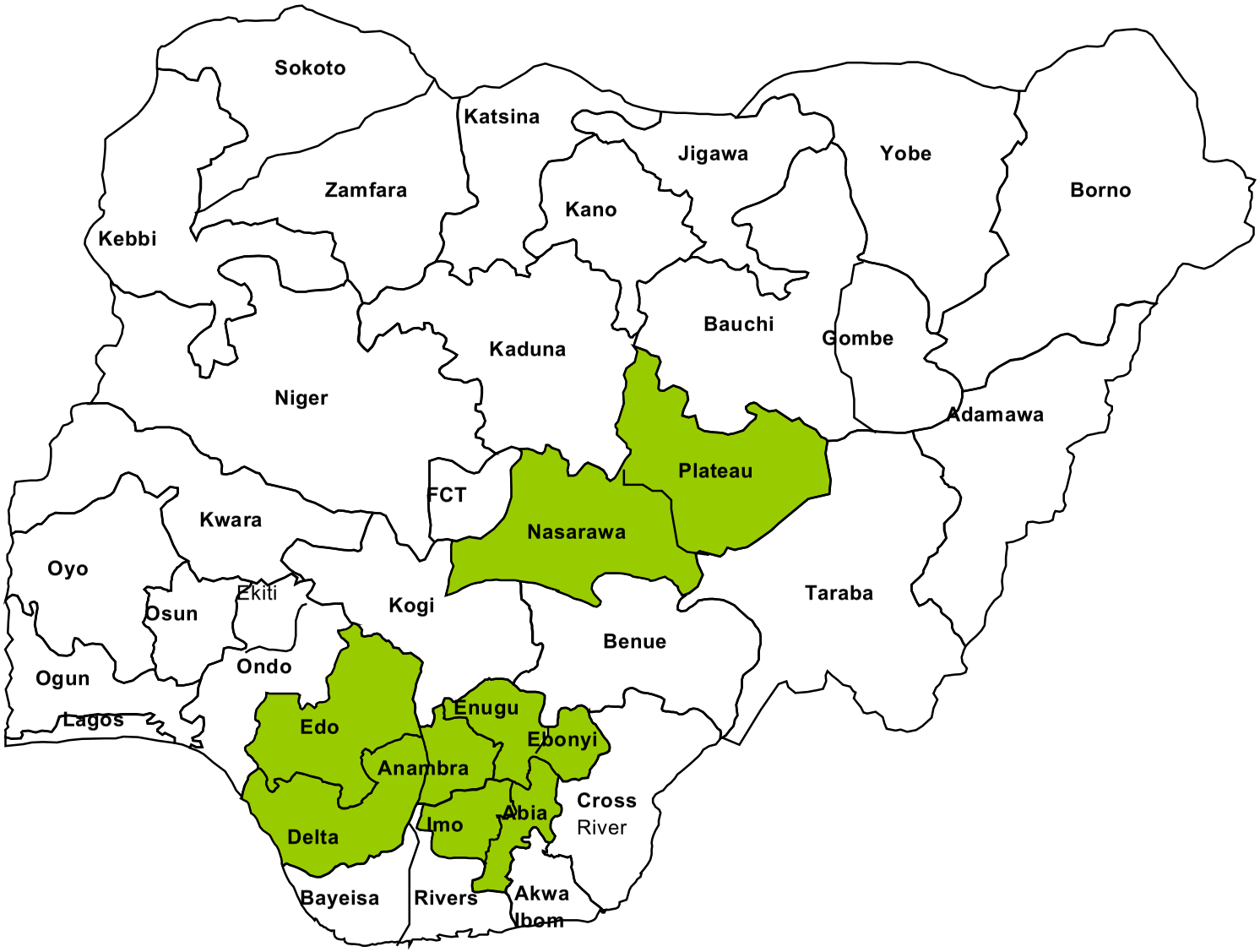


Figure N2

Nigeria: Carter Center-Assisted Areas
2018 River Blindness Semiannual Treatments

State	Number LGAs Targeted	Population in Targeted LGAs	UTG2	Round 1 Treatments	Round 2 Treatments	Total Treatments	% UTG2 reached	Village Goal	Villages Reached	% Village Goal Reached
Enugu	17	3,924,780	6,279,648	2,823,312	2,914,565	5,737,877	91%	6,218	6,219	100%
Anambra	16	4,542,770	7,268,432	3,563,010	3,512,773	7,075,783	97%	2,109	2,109	100%
Edo	5	1,080,064	1,728,102	609,227	823,356	1,432,583	83%	1,016	950	94%
Imo	18	3,720,261	5,952,418	2,744,262	2,598,421	5,342,683	90%	3,646	3,646	100%
Abia	12	2,446,312	3,914,100	1,844,298	1,721,478	3,565,776	91%	2,541	2,540	100%
Total	**68**	**15,714,187**	**25,142,700**	**11,584,109**	**11,570,593**	**23,154,702**	**92%**	**15,530**	**15,464**	**100%**

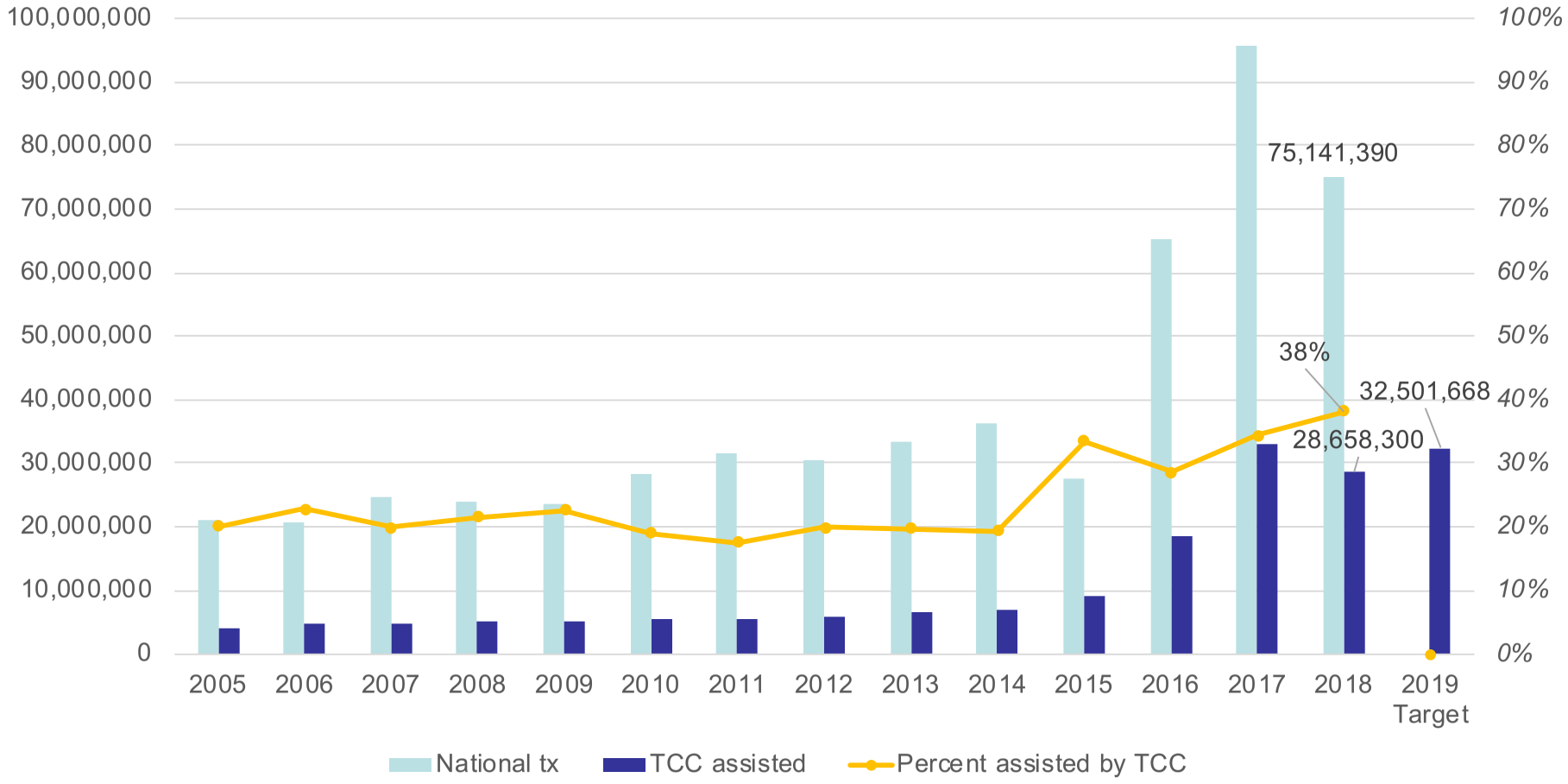
Figure N3

Nigeria: Carter Center-Assisted Areas
2018 River Blindness Annual Treatments

State	LGAs Targeted	Total population in targeted LGAs	UTG	Treatments	Percent of UTG Reached	Village Goal	Villages Reached	Percent of Village Goal Reached
Enugu	10	2,243,771	364,739	344,001	94%	189	189	100%
Ebonyi	2	455,924	1,795,017	1,730,795	96%	2,357	2,357	100%
Edo	11	2,287,217	1,829,774	1,529,971	84%	1,256	1,206	96%
Delta	15	3,228,883	2,583,106	1,898,831	74%	1,834	1,639	89%
TOTAL	**38**	**8,215,795**	**6,572,636**	**5,503,598**	**84%**	**5,636**	**5,391**	**96%**

Figure N4

Nigeria: Annual Carter Center-Assisted and National* Mectizan® Treatments for River Blindness, and 2019 Target



* Source of national figures: Federal Ministry of Health, Nigeria

Figure N5

Nigeria: Carter Center-Assisted Lymphatic Filariasis Treatments (with Mectizan® and Albendazole) and 2019 Target

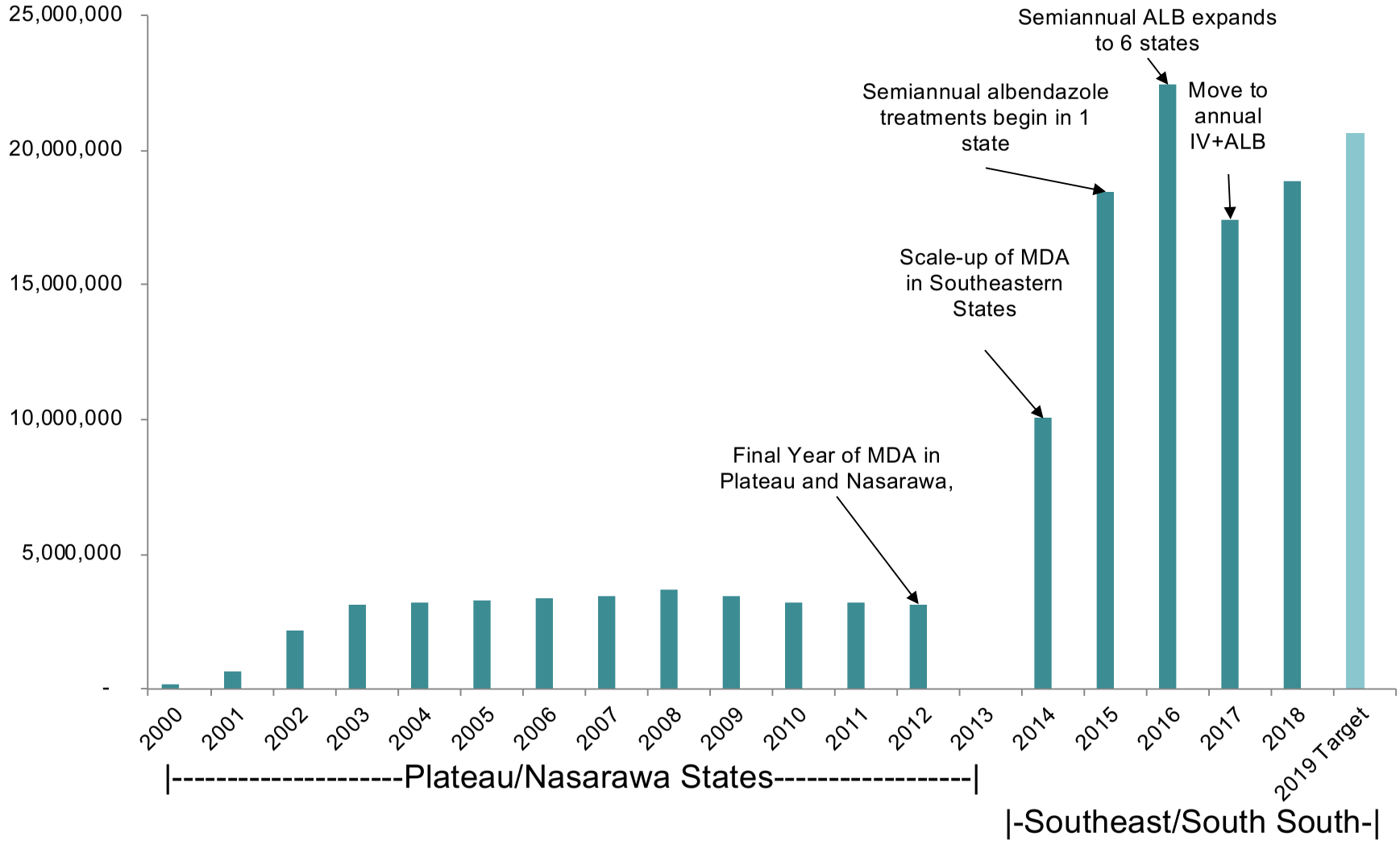


Figure N6

Nigeria: Carter Center-Assisted Areas 2018 Lymphatic Filariasis Treatments

State	Number of LGAs targeted	Total population in targeted LGAs	UTG	Treatments	Percent of UTG Reached	Village Goal	Villages reached	Percent Village Goal reached
Enugu	14	3,684,543	2,947,634	2,689,847	91%	5,356	5,357	100%
Anambra	21	5,624,370	4,499,496	4,915,142	109%	2,935	2,935	100%
Ebonyi	9	2,051,596	1,641,277	1,577,518	96%	2,541	2,541	100%
Edo	7	1,521,206	1,216,965	1,016,323	84%	1,187	1,187	100%
Delta	16	3,171,533	2,537,226	1,986,238	78%	2,392	2,290	96%
Imo	27	5,292,000	4,233,600	3,868,907	91%	5,325	5,311	100%
Abia	17	3,811,414	3,049,131	2,819,059	92%	3,550	3,548	100%
Total	**111**	**25,156,663**	**20,125,329**	**18,873,034**	**94%**	**23,286**	**23,169**	**99%**

Figure N7

Nigeria: 2018 Carter Center-Assisted Schistosomiasis Treatments with Praziquantel

State	Number of LGAs Targeted	Total population in targeted LGAs	UTG	Treatments	Percent of UTG Reached	Village Goal	Villages Reached	Percent of Village Goal Reached
Enugu	12	3,229,770	904,336	0	0%	4,891	0	0%
Anambra	1	225,156	63,044	56,366	89%	212	212	100%
Ebonyi	9	2,121,454	594,007	0	0%	1,935	0	0%
Edo	3	676,050	189,294	0	0%	189,294	0	0%
Delta	8	1,596,097	446,905	41,450	9%	446,905	41,450	9%
Plateau	17	4,275,015	1,197,004	751,911	63%	7,000	5,516	79%
Nasarawa	13	2,507,898	702,211	567,758	81%	3,969	3,284	83%
Total	**63**	**14,631,440**	**4,096,801**	**1,417,485**	**35%**	**654,206**	**50,462**	**8%**

Figure N8

Nigeria: 2018 Carter Center-Assisted Annual Soil-Transmitted Helminthiasis Treatments

State	Number of LGAs Targeted	Total population in targeted LGAs	UTG	Treatments	Percent of UTG Reached	Village Goal	Villages Reached	Percent of Village Goal Reached
Enugu	9	2,445,814	684,828	607,163	89%	3,391	3,391	100%
Anambra	12	3,068,942	859,304	698,146	81%	1,533	1,533	100%
Ebonyi	7	1,612,074	451,381	415,269	92%	1,409	1,409	100%
Edo	10	2,578,042	721,852	509,476	71%	1,134	870	77%
Delta	9	2,004,940	561,383	446,656	80%	1,268	1,268	100%
Imo	2	437,824	1,228,764	1,055,070	86%	4,451	4,453	100%
Abia	2	487,276	848,052	637,609	75%	3,019	3,017	100%
Plateau	17	4,275,015	1,197,004	1,115,568	93%	7,000	6,183	88%
Nasarawa	13	2,507,898	702,211	675,097	96%	3,969	3,885	98%
Total	**81**	**19,417,824**	**7,254,779**	**6,160,054**	**85%**	**27,174**	**26,009**	**96%**

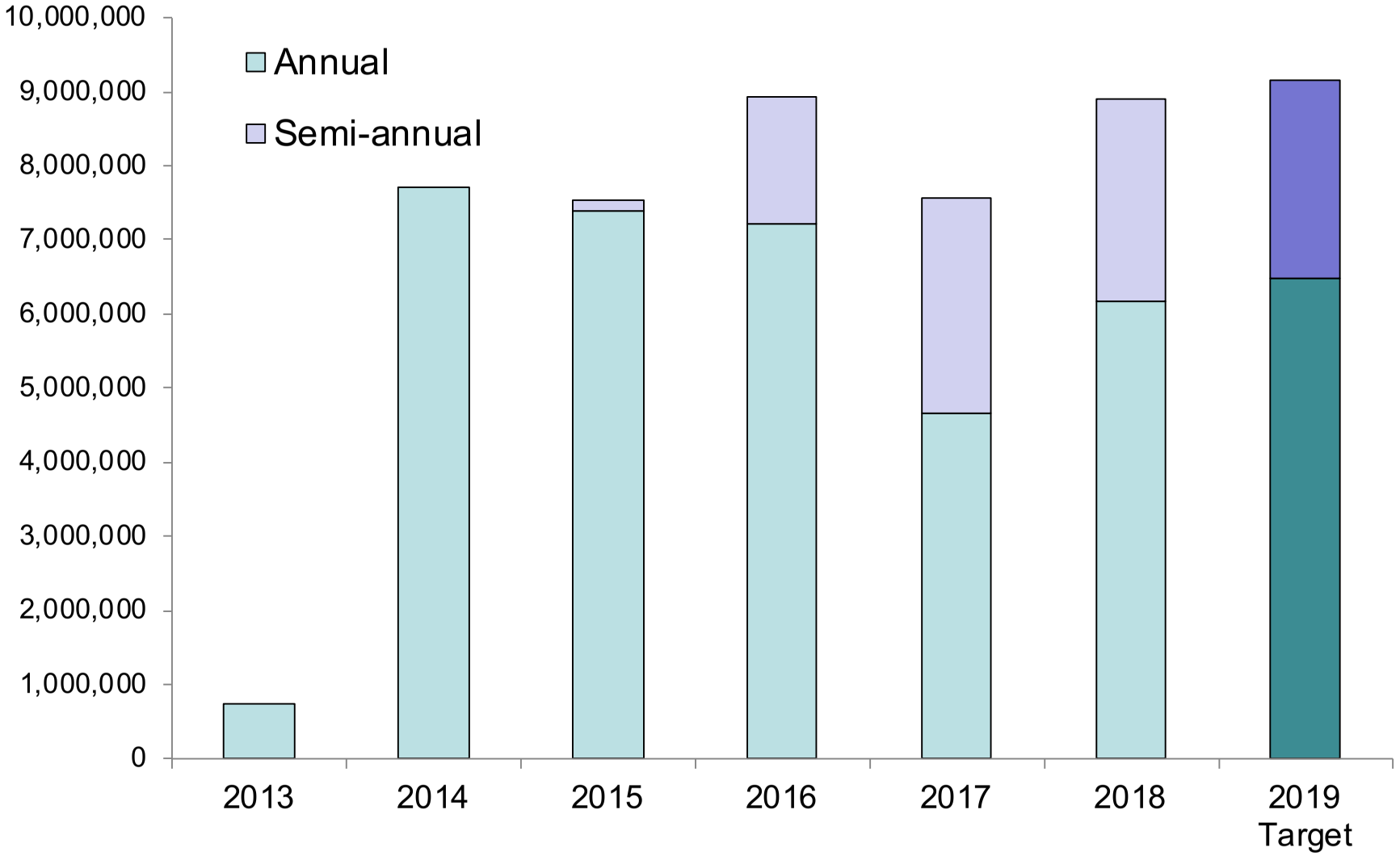
Figure N9

Nigeria: 2018 Carter Center-Assisted Semiannual Soil-Transmitted Helminthiasis Treatments

State	No. of LGAs targeted	Total population in targeted LGAs	UTG2	Round 1 Treatments	Round 2 Treatments	Total Treatments	% of UTG2 Reached	Village Goal	Villages Reached	% of Village Goal Reached
Enugu	1	179,842	100,712	38,570	40,513	79,083	79%	176	176	100%
Ebonyi	3	663,036	371,300	179,691	165,049	344,740	93%	1,292	1,292	100%
Edo	8	1,750,257	980,144	229,776	291,627	521,403	53%	1,014	912	90%
Delta	16	3,506,940	1,963,886	719,137	614,830	1,333,967	68%	937	588	63%
Imo	2	437,824	245,182	95,615	123,053	218,668	89%	514	514	100%
Abia	2	487,276	272,874	117,195	119,414	236,609	87%	280	280	100%
Total	**32**	**7,025,174**	**3,934,098**	**1,379,984**	**1,354,486**	**2,734,470**	**70%**	**4,213**	**3,762**	**89%**

Figure N10

Nigeria: Carter Center-Assisted Soil-Transmitted Helminth Treatments and 2019 Target*



** Treatments are with either Albendazole or Mebendazole. Targets change annually based on WHO guidelines*

ETHIOPIA

Summary: The River Blindness Elimination Program (RBEP) assisted five regions in Ethiopia in 2018 (Amhara, Beneshangul-Gumuz, Gambella, Oromia, and Southern Nations, Nationalities, and Peoples' Region -SNNPR, see Figure E1). These regions provided 17,767,222 ivermectin treatments under the twice-per-year approach, a similar number to those provided in 2017 (Figure E2). Mass drug administration (MDA) was halted in 2018 in parts of Amhara after transmission was demonstrated to have been interrupted in 2017. A major challenge for the RBEP is to help Ethiopia's Federal Ministry of Health (FMOH) complete RB mapping in areas ecologically conducive for onchocerciasis transmission in the eastern part of the country.

The Carter Center Lymphatic Filariasis Program (LF) assisted Ethiopia in providing 1,291,864 ivermectin-albendazole treatments in 2018 (Figure E3), an increase of 60% over the previous year, one driven by expansion into South Omo zone of SNNPR.

Background: Rapid Epidemiological Mapping of Onchocerciasis (REMO) conducted in Ethiopia in 2001 with support from the African Programme for Onchocerciasis (APOC) showed that meso-hyper endemic onchocerciasis was present in the western part of the country. The eastern extent of onchocerciasis transmission was never definitively determined.

In 2012, the FMOH of Ethiopia declared the goal of elimination of onchocerciasis transmission by 2020. The strategy to achieve the goal was primarily 1) completion of national mapping and 2) twice-per-year treatment in all areas (including previously untreated hypo-endemic zones).

Key 2018 elimination program partners with The Carter Center in Ethiopia include the Federal Ministry of Health, Lions Clubs International Foundation, the Lions Clubs of Ethiopia, the END Fund, and the Reaching the Last Mile Fund.[1] Under the leadership of the Most Honorable World Laureate Dr. Tebebe Y. Berhan, the Lions Clubs of District 411-A play a key role in both the River Blindness and Trachoma Programs in the Lions-Carter Center SightFirst Initiative areas of Ethiopia.

The Ethiopia Onchocerciasis Elimination Expert Advisory Committee (EOEEAC): With the declaration of an elimination strategy, the EOEEAC was launched to provide recommendations to the FMOH on their national program. The committee is composed of national and international experts. The EOEEAC Chairperson is Professor Rory Post of Liverpool John Moores University, Dr. Zerihun Tadesse (Ethiopia Country Representative of The Carter Center), serves as the EOEEAC co-secretary with Mr. Nebiyu Negussu (FMOH, Neglected Tropical Disease Coordinator). At its October 2017 meeting, the EOEEAC recommended that MDA for onchocerciasis be stopped in the Metema subfocus of the Galabat/Metema cross-border focus, except in the entomological hotspot of Wudi Gemzu, where vector black flies tested positive for *onchocerca* DNA on two occasions. MDA will continue in Wudi Gemzu on a four-times-per year schedule. In 2018, the committee reviewed mapping results from central and eastern Ethiopia, which showed a potential new focus of transmission (based on OV16 serology in adults in 20 communities of $\geq$5%) in East and West Hararge zones. The program is investigating the area more thoroughly to confirm its endemicity.

[1] 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.

RB Treatments: The total number of treatments provided in 2018 was 17,767,222, all of which were delivered semi-annually (Figure E3). Coverage of the ultimate treatment goal (UTG) UTG2 reached 99%, slightly higher than the 97% reached 2017. Geographic coverage was 96% of the 47,982 targeted villages across both rounds, and nearly all communities were reached at least once. Carter Center-assisted treatments represented 74% of all ivermectin treatments given in Ethiopia in 2018.

Training and Health Education: In accordance with the terminology of the Ethiopian health system, Community Drug Distributors (CDDs) are referred to as members of the Health Development Army (HDA) and Community Supervisors (CSs) are synonymous with Health Extension Workers (HEWs). Training was provided to 230,266 HDAs in 2018, slightly more than in 2017 (Figure E4). The percent of female members of the HDA was 63% in 2018, continuing the trend of increasing female participation that began in 2012 (Figure ES5). The average population per HDA was a remarkable 46 to 1, and all zones reached ratios below the target of 1 HDA per 100 population.

A total of 77,085 HEWs were trained in 2017, overseeing an average of 3 HDAs each, on par with the preceding year and beating the goal of 1:5.

Lymphatic Filariasis: The LF Program in Ethiopia began in 2008 with GSK support, integrating LF with RB treatments (Shiferaw *et al*. 2011). The current Carter Center policy is to assist the FMOH's LF program in zones where RB is also endemic. Thus, as the RBEP expands eastward with mapping activities into new, co-endemic areas, the LF Program will likewise continue to grow in scope. The LF Program provides assistance to Gambella SNNPR, Beneshangul-Gumuz, and Amhara regions; There were 1,291,864 treatments in 2018 (Figure E6). Also, in 2018, 431,496 LF treatments were stopped in North Gondar zone after passing the first transmission assessment survey (TAS) in 2017.

2019 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, ETHIOPIA

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

Conduct treatment coverage surveys in consultation with Headquarters.

Onchocerciasis

Publish the experience of binational collaboration in assessment of and the joint decision with Sudan for halting MDA in the cross-border Special Intervention Zone (SIZ) between Galabat and Metema in a peer reviewed journal.

Explore the possibility that the change in gender ratio (from male dominated to female dominated) in the CDD work force in the last decade had a measurable impact on health outcomes.

Conduct an entomological study in the Wadi Gemzu 'hot spot' area to determine if four-times-per-year MDA has suppressed transmission. Results should be presented at the 2019 EOEEAC meeting and at next year's Program Review.

Collect additional data to support the buffer zone surrounding the Metema focus where MDA was halted. Consider conducting genetic studies of the vectors in collaboration with Professor Rory Post.

Continue four-times-per-year MDA in the Wadi Gemzu 'hot spot'.

Expand mapping activities as resources allow and in consultation with HQ and FMOH. Decision on endemicity is determined in consultation with FMOH.

Establish twice-per-year MDA in East and West Hararge and in untreated 'hypoendemic' districts if they meet the threshold recommended by the WHO OTS and agreed to by the EOEEAC. Note that baseline skin snip prevalence in sentinel areas as well as vector prospecting is needed in East and West Hararge zones prior to launching MDA.

Provide financial and administrative support for the 2019 EOEEAC meeting.

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 continue to provide treatment to the refugees from RSS in Gambella and other migratory populations as needed.

The program should work with Sudan to complete cross border assessments to determine all areas that need to be placed under the MDA program.

Lymphatic Filariasis

In consultation with HQ and FMOH- NTD secretariat, conduct pre-TAS and TAS studies in 2019. Pre-TAS studies should use only filarial antigen testing and not nocturnal mf assessments. Consider obtaining DBS for OV16 testing during pre-TAS and TAS studies, if indicated.

The program should continue to provide treatment to the refugees from RSS in Gambella.

2019 Treatment and Training Objectives:

River Blindness	
Semiannual (UTG2)	26,100,746
Lymphatic Filariasis	
Annual (UTG)	1,435,414
Training Objectives	
CDDs	235,566
CSs	77,200

Figure E1

Map of RB & LF Areas Assisted by The Carter Center

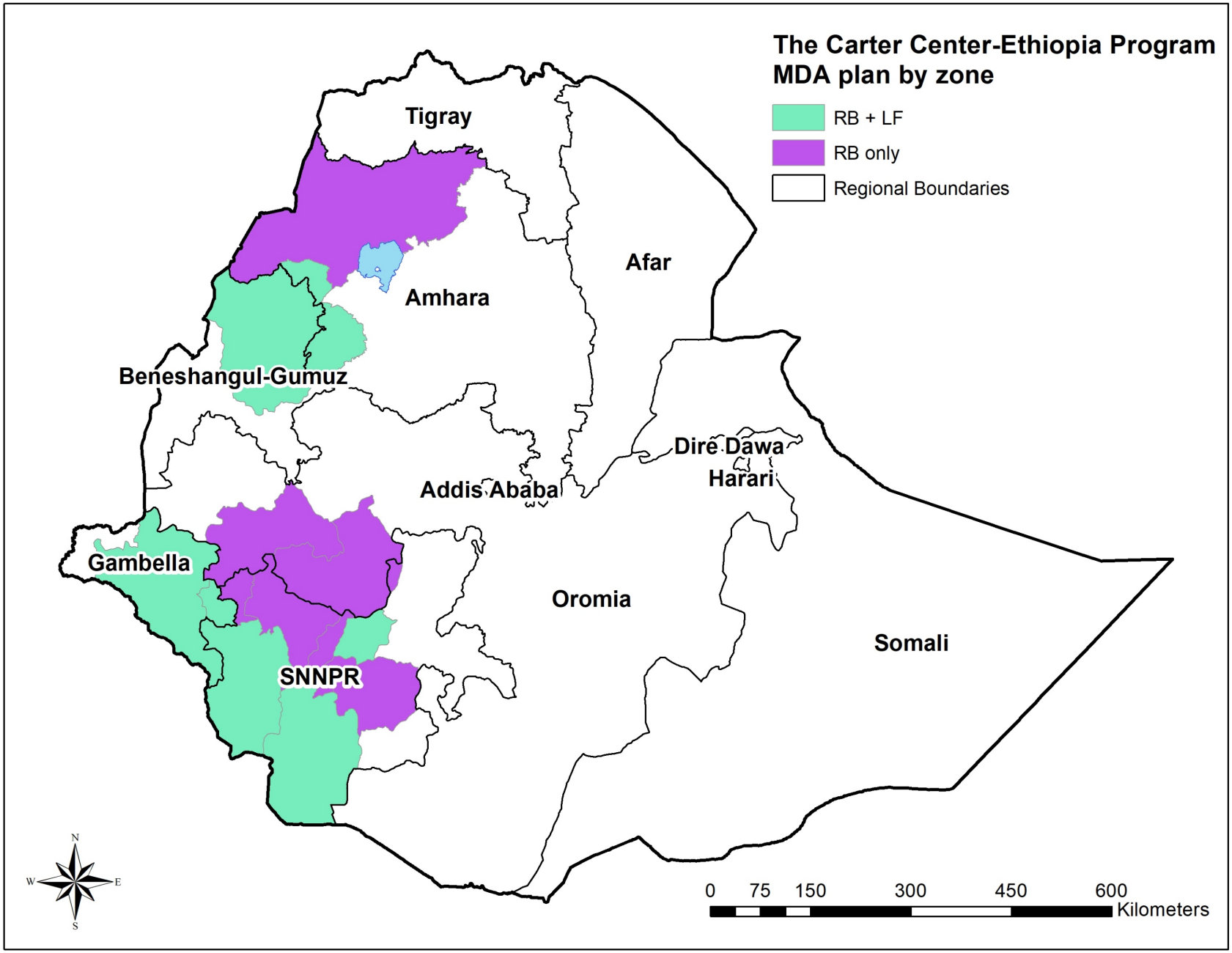


Figure E2

Lymphatic Filariasis Treatments - 2018

Region	Zone	# of Districts	# of Comm-unities	Total Population	Eligible Pop	# people treated	% treated (UTG)	No. of Comm-unities treated	% of Comm-unities treated
SNNPR	Bench-Maji	6	2,657	489,397	384,667	402,267	98%	2,657	100%
	Dawuro	1	321	79,245	64,690	138,088	207%	321	100%
	South Omo	5	443	539,615	453,277	417,252	92%	443	100%
Amhara	Awi	3	1,504	296,127	241,736	249,686	100%	1,504	100%
Benshangul G.	Metekel	2	459	93,056	75,964	0	0%	0	0%
Gambella	Agnuwa	4	238	71,932	58,720	55,961	93%	200	84%
	Mezheng	2	198	88,807	72,496	28,610	38%	88	44%
	Itang Sp. Woreda	1	90	50648	41,345	0	0%	0	0%
Total		**24**	**5,910**	**1,708,827**	**1,392,895**	**1,291,864**	**85%**	**5,213**	**88%**

Note: two rounds of MDA occurred in Dawuro zone due to scheduling anomalies.

Figure E3

River Blindness: Semi-Annual Treatments, 2018

Region	Zone	No. of Districts	Total Pop	UTG 1	UTG 2	Treatments R1	Treatments R2	Treatments R 1 & 2	% UTG 1	% UTG 2	No. Comm	% Comm Treated
SNNPR	Kaffa	11	1,184,613	995,075	1,990,150	81,6703	1,160,467	1,977,170	82	99	4,699	100
	Sheka	5	235,654	197,950	395,899	0	338,552	338,552	0	86	1,310	94
	Bench-Maji	11	865,834	727,301	1,454,601	744,470	723,591	1,468,061	102	101	3,028	100
	Dawuro	6	536,251	450,451	900,902	488,151	496,217	984,368	108	109	2,029	100
	Konta	1	127,763	107,321	214,642	0	204,675	204,675	0	95	499	100
	Yem	1	88,982	74,745	149,490	70,259	70,466	140,725	94	94	523	100
	South Omo	1	59,141	49,679	99,357	31,529	37,262	68,791	63	69	128	98
	Gamogofa	1	160,586	134,892	269,784	139,905	115,050	254,955	104	95	802	95
	Basketo	1	75,843	63,708	127,416	60,587	60,509	121,096	95	95	405	100
Oromia	Illubabor	24	1,674,348	1,406,453	2,812,905	750,819	2,126,938	2,877,757	53	102	8,357	100
	Jimma	22	3,513,527	2951,363	5,902,725	0	6,145,736	6,145,736	0	104	15,834	100
Amhara	North Gondar	8	121,249	101,849	203,698	99,313	120,531	219,844	98	108	719	107
	Awi	11	1,122,061	942,531	1,885,062	898,664	1,100,988	1,999,652	95	106	6,760	105
Benshanghul Gumuz	Metekel	7	408,551	343,183	686,366	178,994	184,835	363,829	52	53	1,929	76
	Dam workers		8,449	7,097	14,194	0	7,265	7,265	0	51		
Gambella	Agnuwa	5	118,662	99,676	199,352	116,222	55,961	172,183	117	86	273	100
	Mezheng	2	86,810	72,921	145,841	67,435	28,610	96,045	92	66	198	100
	Itang	1	49,509	41,588	83,175	43,607	0	43,607	105	52	45	50
	Refugees		215,000	180,600	361,200	143,440	139,471	282,911	79	78		
Total	**17**	**118**	**10,652,833**	**8,948,380**	**17,896,759**	**4,650,098**	**13,117,124**	**17,767,222**	**71**	**87**	**47,538**	**96**

Figure E4

Ethiopia: Community Directed Distributors (CDDs*) and Community Supervisors (CSs*) Trained (2005 – 2018) in Carter Center-Assisted Areas

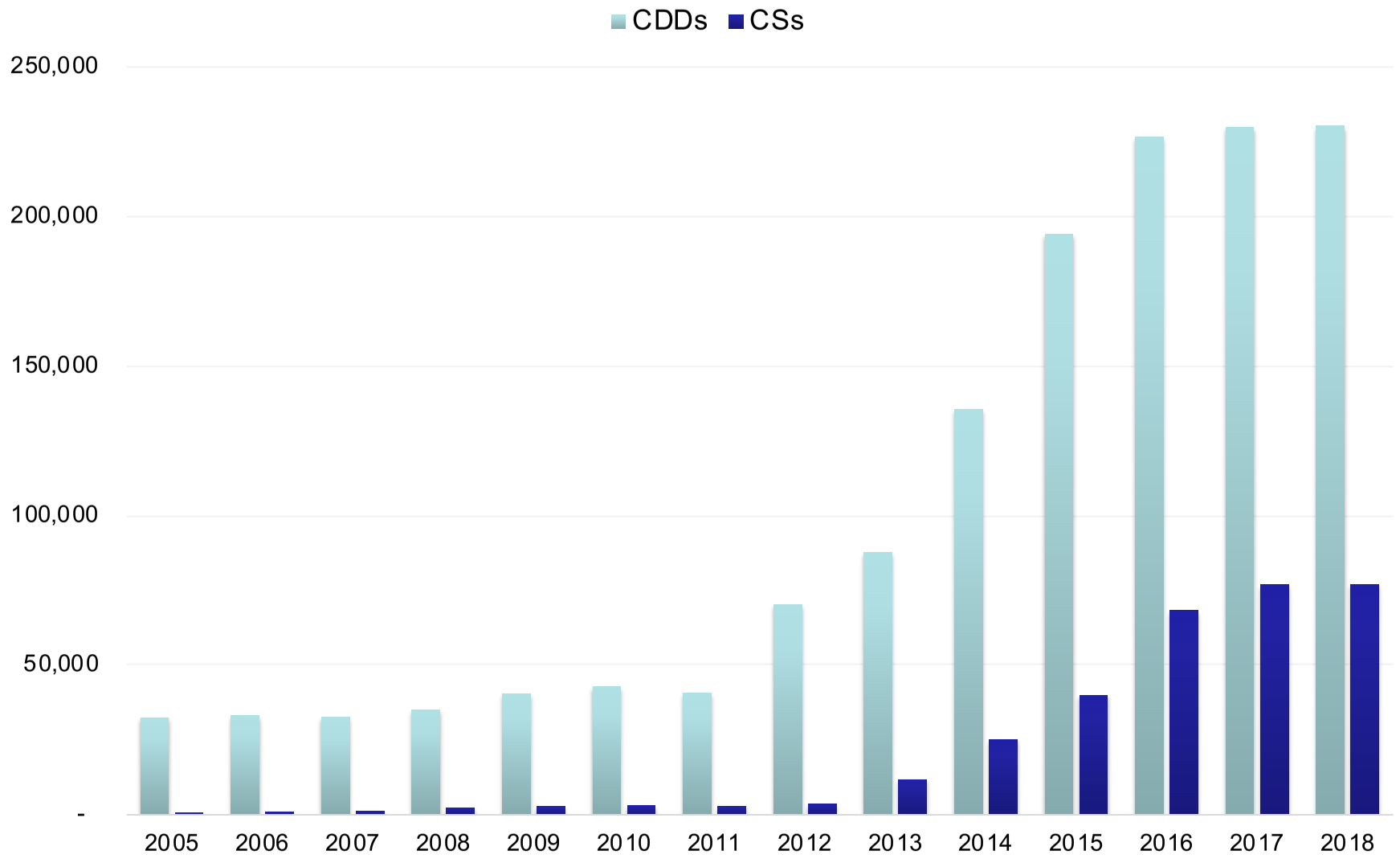


Figure E5

Ethiopia: Training of Community Directed Drug Distributors: 2001 – 2018 and Percentage Female

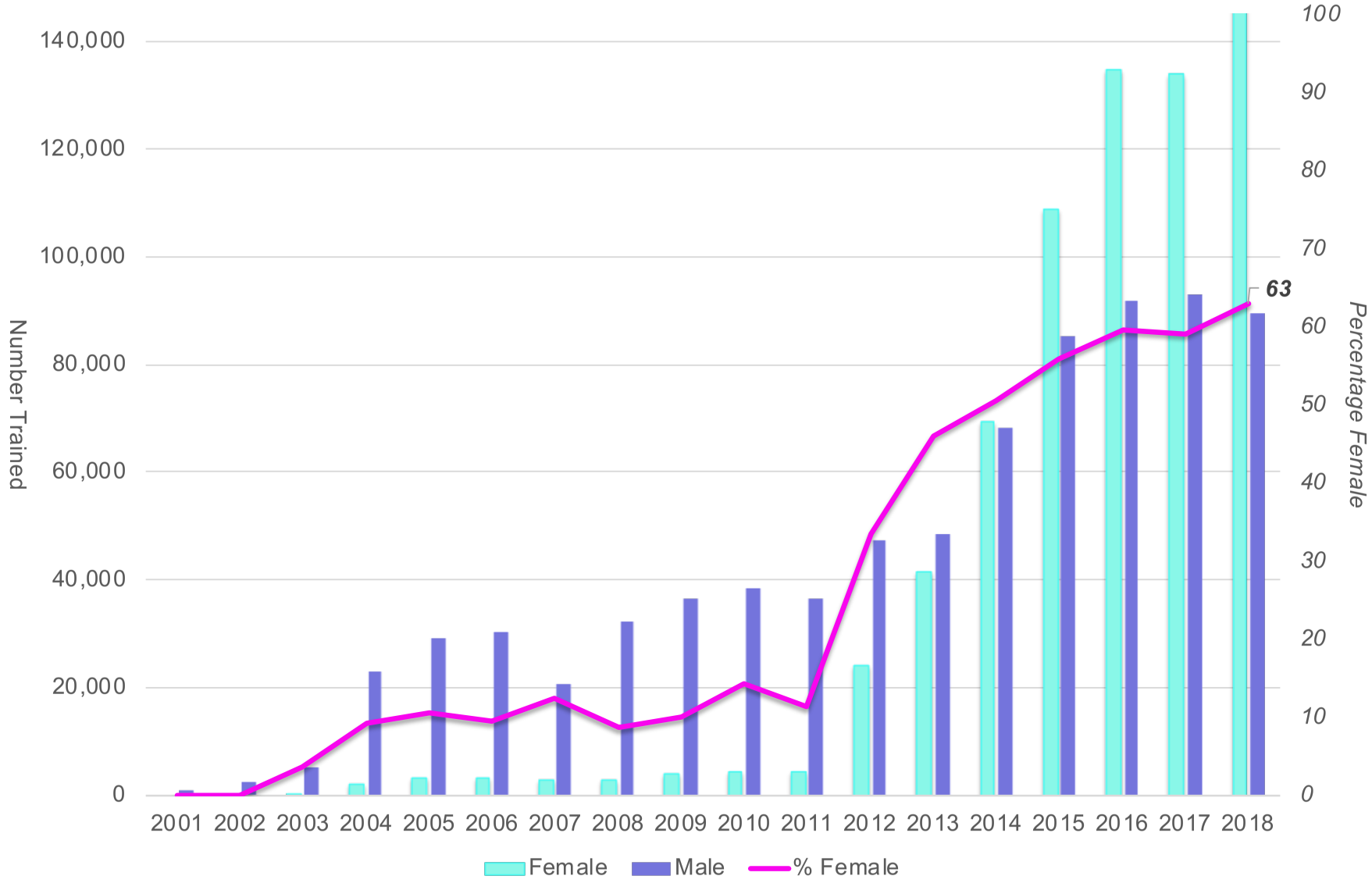
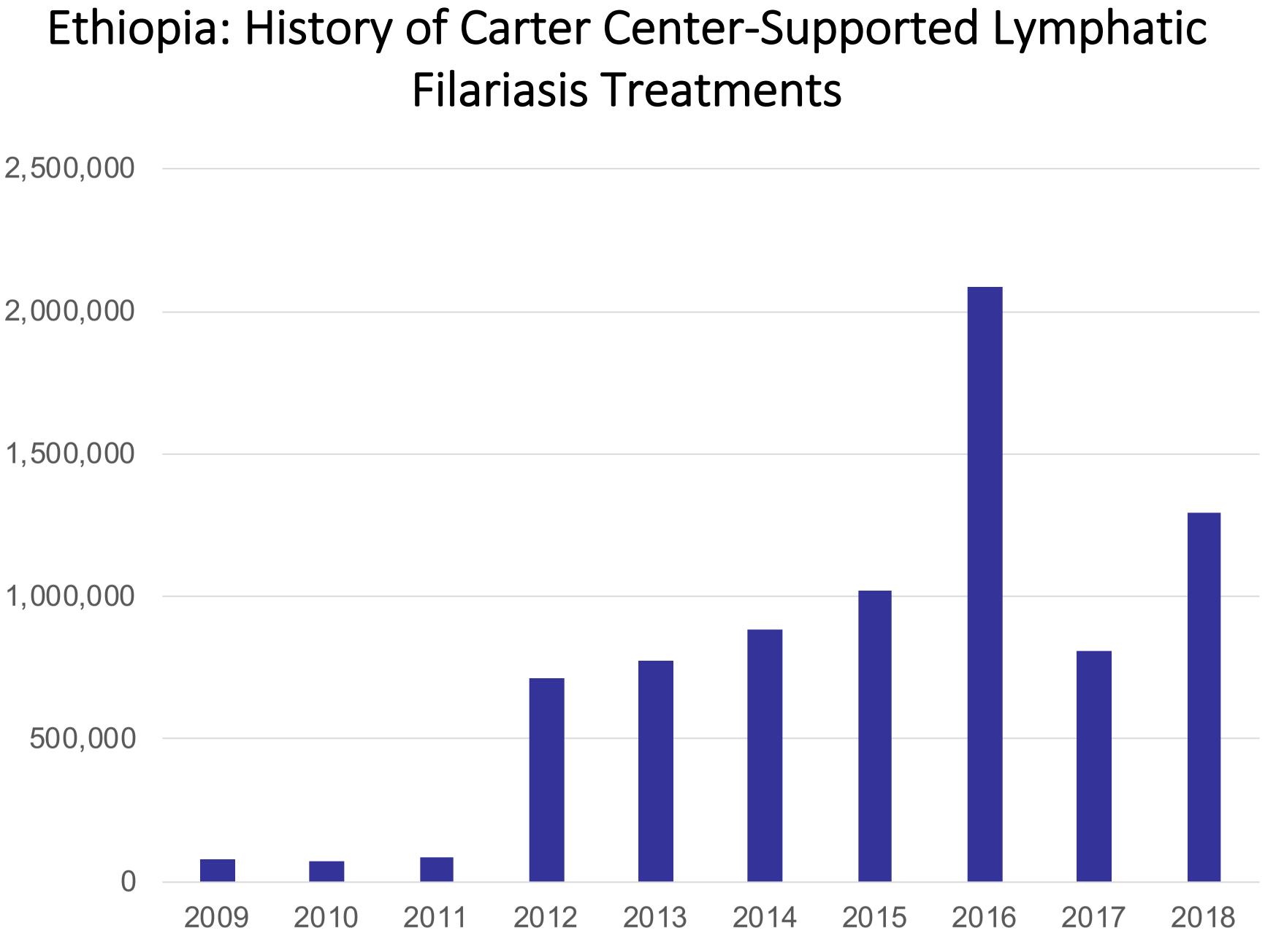


Figure E6



Note: The LF program expanded in 2016 and 2018. Drops in 2017 are due to successfully passing transmission assessment surveys and shifts in MDA scheduling.

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 approximately 20.9 million people are infected and one million have vision loss in 33 endemic countries. Approximately 205 million people live in endemic areas worldwide and are therefore at risk of infection; more than 99% of those at risk are in sub-Saharan Africa. 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 in November 2018 (No 47, 2018, 93, 633–648).

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 The Carter Center 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 calculation 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 (CS). 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 NTD control efforts.

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

- **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 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. 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.

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

- **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 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).

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

- **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 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%.[1]

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 OEPA program 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 microscopy to identify *O. volvulus* microfilaria in skin. Villages in which one or more persons are positive (sample prevalence ≥2%) are considered

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

"at risk" and are recommended for the twice per year (or four times per year) 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 headquarters in Atlanta. 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.

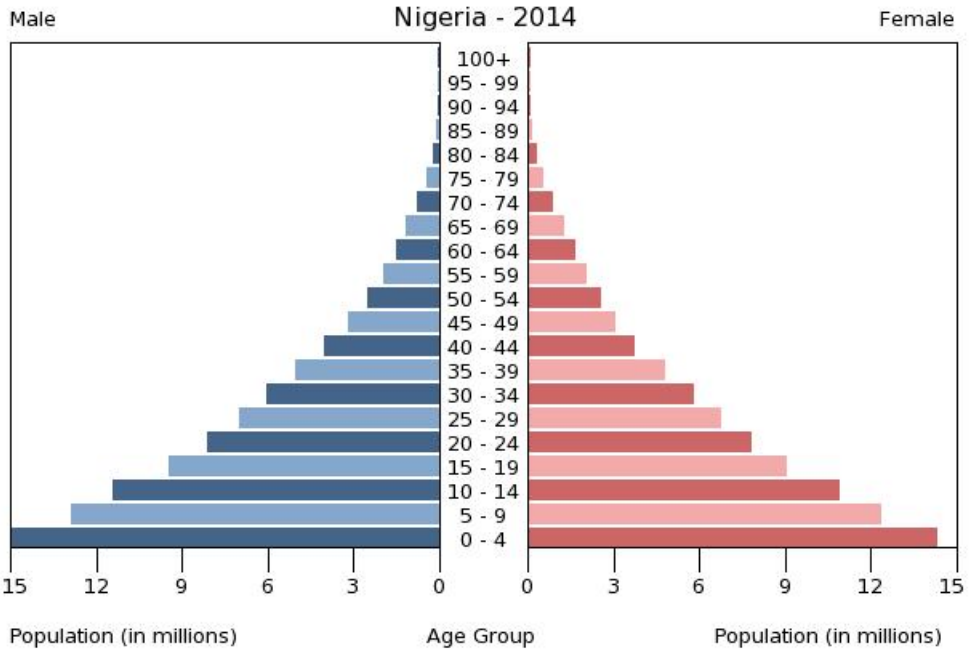
Summary reports of numbers of villages and persons treated are compiled from the village registers by the CDDs and their Community Supervisors, then forwarded to the district level. District-level summary reports are forwarded (whenever possible through MOH surveillance and reporting channels) to both the state MOH headquarters 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/World Health Organization (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 NGDO Onchocerciasis Coordination Group.

RBEP Treatment Indices: Treatments are reported (see Figure ES5) as number of persons and number of at-risk villages (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%).



[2]

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)

[2] 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: List of Program Review Participants

The Carter Center Atlanta

Ms. Lauri Bernard
Dr. Stephen Blount
Ms. Eve Byrd
Ms. Kelly Callahan
Ms. Kenya Casey
Mr. Yohannes Dawd
Mr. Don Denard
Ms. Janie French
Ms. Felicia Griffin
Ms. Emily Griswold
Ms. Madelle Hatch
Mr. Andrew Heacox
Dr. Moses Katabarwa
Mr. Jim Kavanagh
Mr. Curtis Kohlhaas
Ms. Nicole Kruse
Ms. Emily Mooney
Dr. Scott Nash
Dr. Gregory Noland
Amb. Mary Ann Peters
Ms. Lindsay Rakers
Ms. Faith Randolph
Dr. Frank Richards
Ms. Lauren Shewmaker
Dr. Dean Sienko
Mr. Randall Slaven
Ms. Emily Staub
Mr. Marc Tewari
Mr. Adam Weiss
Mr. Craig Withers
Ms. Zeldayah Wright
Ms. Eva Zamarripa

The Carter Center Field Office Staff

Mr. Alex Arinaitwe
Dr. Nabil AwadAlla
Mr. Luccene Desir
Mrs. Attamah-Isiani Egeonu
Dr. Abel Eigege
Mr. Yemane Kejela Elill
Dr. Emmanuel Emukah
Mr. Abate Tilahun Habtemariam
Dr. Cephas Ityonzughul
Ms. Annet Khainza
Mr. Tewodros Mehamed
Dr. Emmanuel Miri
Mr. Aderajew Mohammed
Dr. Christopher Nwuzor
Mr. Justine Ocaka
Dr. Adamu Sallau
Dr. Mauricio Sauerbrey
Mr. Fetene Mihretu Sheta
Dr. Zerihun Tadesse

Country Representatives

Hon. Dr. Jane Ruth Aceng
Dr. Chukwuma Anyaike
Dr. Narcis Kabatereine
Dr. Babikir Assidig Gabir Kaballo
Ms. Jean Marie da Rocha Marcelino
Ms. Joyce Ester Naluyiga
Dr. Oscar Noya Alarcon
Mr. David Oguttu
Mr. Makoy Samuel Yibi
Dr. Edridah Muheki Tukahebwa
Mr. Nebiyu Negussu
Dr. Evelyn Ngige
Mr. Asam Zroug

University and NGDO Personnel & Special Guests

Hon. Tebebe Y. Berhan – LCIF
Ms. Margaret Baker – RTI International
Mr. Taher Alkhateeb – Kuwait Fund
Mr. Abdulridha Bahmen – Kuwait Fund
Ms. Heather Brooks – The Task Force for Global Health
Ms. Lauren Brown – RTI/ENVISION
Dr. Vitaliano Cama – CDC
Dr. Rand Carpenter – The Task Force for Global Health
Ms. Jessica Cheng – LUI Che Woo Prize
Mr. Philip Downs – Sightsavers
Mr. Darin Evans – USAID
Dr. Katherine Gass – The Task Force for Global Health
Dr. Julie Gutman – CDC
Mr. Matthew Hallas – DigitalGlobe
Ms. Louise Hamill – Sightsavers
Ms. Megan Hill – Ithaca College
Mr. Richard Killian – RTI International
Dr. Patrick Lammie – The Task Force for Global Health
Ms. Joni Lawrence – The Task Force for Global Health
Dr. Charles Mackenzie – The Task Force for Global Health
Prof. Edwin Michael – University of Notre Dame
Ms. Molly Mort – Bill & Melinda Gates Foundation
Mr. Benjamin Nwobi – RTI International
Prof. B.E.B Nwoke – Imo State University Owerri
Dr. Kisito Ogoussan – The Task Force for Global Health
Capt. Monica Parise – CDC
Prof. Rory Post – LSHTM
Ms. Maria Rebollo Polo – WHO
Dr. Anders Seim - Health & Development International
Ms. Sarah Sullivan – The Task Force for Global Health
Ms. Carly Smith – USAID
Ms. Gretchen Stoddard – IZUMI Foundation
Dr. Wilma Stolk – NTD Modeling Consortium

ANNEX 4: List of Program Review Participants

University and NGDO Personnel & Special Guests – cont'd

Ms. Sarah Sullivan – Task Force for Global Health
Ms. Jamie Tallant – The END Fund
Dr. Jordan Tappero – Bill & Melinda Gates Foundation
Ms. Angela Udongwo – Emory University
Dr. Thomas Unnasch – University of South Florida
Ms. Ellen Wild – The Task Force for Global Health

The Carter Center
Meeting Agenda
March 25-27, 2019

Title:	23rd Carter Center River Blindness Elimination Program Review
Location:	Ivan Allen Chapel
Date:	Monday, March 25, 2019

Start	End	Title	Speaker
8:00 AM	*8:30 AM*	*Shuttle Pickup at the Sheraton*	
8:30 AM	*9:00 AM*	*Continental Breakfast*	
9:00 AM	9:05 AM	Welcome	Dr. Dean Sienko
9:05 AM	9:30 AM	Overview and Introduction	Dr. Frank Richards
Morning Session Chair:		*Dr. Mauricio Sauerbrey*	
9:30 AM	10:00 AM	Nigeria: Treatments-Southeast and Plateau/Nasawara	Dr. Emmanuel Miri
10:00 AM	10:15 AM	*Discussion*	
10:15 AM	10:30 AM	Nigeria: Assessing LF Elimination: the Plateau-Nasarawa experien	Dr. Gregory Noland
10:30 AM	10:40 AM	*Discussion*	
10:40 AM	11:10 AM	*Morning Break (Group Photo)*	
11:10 AM	11:25 AM	Nigeria: SCH/STH Survey Results	Dr. Abel Eigege
11:25 AM	11:35 AM	*Discussion*	
11:35 AM	11:50 AM	SCH/STH - Transition & Health Systems Strengthening	Mr. Richard Killian
11:50 AM	12:00 PM	*Discussion*	
12:00 PM	1:30 PM	*Lunch*	
Afternoon Session Chair		*Dr. Zerihun Tadesse*	
1:30 PM	2:00 PM	Nigeria: Training Costs and Mainstreaming	Dr. Adamu Sallau
2:00 PM	2:15 PM	*Discussion*	
2:15 PM	2:30 PM	Nigeria: LF and Onchocerciasis in Nigeria: a Status Report	Dr. Chukwuma Anyaike
2:30 PM	2:40 PM	*Discussion*	
2:40 PM	2:55 PM	Nigeria: Hypo RB Results from *Loa loa* Study	Dr. Emmanuel Emukah
2:55 PM	3:05 PM	*Discussion*	
3:05 PM	3:20 PM	Nigeria: Hypo 6 LGA Survey	Dr. Cephas Ityonzughul
3:20 PM	3:30 PM	*Discussion*	
3:30 PM	4:00 PM	*Afternoon Break*	
4:00 PM	4:15 PM	Modelling - Impact of IVM for LF on hypo-endemic oncho	Dr. Wilma Stolk
4:15 PM	4:25 PM	*Discussion*	
4:25 PM	4:40 PM	MMDP for LF in Plateau/Nasarawa (Dossier)	Dr. Charles Mackenzie
4:40 PM	4:50 PM	*Discussion*	
4:50 PM		*Session Adjourns*	
4:55 PM		*Shuttle Departs for Hotel*	
6:00 PM		*Shopping trip - Pick up from Hotel*	

The Carter Center
Meeting Agenda
March 25-27, 2019

Title:	23rd Carter Center River Blindness Elimination Program Review
Location:	Ivan Allen Chapel
Date:	Tuesday, March 26, 2019

Start	End	Title	Speaker
8:00 AM	*8:30 AM*	*Shuttle Pickup at the Sheraton*	
8:30 AM	*9:00 AM*	*Continental Breakfast*	
Morning Session Chair:		*Dr. Frank Richards*	
9:00 AM	9:30 AM	OEPA: Overview 2018	Dr. Mauricio Sauerbrey
9:30 AM	9:45 AM	*Discussion*	
9:45 AM	10:00 AM	OEPA: DigitalGlobe Satellite Imagery	Mr. Matthew Hallas
10:00 AM	10:10 AM	*Discussion*	
10:10 AM	10:25 AM	Venezuela: Landing Strips	Dr. Oscar Noya-Alarcón
10:25 AM	10:35 AM	*Discussion*	
10:35 AM	11:05 AM	*Morning Break*	
11:05 AM	11:20 AM	Brazilian Onchocerciasis Program: Progress on the Score Card for Tracking Community Performance	Dr. Jean Marie Marcelino
11:20 AM	11:30 AM	*Discussion*	
11:30 AM	12:00 PM	Ethiopia: Treatments and Impact	Mr. Abate Tilahun
12:00 PM	12:15 PM	*Discussion*	
12:15 PM	1:45 PM	*Lunch*	
Afternoon Session Chair:		*Dr. Nabil Aziz*	
1:45 PM	2:15 PM	Ethiopia: Training, Integration & Community Ownership	Dr. Zerihun Tadesse
2:15 PM	2:30 PM	*Discussion*	
2:30 PM	3:00 PM	Metema Buffer Zones	Dr. Moses Katabarwa
3:00 PM	3:15 PM	*Discussion*	
3:15 PM	3:45 PM	*Afternoon Break*	
3:45 PM	4:00 PM	Ethiopia: Wude Gemuz Hot Spots	Mr. Aderajew Mohammed
4:00 PM	4:10 PM	*Discussion*	
4:10 PM	4:30 PM	*S. ethiopiense* & Proposed Molecular Studies of Transmission Zones	Dr. Rory Post
4:30 PM	4:40 PM	*Discussion*	
4:40 PM	4:55 PM	Ethiopia: New Focus in Eastern Ethiopia	Mr. Tewodros Seid
4:55 PM	5:05 PM	*Discussion*	
5:05 PM	5:35 PM	Mectizan Donation Program: Update	Dr. Rand Carpenter
5:35 PM	5:45 PM	*Discussion*	
5:45 PM		*Session Adjourned*	
5:45 PM	*7:30 PM*	*RBEP Reception: Jimmy Carter Library & Museum Lobby*	
7:30 PM		*Shuttle Departs for Hotel*	

The Carter Center
Meeting Agenda
March 25-27, 2019

Title:	23rd Carter Center River Blindness Elimination Program Review
Location:	Ivan Allen Chapel
Date:	Wednesday, March 27, 2019

Start	End	Title	Speaker
8:00 AM	*8:30 AM*	*Shuttle Pickup at the Sheraton*	
8:30 AM	*9:00 AM*	*Continental Breakfast*	
Morning Session Chair:		*Dr. Emmanuel Miri*	
9:00 AM	9:30 AM	Uganda: Treatment and Impacts	Dr. Edridah Muheki
9:30 AM	9:45 AM	*Discussion*	
9:45 AM	10:15 AM	Uganda: Training, Integration & Community Ownership	Ms. Annet Khainza
10:15 AM	10:30 AM	*Discussion*	
10:30 AM	11:00 AM	*Morning Break*	
11:00 AM	11:20 AM	Uganda: DRC/RSS Crossborder	Dr. David Oguttu
11:20 AM	11:30 AM	*Discussion*	
11:30 AM	11:45 AM	Uganda: Final Results on Victoria Focus	Dr. Moses Katabarwa
11:45 AM	11:55 AM	*Discussion*	
11:55 AM	12:25 PM	Sudan: Treatments and Impact	Dr. Nabil Aziz
12:25 PM	12:40 PM	*Discussion*	
12:40 PM	2:10 PM	*Lunch*	
Afternoon Session Chair:		*Dr. Frank Richards*	
2:10 PM	2:25 PM	Refugee and IDP Treatment: TCC-Assisted Countries	Ms. Emily Griswold
2:25 PM	2:35 PM	*Discussion*	
2:35 PM	3:05 PM	*Afternoon Break*	
3:05 PM	3:25 PM	Uganda: A Radical Plan for Schistosomiasis	Dr. Narcis Kabatereine
3:25 PM	3:35 PM	*Discussion*	
3:35 PM	3:50 PM	OTS and OV16 Update	Dr. Thomas Unnasch
3:50 PM	4:00 PM	*Discussion*	
4:00 PM	4:30 PM	*Summary and Closure of the 23rd RB Program Review*	Dr. Frank Richards
4:30 PM		*2018 Carter Center River Blindness Elimination Program Review Adjourned*	
4:35 PM		*Shuttle Departs for Hotel*	

ANNEX 6: River Blindness Elimination Program Review Contact List

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ANNEX 6: River Blindness Elimination Program Review Contact List

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ANNEX 6: River Blindness Elimination Program Review Contact List - *continued*

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ANNEX 6: River Blindness Elimination Program Review Contact List

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ANNEX 7: 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 GlaxoSmithKline [GSK]/The Task Force for Global Health), or diethylcarbamazine (DEC, donated by Eisai pharmaceuticals) 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 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 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 120 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 the 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 long lasting insecticidal net (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 will work with its ministry of health partners to conduct a needs assessment survey 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.

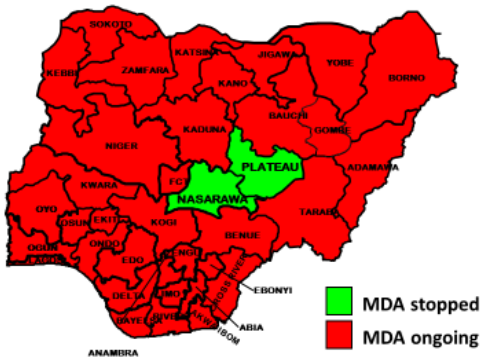


Figure 1: Elimination of LF in Plateau and Nasarawa states in 2017

***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 USAID ENVISION project led by 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., *AJTMH* 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 field 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 one million treatments each year, and 5 districts have passed TAS1, stopped over 431,000 treatments and begun post-treatment surveillance (TAS2 and TAS3).

ANNEX 8: The Schistosomiasis/Soil-Transmitted Helminthiasis Control Program

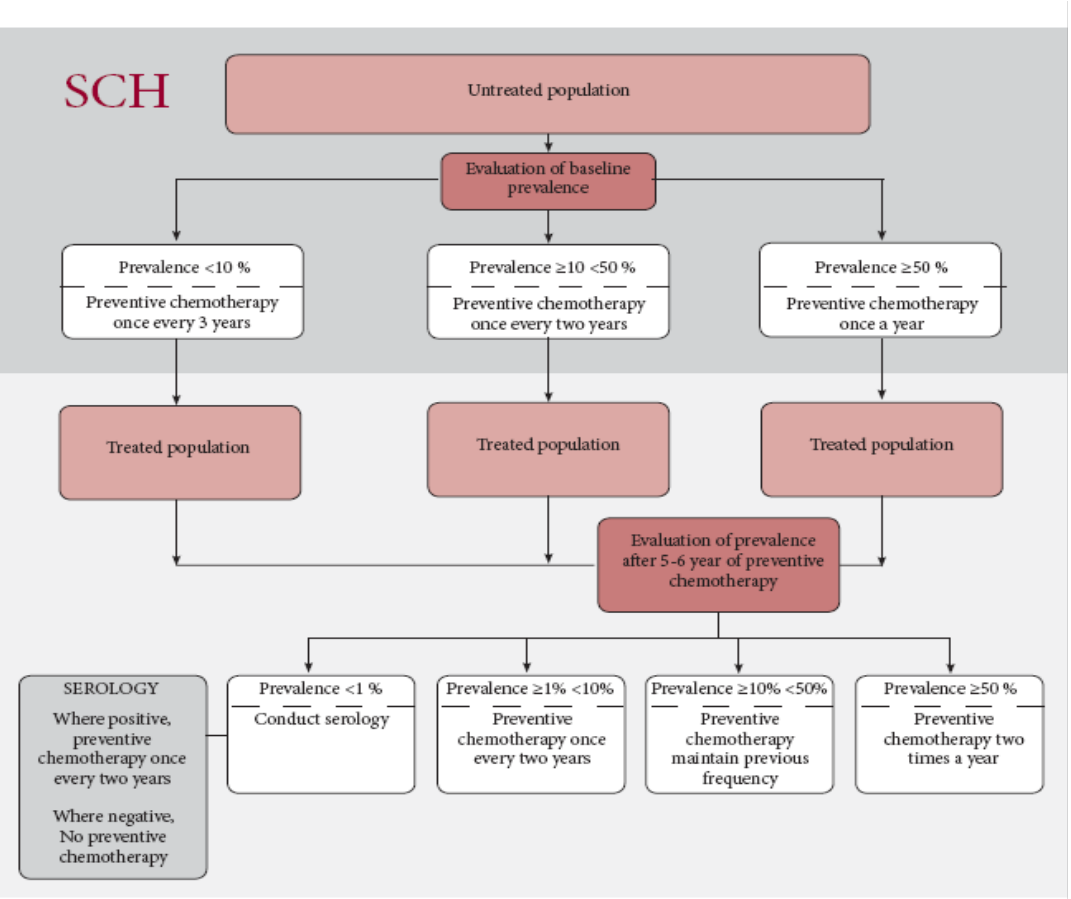
SCHISTOSOMIASIS

Schistosomiasis (SCH) is a parasitic disease acquired from skin contact with fresh water 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. 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/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 two-three 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 8: The Schistosomiasis/Soil-Transmitted Helminthiasis Control Program - *continued*

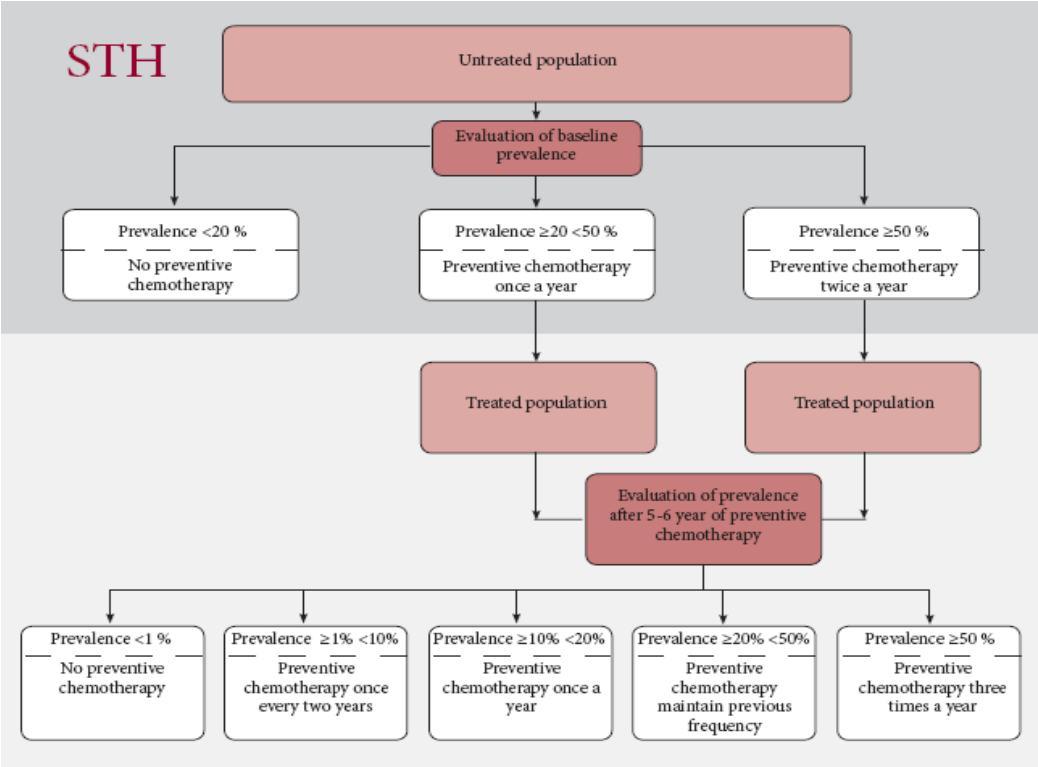


Transmission is unlikely to be interrupted by this paradigm of MDA targeted at school-aged children because: 1) all age groups would need to be treated to have the greatest impact on transmission; 2) praziquantel does not kill the migrating schistosomula forms, thus single dose treatment in children 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 hookworm, which have their heaviest infections in adults.

ANNEX 8: 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 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.

ANNEX 8: The Schistosomiasis/Soil-Transmitted Helminthiasis Control Program - *continued*

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 TAS assessments cease treatment.

The written description of SCH/STH work under the new USAID/RTI Act to End NTDs | East focuses on “mainstreaming” the two diseases into the large health care delivery system and to abandon the vertical MDA approach to control. Although this is yet to be confirmed, we believe it is highly likely that there will be less support in the near future for the TCC SCH/STH program. Accordingly, in LGAs where RB or LF community-wide MDA is ongoing, we will seek to integrate the SCH/STH treatments into the RB or LF platform, co-administering drugs. A priority activity will be to reassess SCH/STH prevalence in LGAs where the RB or LF platform does not exist, and consider options for either stopping MDA (if WHO guidelines and the FMOH permit) or transferring (‘mainstreaming’) MDA to the Ministry of Education where national funds will begin to support the program.

Annex 9: Publications by Year Authored or Coauthored by RBEP Personnel

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ANNEX 10: Acknowledgements

The River Blindness Elimination Program is indebted to the following individuals for their help in planning and executing the Program Review and in the preparation of these proceedings:

Ms. Lauri Bernard, Ms. Kenya Casey, Ms. Janie French, Mr. Belachew Gebresadik, Ms. Felicia Griffin, Ms. Emily Griswold, Ms. Madelle Hatch, Mr. Andrew Heacox, Ms. Molly Ison, Dr. Moses Katabarwa, Ms. Nicole Kruse, Dr. Gregory Noland, Ms. Anne Nguyen, Mr. Donald Oliver, Ms. Lindsay Rakers, Dr. Frank Richards, Dr. Dean Sienko, Mr. Randall Slaven, Ms. Emily Staub, Ms. Shandal Sullivan, Mr. Marc Tewari, Mr. Arjan Wietsma, Mr. Craig Withers, Mr. Joshua Woodson, and Ms. Zeldayah Wright.

We would also like to send a special thanks to our dignitaries, the Honorable Minister of Health of Uganda, Dr. Jane Ruth Aceng; the Honorable Minister of Health of Sudan, Dr. Babikir Kaballo; and World Laureate Lion, Honorable Dr. Tebebe Berhan; as well as to all the presenters, Ms. Denise Bomberger, and the many Carter Center interns and volunteers.

Certain sections of this report are based upon work made possible thanks to the generous support of the American People through the United States Agency for International Development[1] (USAID) and the ENVISION project led by RTI International.[2] Its contents are solely the responsibility of the authors and do not necessarily represent the official views of RTI International or the U.S. Agency for International Development.

1 Through Cooperative Agreement # AID-OAA-G-12-00020
2 Through Subagreement # 7-330-0213210-51113L