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CARTER CENTER

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SUMMARY
2017 PROGRAM REVIEW
RIVER BLINDNESS ELIMINATION PROGRAMS
ETHIOPIA, NIGERIA, OEPA, SUDAN, AND UGANDA
MARCH 14-16, 2018
THE CARTER CENTER
ATLANTA, GA

SEPTEMBER 2018

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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 2017 for the activities described in these proceedings.

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ACRONYMS

ACT	Artemisinin Combination Therapy
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
CDHSs	Community-Directed Health Supervisors
CDTI	Community-Directed Treatment with Ivermectin
CS	Community Supervisors
DEC	Diethylcarbamazine
DRC	Democratic Republic of Congo
EOEEAC	Ethiopia Onchocerciasis Elimination Expert Advisory Committee
ELISA	Enzyme-linked immunosorbent assay
ESPEN	Expanded Special Project for Elimination of NTD's
FMOH	Federal Ministry of Health
FTS	Filarial Test Strip
GSK	GlaxoSmithKline
HDA	Health Development Army
HE	Health Education
HEWs	Health Extension Workers
IACO	InterAmerican Conference on Onchocerciasis
IHAs	Indigenous Health Agents
IRB	Institutional Review Board
ITFDE	International Task Force for Disease Eradication
IVT	International Verification Team
KAP	Knowledge Attitude & Perceptions
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
Mectizan®	Ivermectin (Merck & Co., Inc., product name)
MOHs	Ministry/Ministries of Health
MSD	Merck & Co., Inc.
NGDO	Non-Governmental Development Organization

ACRONYMS (Continued)

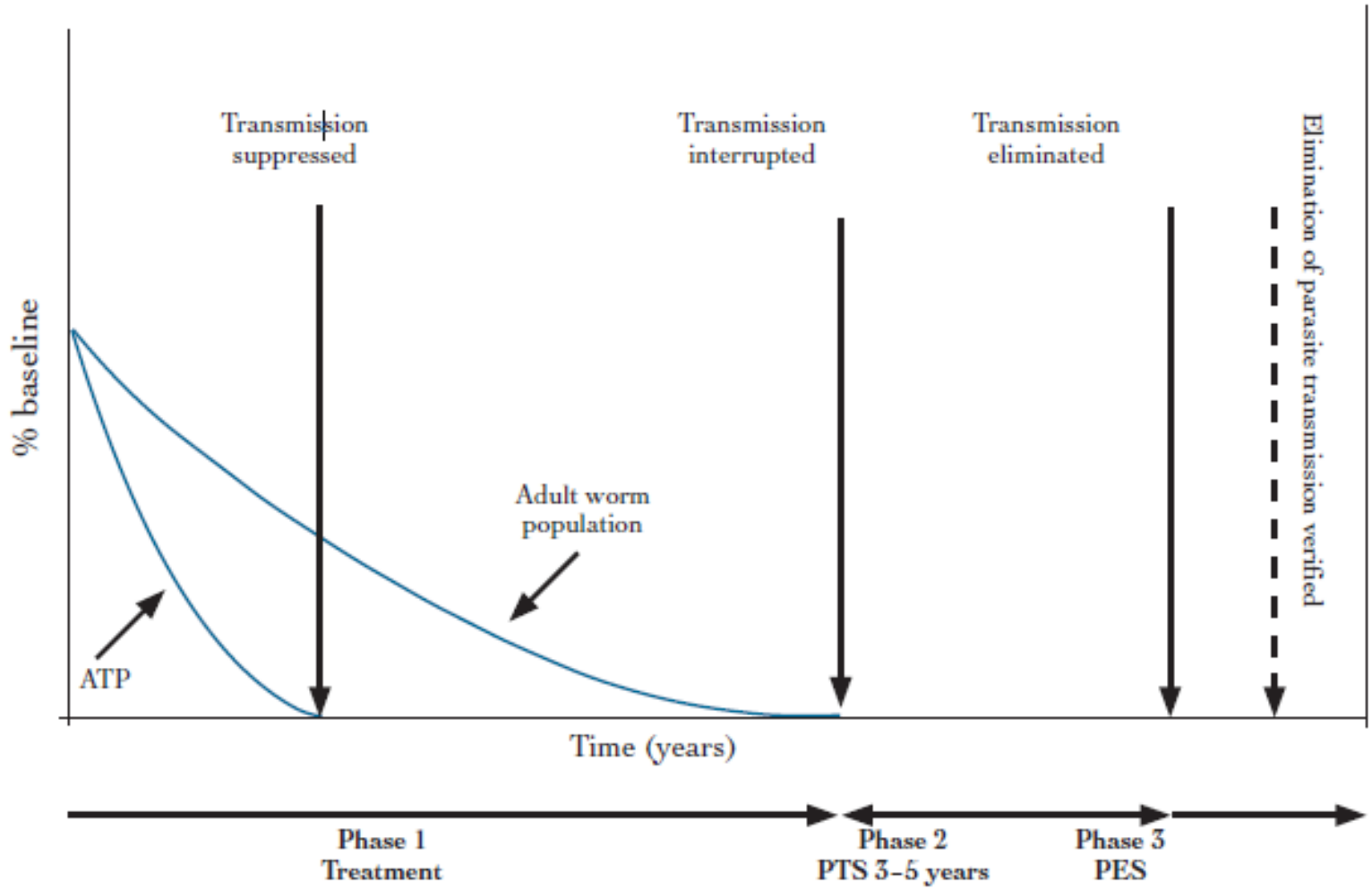
NGO	Non-Governmental Organization
NOEC	The Nigerian Onchocerciasis Elimination Committee
NOTF	National Onchocerciasis Task Force
NTDs	Neglected Tropical Diseases
OEPA	Onchocerciasis Elimination Program for the Americas
OTS	Onchocerciasis Technical Subgroup/Subcommittee
PAHO	Pan American Health Organization
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
RDTs	Rapid Diagnostic Tests
REMO	Rapid Epidemiological Mapping of Onchocerciasis
RSS	Republic of South Sudan
RTI	Research Triangle Institute
SAE	Severe Adverse Events
SCH	Schistosomiasis
SIZs	Special Intervention Zones
STH	Soil Transmitted Helminths
TAS	Treatment Assessment Survey
TCC	The Carter Center
TDA	Triple Drug Administration
UOEEAC	Ugandan Onchocerciasis Elimination Expert Advisory Committee
USAID	United States Agency for International Development
USF	University of Southern Florida
UTG	Ultimate Treatment Goal
WHO	World Health Organization
YFA	Yanomami Focus Area

Figure ES1

2017 River Blindness Elimination Program Review Participants

Figure ES2

Phases of the Elimination of Onchocerciasis (Recent 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, 6.5 million people no longer need Mectizan® treatment in Carter-Center assisted areas in nine countries. 3.8 million (58%) of these people were able to stop their treatment at the end of 2017, the most ever!

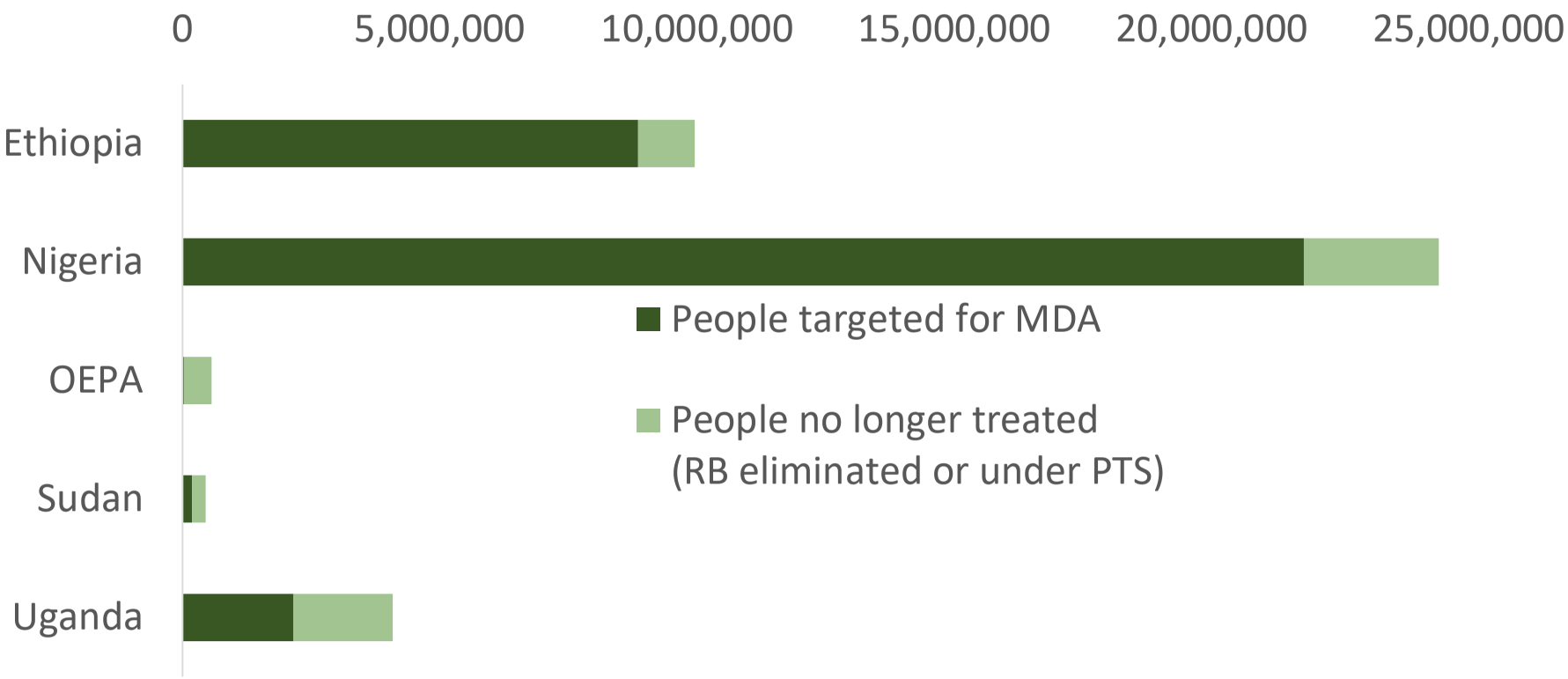


Figure ES4

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

RIVER BLINDNESS		
Country	NOT on MDA in 2018 (both eliminated and on PTS)	Stopped MDA in 2017
ETHIOPIA	1,100,000	1,100,000
OEPA	538,517	
NIGERIA	2,618,861	2,618,861
SUDAN	264,811	144,811
UGANDA	1,928,555	
TOTAL	**6,450,744**	**3,863,672**

Note: Uganda's figure excludes Victoria focus, popn 2.6 million

LYMPHATIC FILARIASIS		
Country	NOT on MDA in 2018 (both eliminated and on PTS)	Stopped MDA in 2017
ETHIOPIA	431,495	431,495
NIGERIA	7,258,307	
TOTAL	**7,689,802**	**431,495**

Note: Ethiopia's 2017 figure combines Metema, Quara and the 3 districts in Bench Maji, even though TAS were in different years

Figure ES5

2017 Mectizan® Mass Treatment Figures for Carter Center RBEP-Assisted Areas in Africa, Latin America (OEPA) and Sudan

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	TOTAL	UTG	% UTG	% All RBEP
Nigeria																
Treatments	-	17,113	66,977	12,899	245,667	821,658	793,158	1,891,343	1,074,663	1,859,911	1,938,462	2,075,421	10,797,272	*12,147,323*	**89%**	**20%**
Villages treate	-	63	-	98	73	1,059	985	2,272	1,831	1,837	1,933	1,459	11,610	*16,329*	**71%**	**14%**
Nigeria 2x																
Treatments	-	-	-	-	-	1,416,560	6,457,070	3,758,610	1,156,704	176,783	1,998,648	7,215,144	22,179,519	*24,431,818*	**91%**	**40%**
Villages treate	-	-	-	-	362	1,743	9,155	5,118	359	276	1,053	13,889	31,955	*30,450*	**105%**	**38%**
Uganda																
Treatments	-	-	-	-	80,992	1,550,977	299,451	31,476	-	130,218	1,329,158	527,898	3,950,170	*4,191,682*	**94%**	**7%**
Villages treate	-	-	-	-	260	3,253	333	-	-	-	-	-	3,846	*7,692*	**50%**	**5%**
OEPA 2x																
Treatments	-	-	8,688	-	-	8,721	-	-	-	-	-	-	17,409	*19,232*	**91%**	**0%**
Villages treate	-	-	43	-	-	139	-	-	-	-	-	-	182	*364*	**50%**	**0%**
OEPA 4x																
Treatments	-	-	11,669	-	-	12,173	-	-	13,042	-	-	12,999	49,883	*63,956*	**78%**	**0%**
Villages treate	-	-	296	-	-	63	-	-	-	-	-	-	359	*1,436*	**25%**	**0%**
Ethiopia 2x																
Treatments	-	-	1,384,057	2,138,176	2,480,498	16,038	212,484	3,088,184	-	-	-	8,460,767	17,780,204	*18,421,949*	**97%**	**32%**
Villages treate	-	-	8,357	523	16,286	9,890	1,397	15,834	-	-	-	19,457	35,872	*104,264*	**34%**	**43%**
Sudan																
Treatments	-	-	9,654	-	23,280	-	8	11	171	13,088	-	-	46,212	*62,587*	**74%**	**0%**
Villages treate	-	-	-	-	-	24	-	-	5	-	-	-	29	*29*	**100%**	**0%**
Sudan 2x																
Treatments	-	-	-	-	-	-	107,856	3,494	17,219	-	-	-	128,569	*123,090*	**104%**	**0%**
Villages treate	-	-	-	-	-	144	-	-	-	-	-	-	144	*306*	**47%**	**0%**
TOTALS																
Treatments	**-**	**17,113**	**1,481,045**	**2,151,075**	**2,830,437**	**3,826,127**	**7,870,027**	**8,773,118**	**2,261,799**	**2,180,000**	**5,266,268**	**18,292,229**	**54,949,238**	***59,461,637***	**92%**	
Villages treat	**-**	**63**	**8,696**	**621**	**16,981**	**16,315**	**11,870**	**23,224**	**2,195**	**2,113**	**2,986**	**34,805**	**83,997**	***160,870***	**52%**	

Cumulative RBEP-Assisted Treatments (1996 - 2017): 333,102,914

2017 Mass Treatments	54,949,238
2017 Passive Treatments	130,377
2017 TOTAL TREATMENTS	**55,079,615**

Figure ES6

RBEP-Assisted Programs: Mectizan® Treatments 1996 – 2017 and 2018 Target

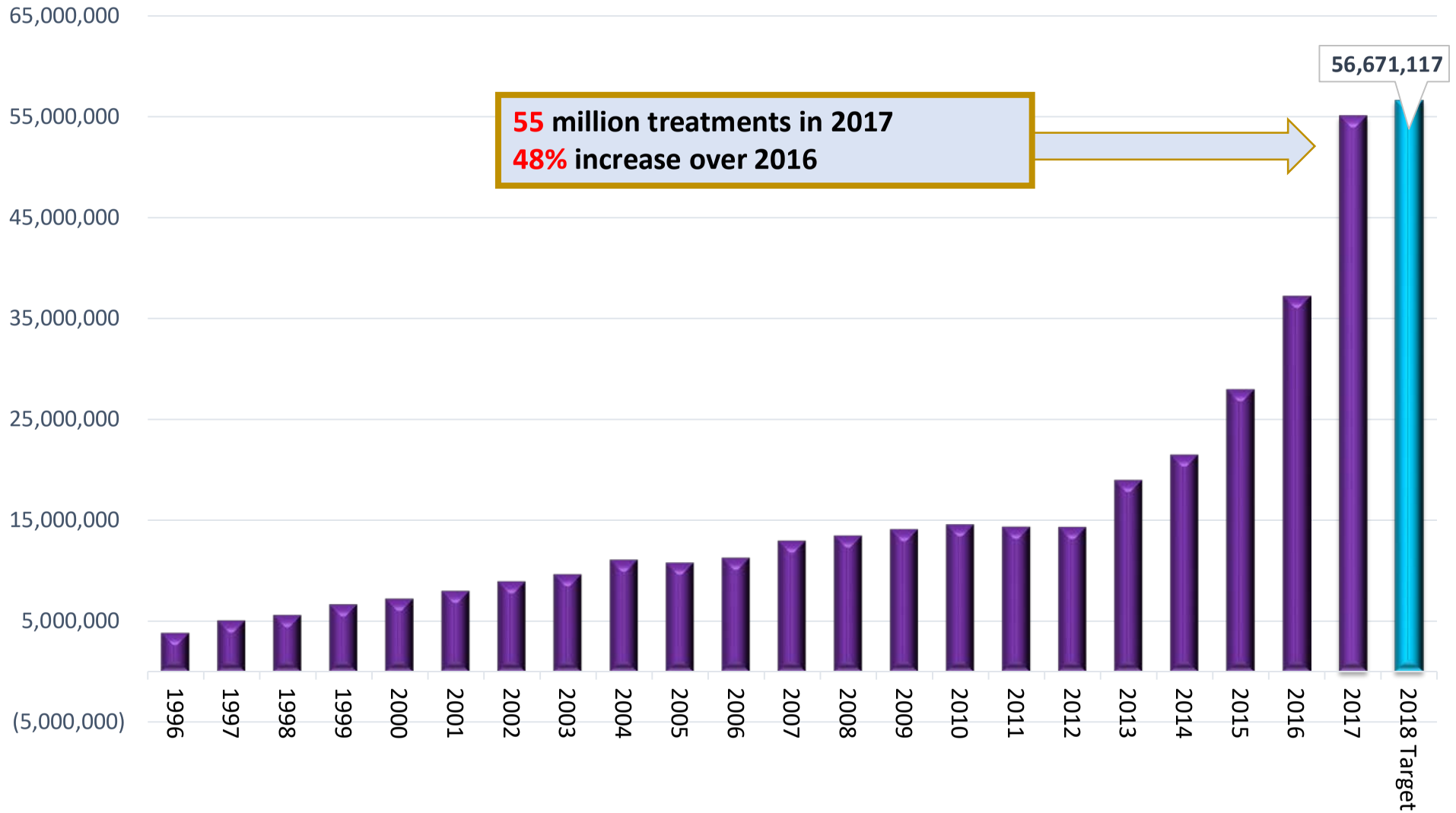


Figure ES7

Carter Center-Supported Treatment Doses, and Persons Treated, for Neglected Tropical Diseases 2015 – 2017

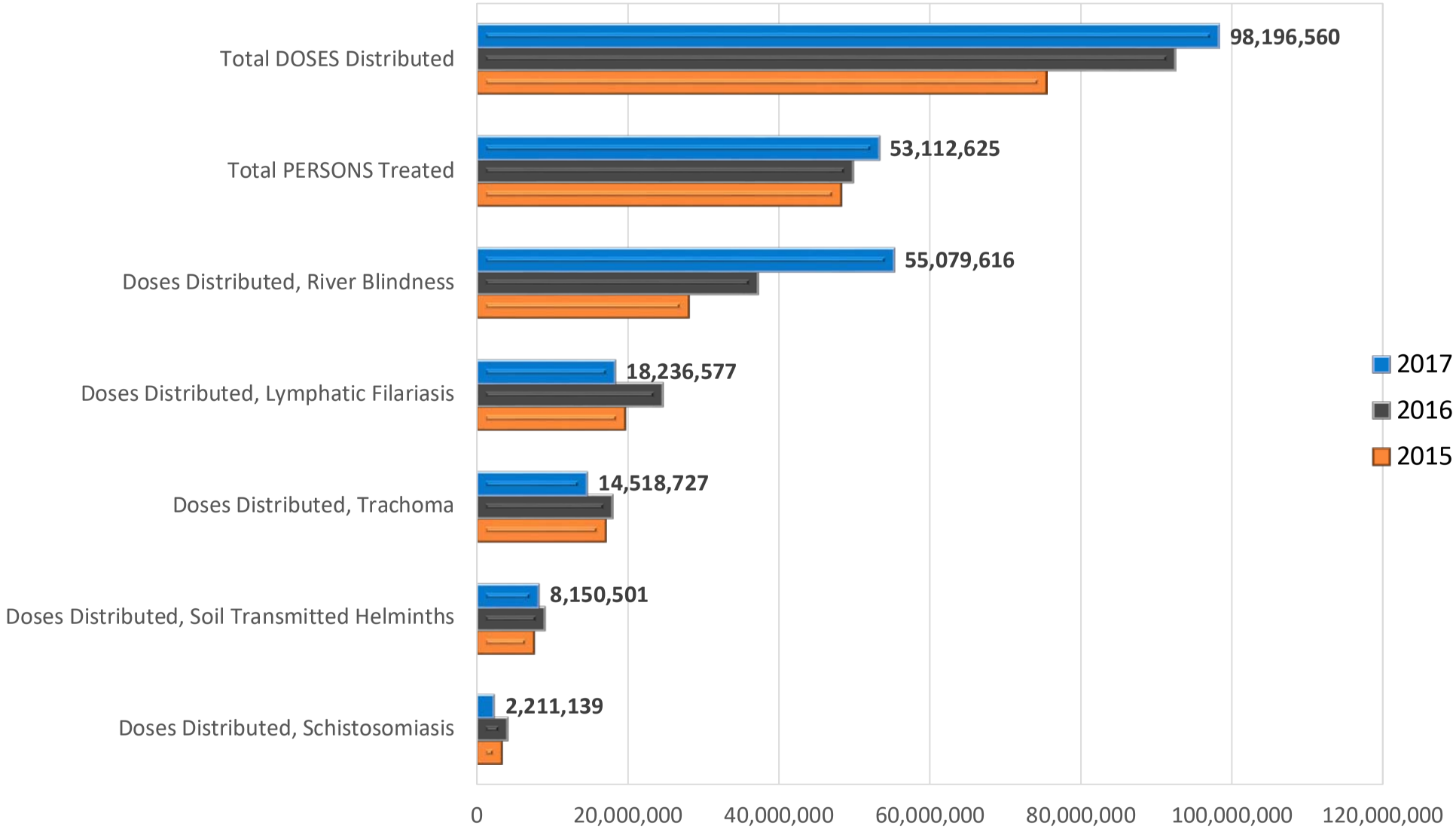


Figure ES8

Carter Center River Blindness Elimination Programs Cumulative Treatments 1996-2017

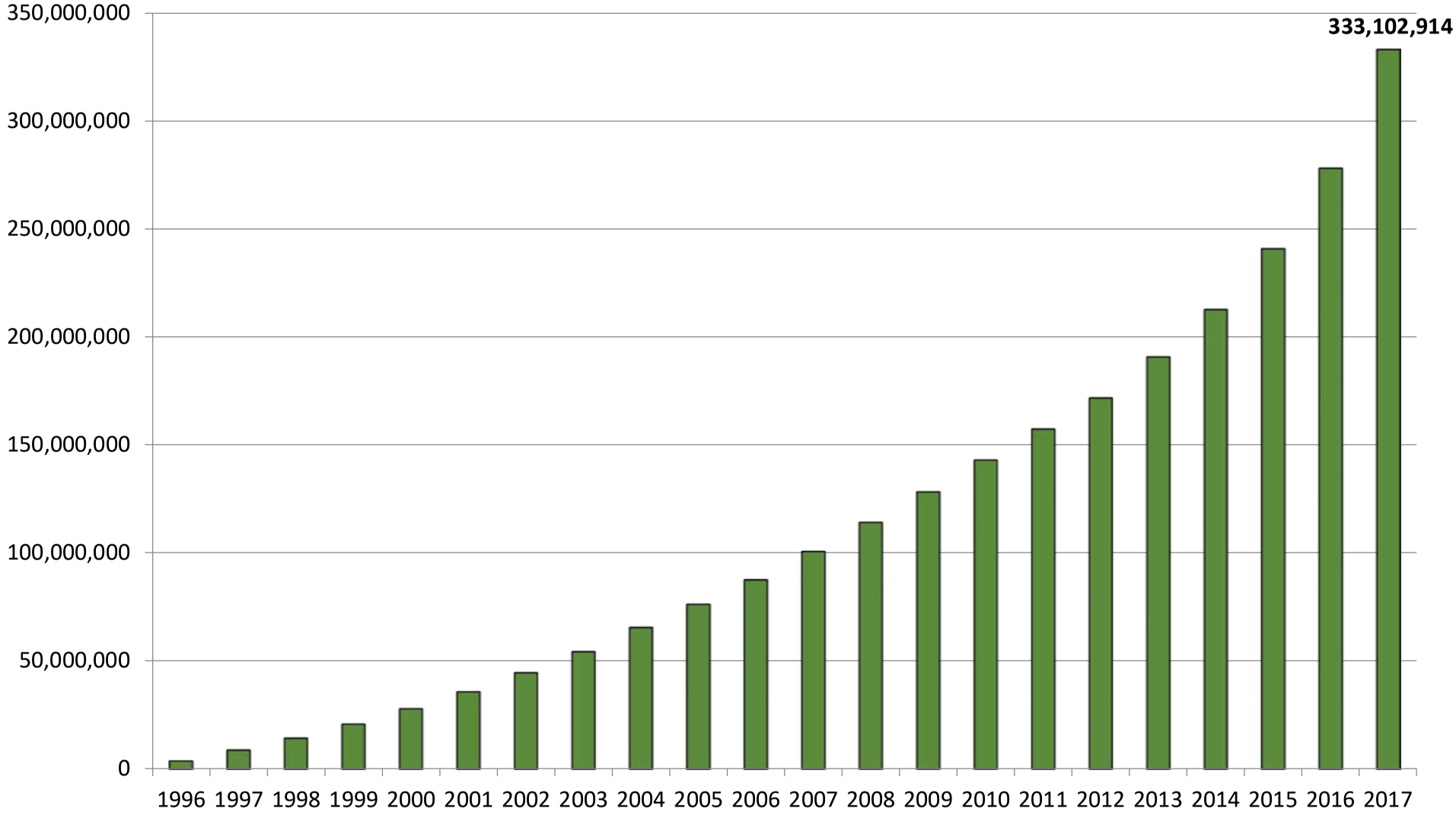


Figure ES9

Carter Center-Assisted Programs: 1996 – 2017 Mectizan® Treatments by Program

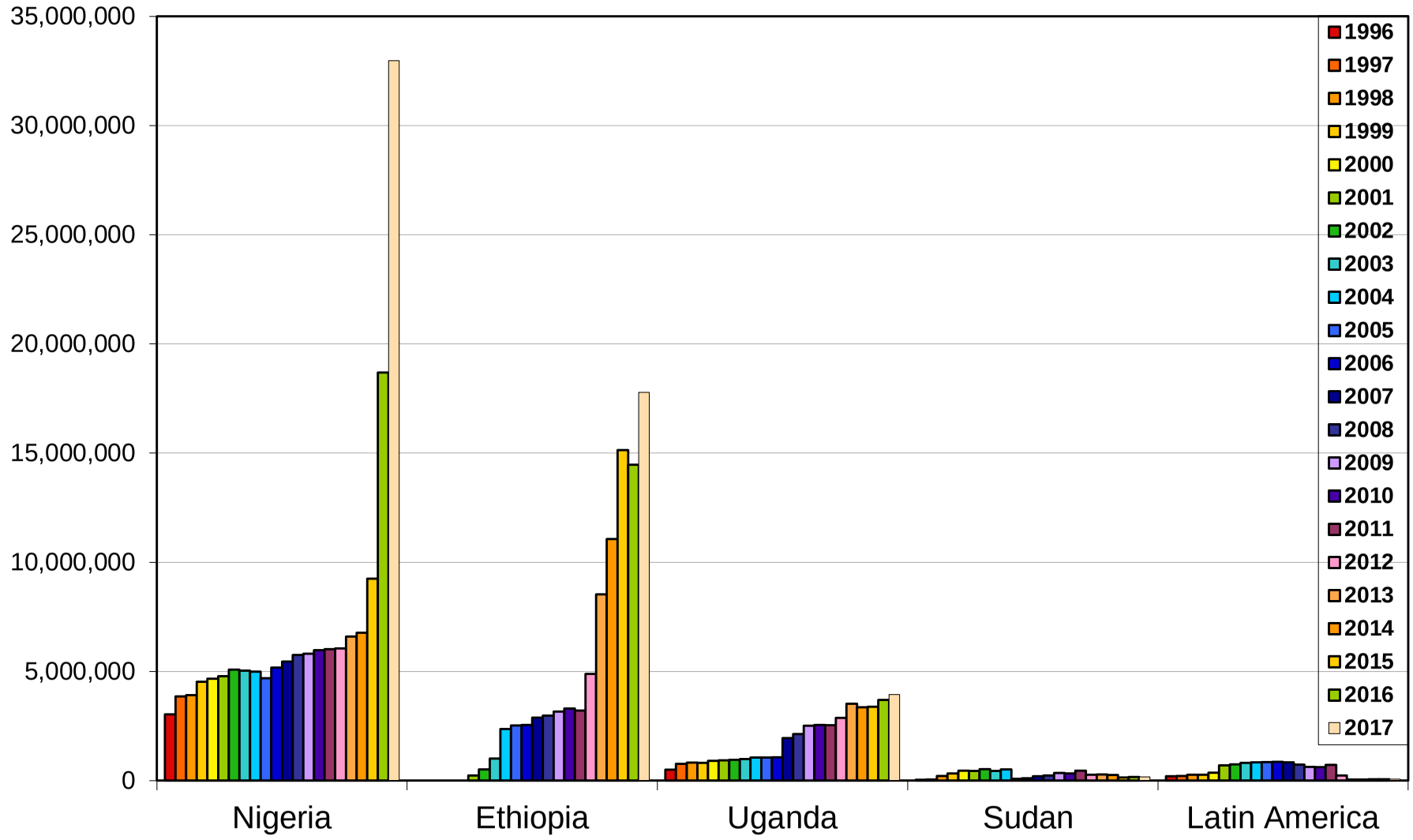


Figure ES10

River Blindness Program: Reported Treatment Coverage (eligible population) by Project: UTG, UTG(2), or UTG(4) 2005 – 2017

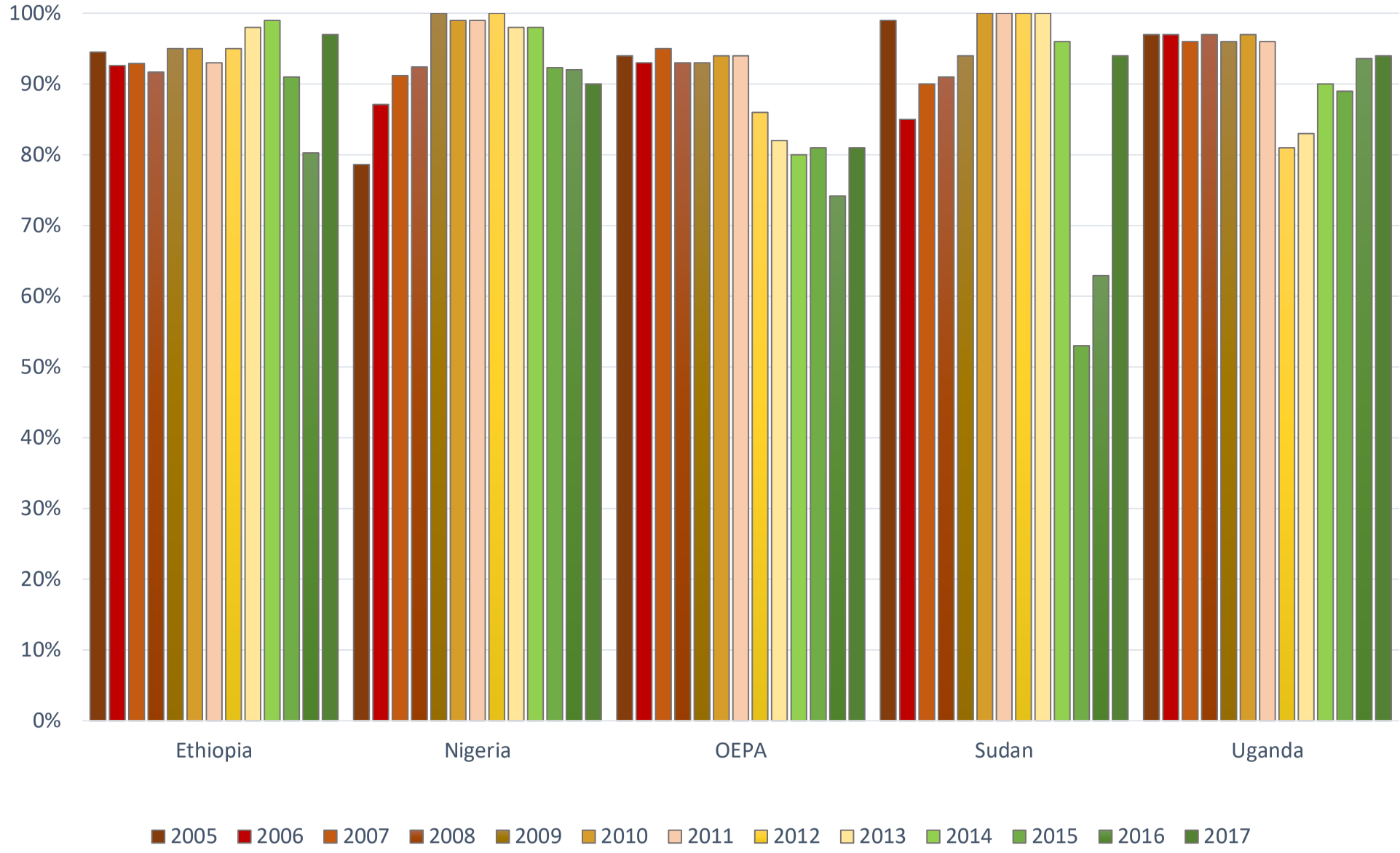


Figure ES11

Community-Directed Distributors (CDDs) Trained 2004 – 2017 and 2018 Total Targets

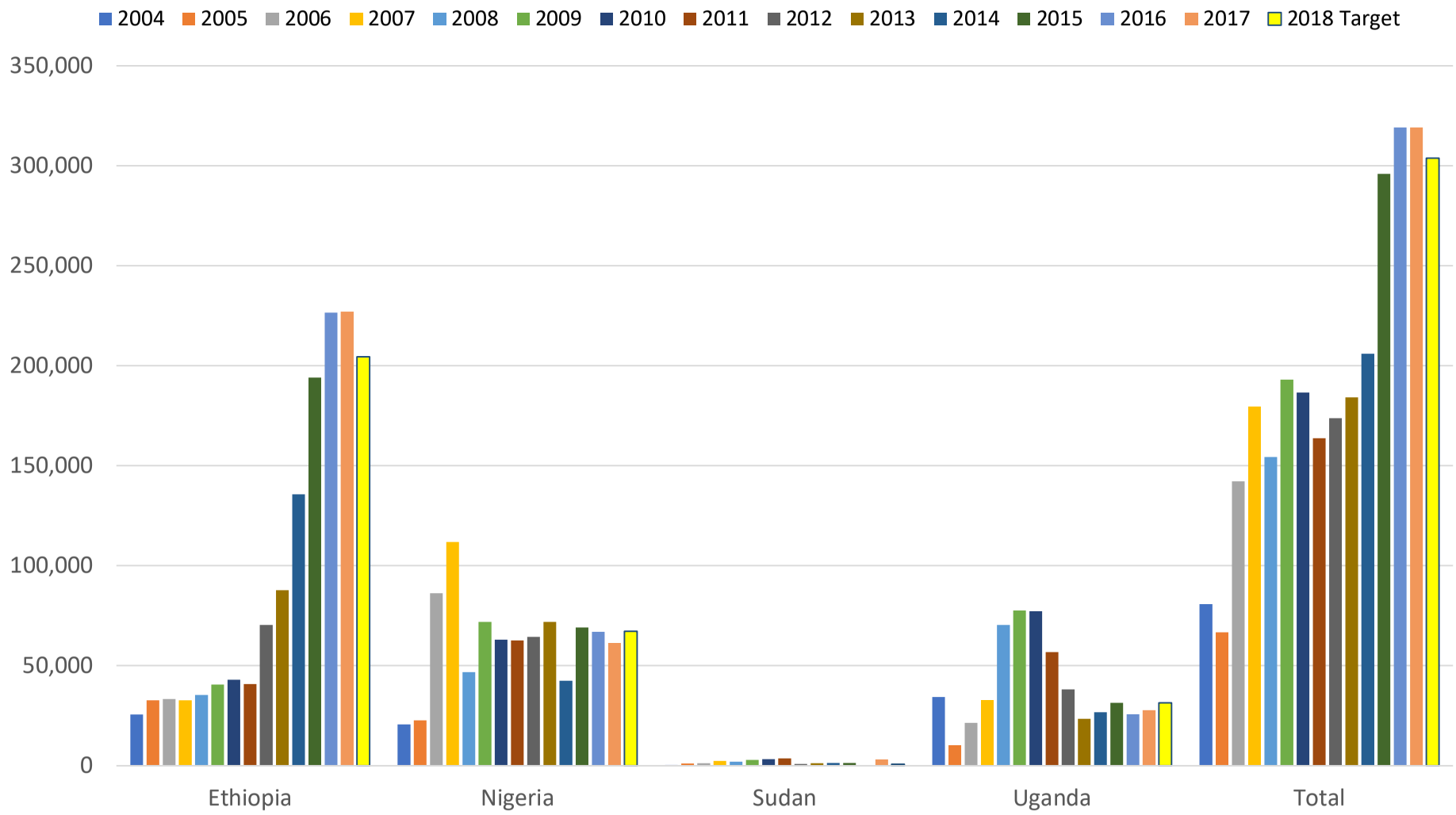
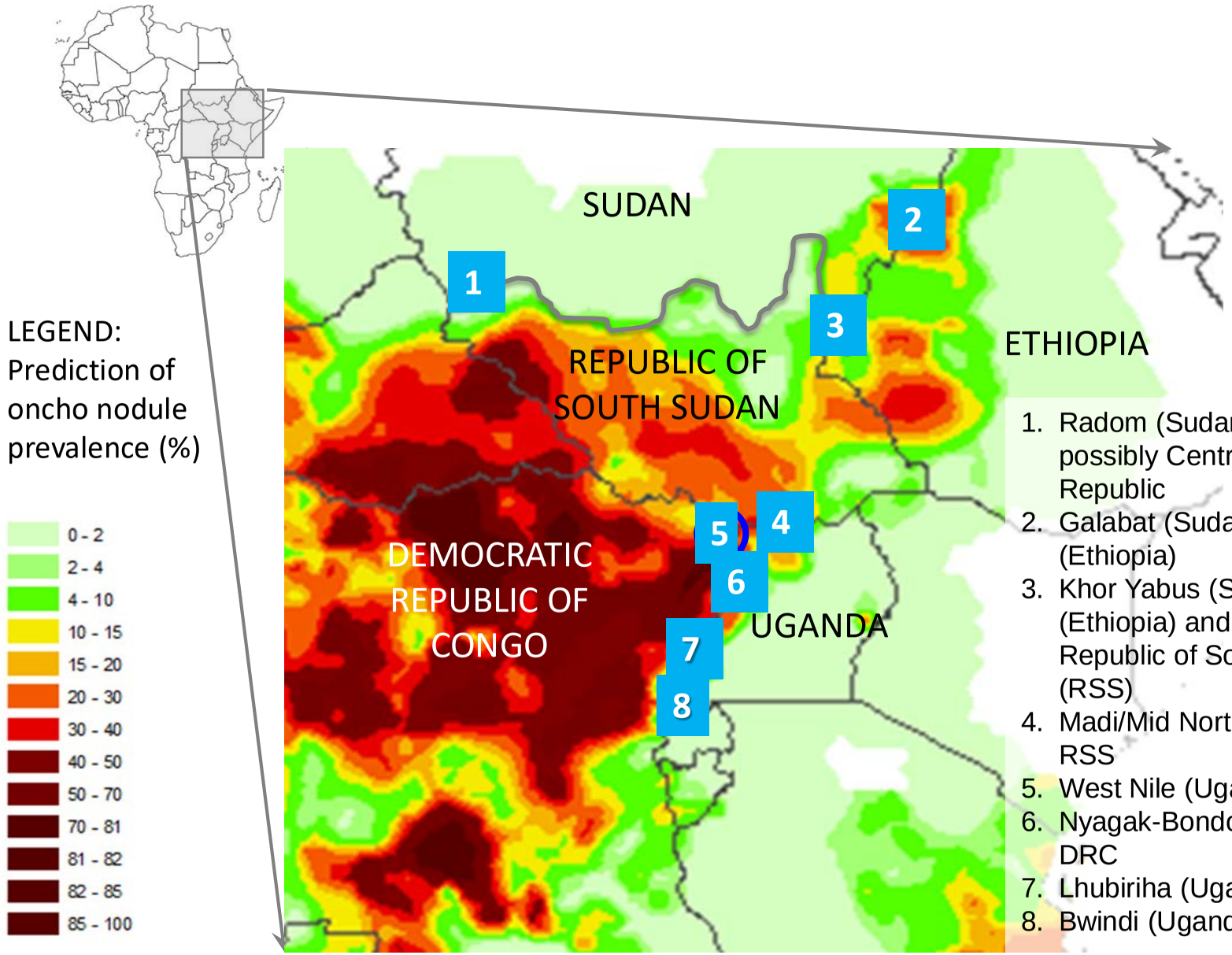


Figure ES12

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



REMO map source: APOC

Figure ES13

Nigeria: Carter Center Assisted River Blindness (RB), Lymphatic Filariasis (LF), Soil Transmitted Helminths (STH) and Schistosomiasis (SCH) Treatments 2012 – 2017 and 2018 Targets

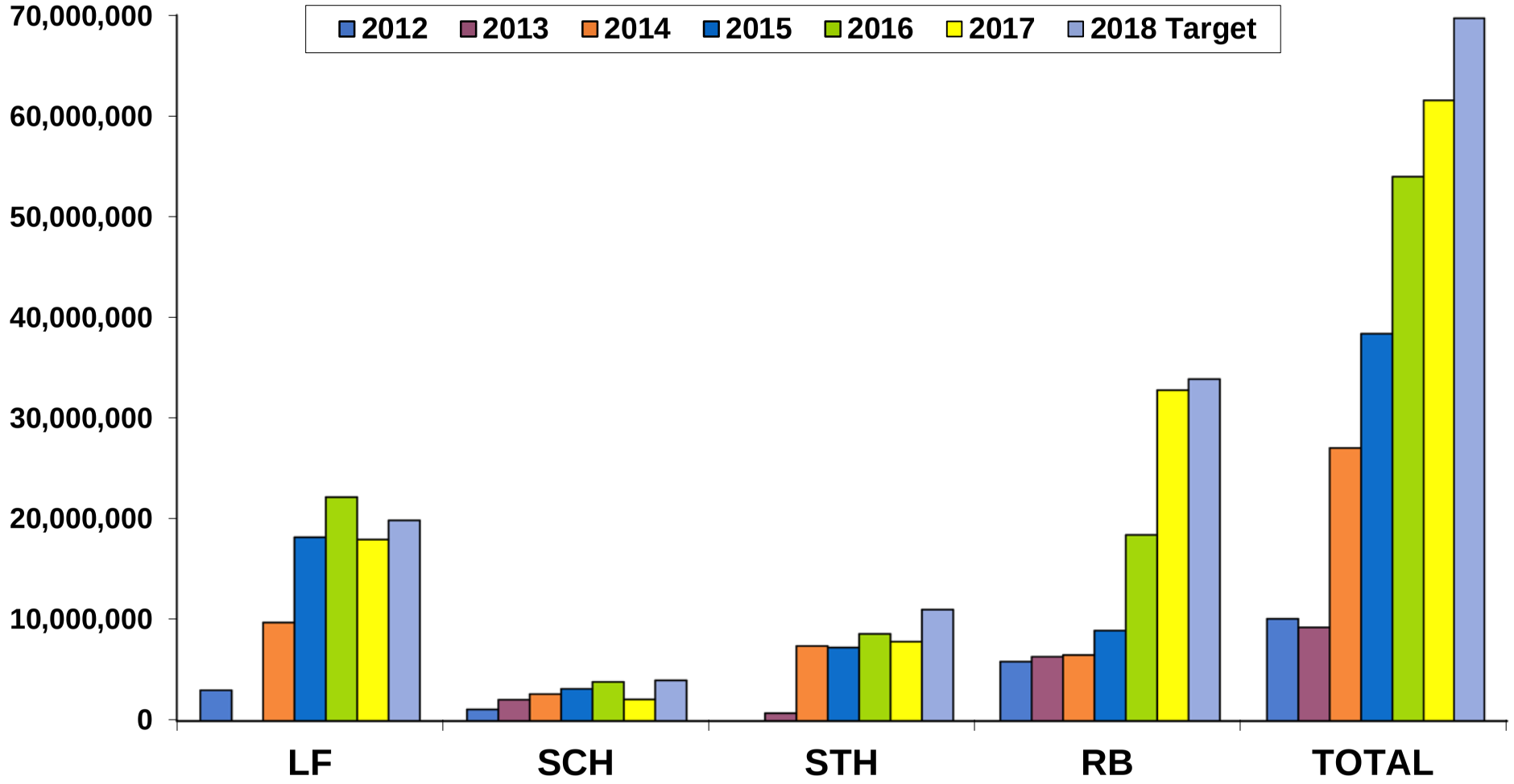


Figure ES14

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

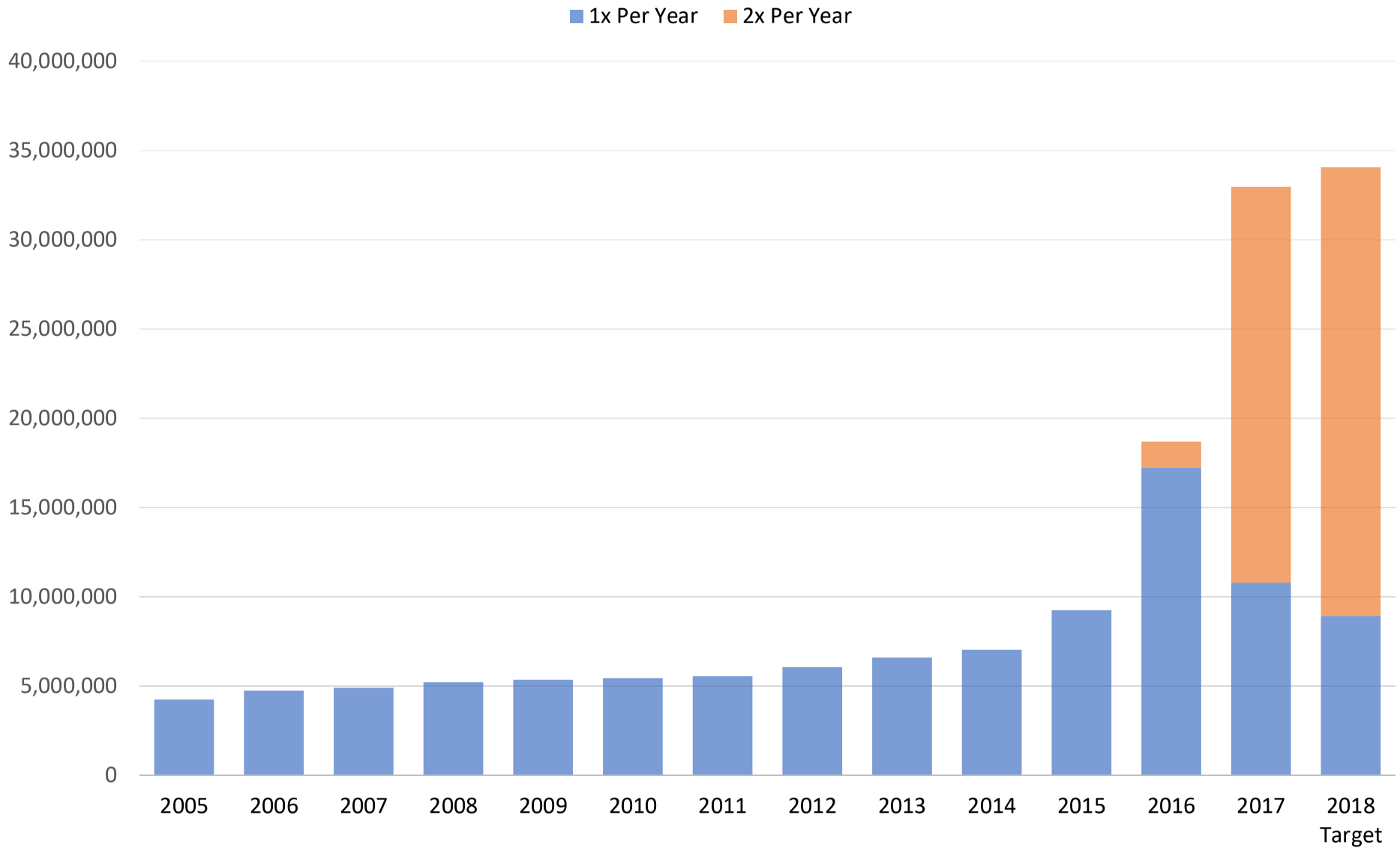
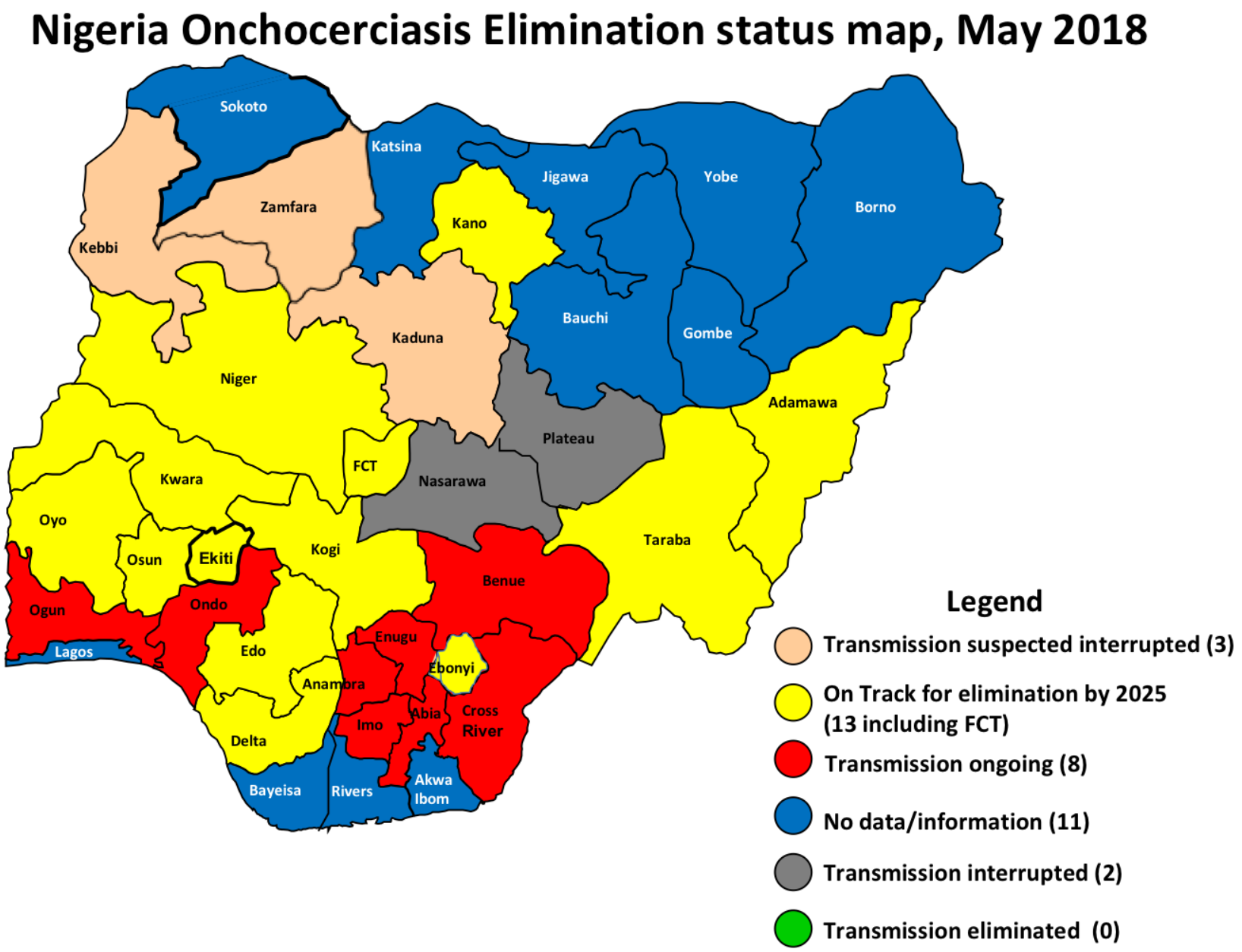


Figure ES15

RBEP-assisted Plateau and Nasarawa States first to stop MDA in Nigeria!



Source: Nigeria Onchocerciasis Elimination Committee

Figure ES16

Ninety–Four Percent of Onchocerciasis in the Americas Eliminated!

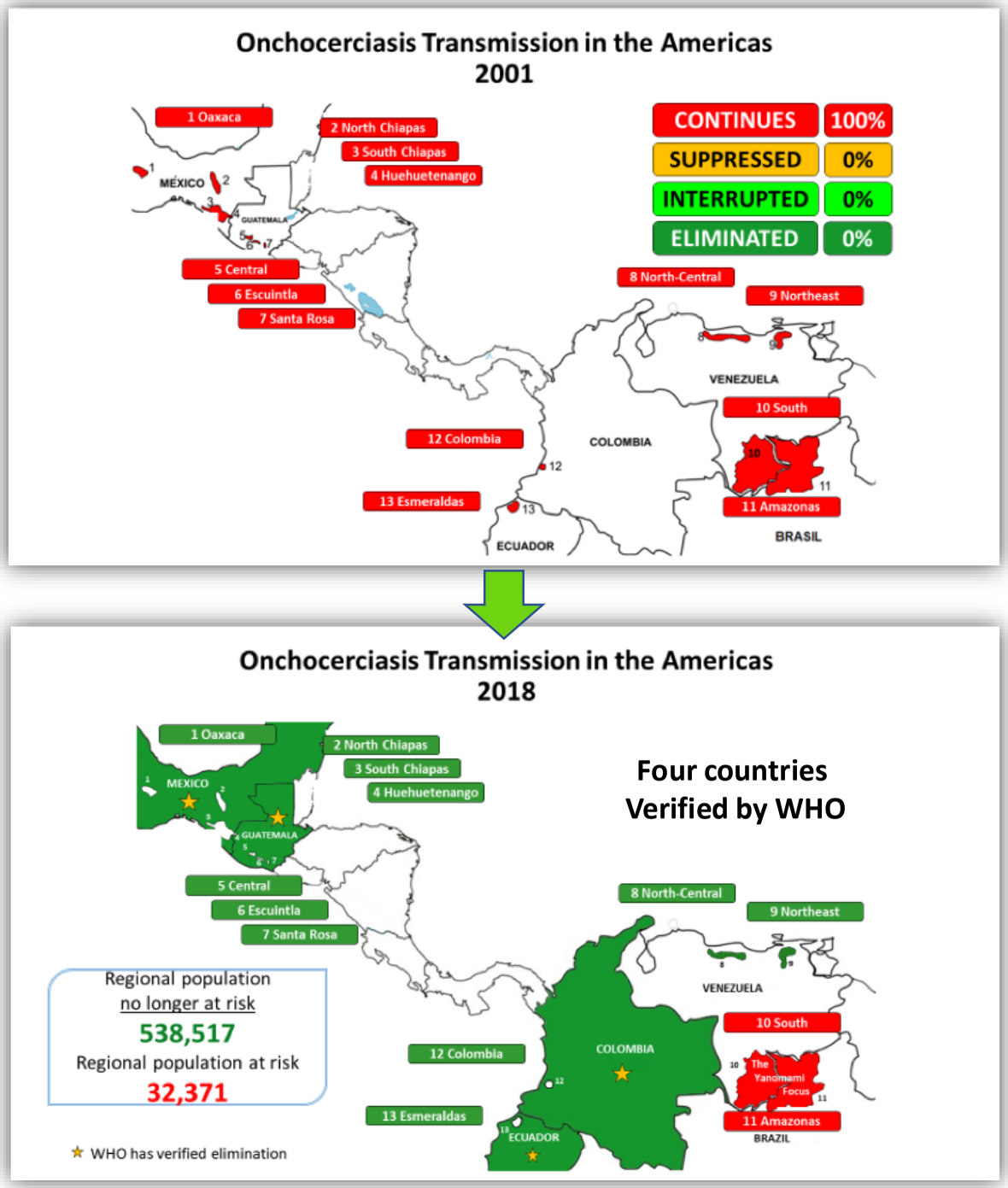


Figure ES17

Mectizan® Treatments Distributed in the Americas 1989 - 2017 2x and 4x/year Treatment Approaches

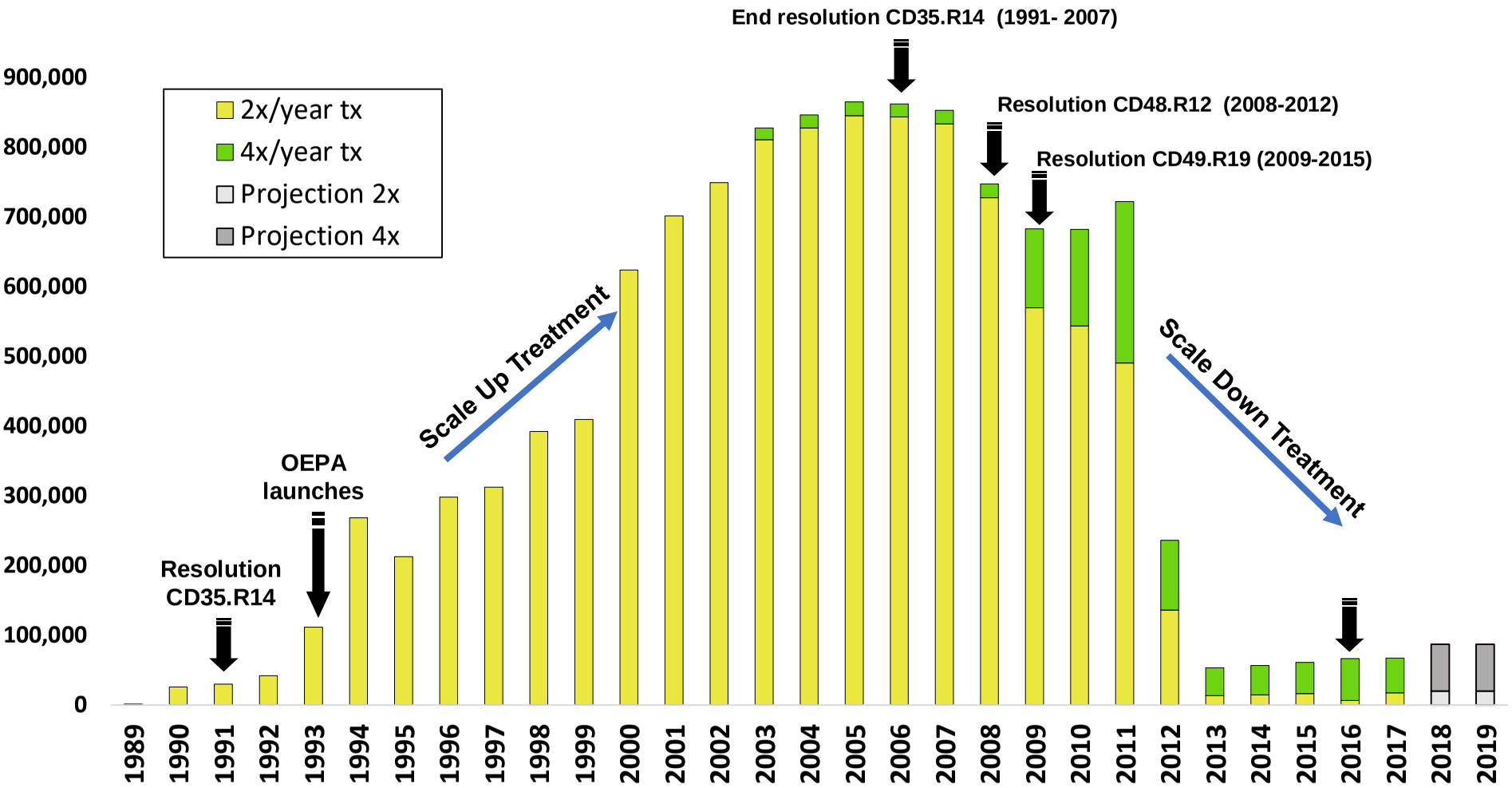
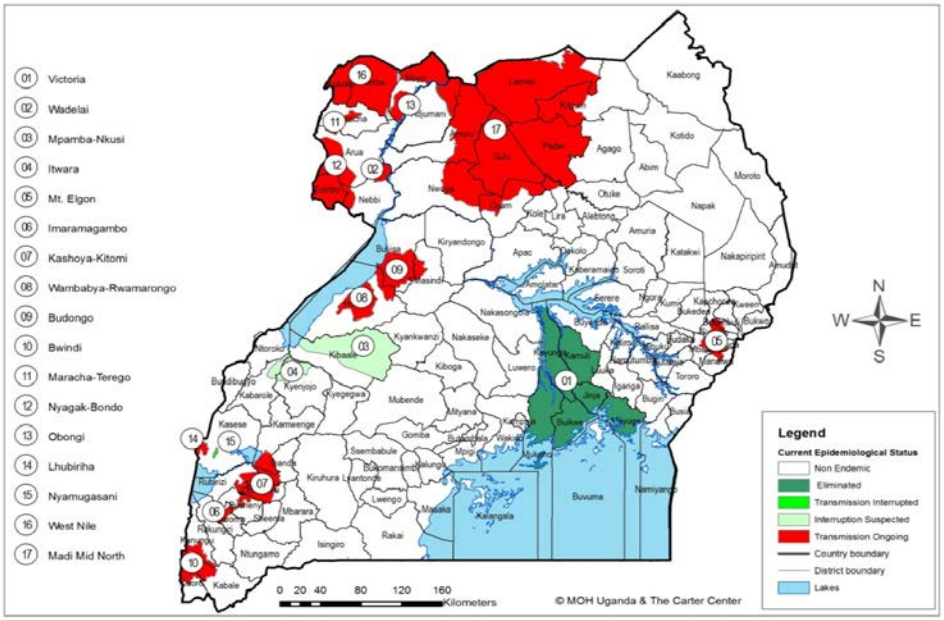


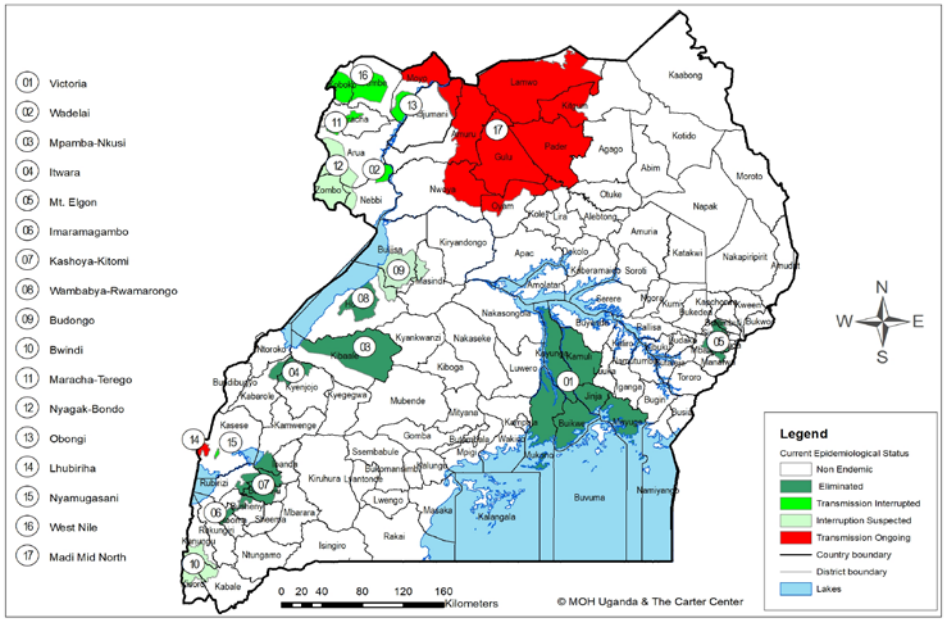
Figure ES18

Uganda: Ten Years of Progress in Eliminating Onchocerciasis Transmission

2007



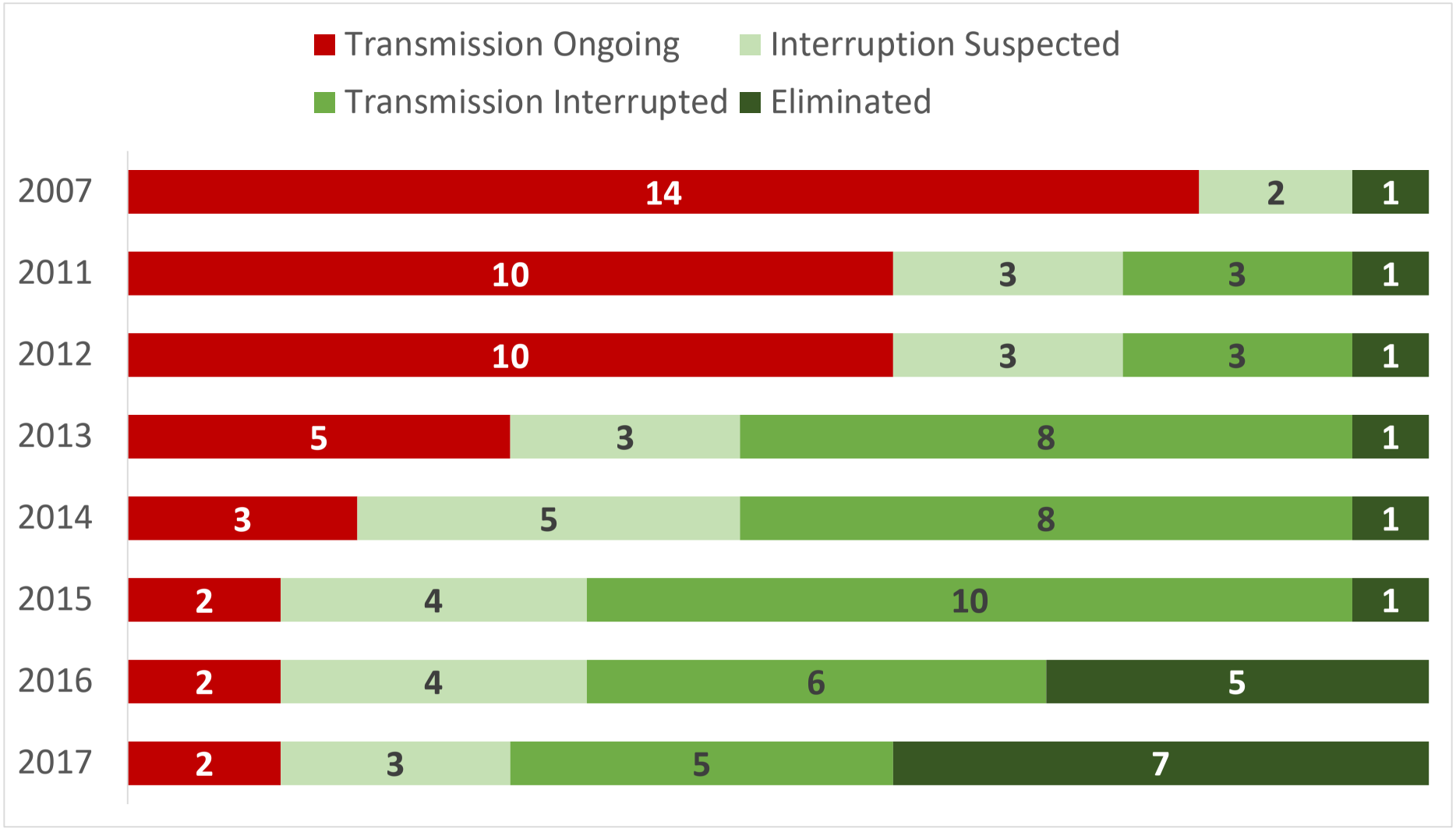
2017



Red = Foci with ongoing transmission

Figure ES19

Uganda Progress in Eliminating Onchocerciasis Transmission (Change in Endemic Status in Foci) 2007-2017



ABSTRACT

The Carter Center (TCC) River Blindness Elimination Program (RBEP) held its 22nd Annual Review, March 14-16, 2018 at its Atlanta headquarters (meeting photo, Figure ES1). The Review focused on the 2017 RBEP achievements, challenges, and operational research, and provided recommendations for 2018 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 eliminate river blindness (RB) transmission everywhere it assists ministries of health (MOHs) in 10 countries.[1] The strategy for elimination in RBEP programs is mass drug administration (MDA) with ivermectin (Mectizan®, donated by Merck & Co., Inc.), preferably given twice-per-year, and spaced by six months. This strategy has been highly successful in the Americas, resulting in 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 with respect to the WHO elimination guidelines, 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) Post Treatment Surveillance (PTS) completed and transmission eliminated.

As a result of our RB elimination partnership, 6.5 million people no longer need Mectizan® treatment in Carter Center-assisted areas in eight countries; 2.7 million (41%) of these stopped their treatment at the end of 2017, the most ever! Details of this notable achievement are shown in Figures ES3 and ES4.

The 2017 Review continued to highlight challenges in cross-border transmission areas that we have termed ‘Special Intervention Zones’ (SIZs).

In 2017, The Carter Center assisted in a total of 55,079,616 mass ivermectin treatments for river blindness (onchocerciasis) in six countries, a 48% increase from 2016 and 92 percent of the 2017 treatment target (Figures ES5 and ES6). A goal of 56.7 million treatments has been set for 2018 (Figure ES6). These treatments represented about 57% of the 97 million MDA treatments assisted by The Carter Center for neglected tropical diseases (NTDs). Figure ES7 shows the last three years of treatments by disease, and the estimated number of persons treated.

RBEP’s cumulative treatments since 1996 have now reached 333 million (Figure ES8). Figures ES9 and ES10 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.

[1] Brazil, Colombia, Ecuador, Ethiopia, Guatemala, Mexico, Nigeria, Sudan, Uganda, and Venezuela.

RBEP is an integrated program and during the Review, treatment numbers were reported for 2017 MDA results for several other TCC Neglected Tropical Disease (NTD) efforts in addition to river blindness, including lymphatic filariasis (LF) in Ethiopia and Nigeria (18,236,577 treatments, 85% of the target), and schistosomiasis (SCH) and soil-transmitted helminthiasis (STH) in Nigeria (2,211,139 and 8,150,501 treatments, for 82% and 94% of the targets, respectively). Donated medicines for these treatments were provided by MSD, also known as Merck & Co., Inc., Kenilworth, N.J. USA (Merck & Co., Inc.), Merck KGaA, Darmstadt, Germany (E-Merck), GSK, Johnson & Johnson, and Pfizer, Inc.

Our work would not be possible without a grassroots network of community-directed drug distributors who provide the treatments along with health education. A combined 409,840 community workers were trained in 2017, all of whom were trained and mentored by Ministry of Health personnel working in affected districts assisted by TCC (Figure ES11).

EXECUTIVE SUMMARY OF THE 22ND PROGRAM REVIEW

Dr. Frank Richards, Director of The Carter Center's River Blindness, Lymphatic Filariasis, and Schistosomiasis Programs, co-chaired the meeting with four RBEP Country Representatives: Ms. Peace Habomugisha (Uganda), 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; British Consulate General Atlanta; The ELMA Philanthropies; Emory University; The END Fund; FHI 360; GSK; The Huffington Post; Imo State University Owerri; Izumi Foundation; Lions Clubs International Foundation; The London School of Hygiene & Tropical Medicine; Mectizan® Donation Program; RTI International; Sightsavers; The Task Force for Global Health; University of Notre Dame; University of South Florida; United States Agency for International Development; U.S. Centers for Disease Control and Prevention (CDC); and the World Health Organization (WHO). Key findings and country reports follow. (See Annexes 1–8 for background on the diseases; a program achievement timeline; lists of participants, contacts, and 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 SIZ that straddles the border between Brazil and Venezuela. In Africa, the SIZs currently addressed are: 1) the Radom focus of Sudan, another very unstable SIZ that extends into Republic of South Sudan (RSS) and possibly Central Africa Republic; 2) the Galabat (Sudan) and Metema (Ethiopia) transmission zones, both of which reached an agreement in 2017, for coordinated stopping of Mass Drug Administration (MDA); 3) Sudan's Khor Yabus focus which is shared between Ethiopia, RSS, and Sudan; 4) the Madi/Mid North 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) Lhubilhia 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 Kaduna, Benue, Bauchi and Taraba States (supported by various 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 2017, Ethiopia delivered a total of 17,864,308 Mectizan® treatments, compared to 14,467,640 in 2016. The TCC-assisted LF program provided 1,118,593 treatments with Mectizan® and Albendazole. A total of 226,529 community drug distributors were trained, about 32,000 more than in 2016 (ES11). Ethiopia's RBEP is aiming for 17.89 million treatments in 2018. 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, and other donors.

Sudan aims to give about 208,600 treatments in 2018 in their Radom focus.

History of Stop MDA in Ethiopia and Sudan: In 2017 Ethiopia and Sudan jointly declared a stop ivermectin MDA decision in the cross-border onchocerciasis transmission zone (focus) straddling the Metema district of the North Gondar Zone of Amhara region, Ethiopia and the Galabat district of Sudan's Gedarif State. This shared SIZ has a population of about 1.2 million people (1.1 million in Ethiopia). Ethiopia stopped over 400,000 treatments for LF at the end of 2017. Together with Galabat and Abu Hamad Sudan has stopped over 400,000 treatments for RB. (ES3-ES4)

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 59.7 million treatments for river blindness, LF, SCH, and STH in nine states of Nigeria in 2017 (Figure ES13).

RBEP assisted in 32,976,792 Mectizan® treatments for river blindness in 2017, a 76% increase over 2016 due to an incredible expansion of twice-per-year treatments under the country's aggressive elimination agenda (Figure ES14). The program also reported that the Nigeria Onchocerciasis Elimination Committee (NOEC) had reviewed results of 2017 serology and entomology assessments and determined that MDA for river blindness could be halted in Plateau and Nasarawa States. The river blindness victory in Plateau and Nasarawa follows on the heels of an October 2017 announcement that the same two states had successfully completed their third LF Transmission Assessment Survey (TAS-3) that showed no evidence of resumed LF transmission six years after stopping LF MDA, thus eliminating that disease as a public health problem (Figure ES15). Our LF MDA in Nigeria is now focused on the seven TCC-assisted southern states, where we helped to provide 17,426,794 combination Mectizan®/albendazole annual treatments in 2017. Our LF target in 2018 is 20 million treatments. Thanks to our *Loa loa* study in 2016, which demonstrated to the FMOH and the Mectizan Expert Committee that these states do not have high-intensity *Loa loa* that would preclude Mectizan® treatment, the LF program was able to switch to annual combination treatment from the twice per year albendazole monotherapy regimen provided in 2016. Albendazole is donated by GSK.

The Carter Center's integrated malaria-LF program provided 9,147 long-lasting insecticidal nets (LLIN) 2017; the Nigerian TCC program has assisted with the distribution of over 11.5 million nets since 2004. Recent support from the Clarke Cares Foundation/Clarke Mosquito Control has funded net distribution and use promotion, and TCC continues to urge the use of the FMOH Guidelines for malaria-LF co-implementation in Nigeria.

The Carter Center assisted in 2,211,139 praziquantel treatments for schistosomiasis in our nine assisted states in Nigeria in 2017. Praziquantel is donated to The Carter Center through the World Health Organization by Merck KGaA (E-Merck) of Germany. Izumi Foundation supports this program in four of the states we assist. Our target in 2018 is 4.2 million treatments (an 88% increase). Treatments in 2017 for STH were 8,150,501, and the 2018 target is 11 million treatments (a 38% increase). The medicines used for STH treatment are donated by GSK (albendazole) or Johnson & Johnson (mebendazole).

History of Stop MDA successes in Nigeria. In Plateau and Nasarawa States, MDA has been stopped among 2.6 million persons for RB (at the end of 2017) and among 7.2 million persons for LF (in 2012) (ES3-ES4).

Uganda

In 2007, Uganda declared a goal of river blindness transmission elimination from all its 17 transmission zones (foci). The program continued to make excellent progress. At the 2017 Ugandan Onchocerciasis Elimination Expert Advisory Committee meeting, two more foci (Kashoya-Kitomi and Wambabya-Rwamarongo) successfully completed post-treatment surveillance and were reclassified as having achieved transmission elimination, based on the WHO elimination guidelines. Two additional foci (Wadelai and West Nile) were reclassified as having interrupted transmission. Three foci (Budongo, Bwindi, and Nyagak-Bondo) are suspected to have interrupted transmission, while the remaining two foci (Lhubiriha and Madi-MidNorth) have active transmission. Uganda administered a total of 3.9 million Mectizan® treatments in 2017, all under the twice-per-year strategy. For 2018, the target is for 4.3 million treatments, most of which will take place in the large Madi-MidNorth Focus bordering South Sudan. Uganda also has important cross-border foci shared with the Democratic Republic of the Congo (Figure ES16). Currently, onchocerciasis elimination in Uganda is supported by The Carter Center, USAID's ENVISION project led by RTI International, and Sightsavers, under the coordination of the Ministry of Health.

History of Stop MDA successes in Uganda (Figure ES19). Since the program launched its elimination policy, approximately 1.9 million ivermectin treatments have been halted in the country. (ES3-ES4)

The Americas

The OEPA initiative has stopped 94% of the ivermectin treatments once required in the Americas; 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 remaining active transmission zone is an SIZ populated by about 30,000 indigenous, migratory people (the Yanomami) residing in the remote Amazon rainforest in an area bordering Brazil and Venezuela. The countries and Carter Center staff are trying to creatively solve the problems of extreme isolation and difficult access to this area, 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 65,000 treatments are planned in the Yanomami Area in 2018. The OEPA program receives financial support from USAID and the Carlos Slim Foundation.

History of Stop MDA successes in the Americas (Figure ES17). Over 500,000 persons are no longer under treatment in the Americas (Figures ES3-ES4).

2018 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) assisted areas in Africa and the Americas. TCC/RBEP work includes:

- Helping to empower national onchocerciasis committees to review their data and make decisions related to enhancing interventions, expanding treatment, stopping interventions, and entering into post-treatment surveillance, guided by (but not restricted to) WHO guidelines.
- Conducting new assessments to help delimit the precise borders of African onchocerciasis transmission zones ('*foci*') that are targeted for elimination 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 (flexibly using 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.

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

Programs should collect more information, to share at the next review, on communities with low coverage.

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

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 work with Ministries of Health to target an April 30 submission in order 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, the 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 seeks onchocerciasis transmission interruption in all the countries that it assists, in both the Americas and in Africa. Accordingly, TCC urges the ministries of health of countries where it works to ask WHO to put a draft resolution before the World Health Assembly calling for elimination of onchocerciasis transmission and halting of MDA, in accord with current WHO guidelines, in countries electing to pursue that goal (which includes all counties where TCC/RBEP assists).

TCC/RBEP and its partners are often unable to assess the status of onchocerciasis in areas of civil strife. In such insecure areas, WHO should establish a rapid assessment protocol to allow programs to enter and assess onchocerciasis endemicity and transmission status when the security situation allows.

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 University of South Florida (USF) (Dr. Thomas Unnasch). 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 first by Dr. Unnasch or his staff before TCC HQ will purchase and ship in a timely manner.

The WHO Onchocerciasis Technical Subgroup (OTS) has recommended that mapping of onchocerciasis hypoendemic areas should be conducted in adult residents and not in children as is being done now by some countries assisted by TCC. Ov16 rates in adults ≥2% is the threshold to launch MDA is currently recommended by OTS.

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

The 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 Helminthiasis (STH) Programs propose to assist ministries of health to provide 93,711,568 treatments for NTDs in 2018.

2018 Treatment and Training Objectives:

UTG = Ultimate Treatment Goal
UTG(2) = Twice-per-year UTG
UTG(4) = Four-times-per-year UTG

River Blindness	
Quarterly UTG(4)	21,520
Semiannual UTG(2)	47,646,642
Annual UTG	8,993,809
Total RB Treatments	**56,661,971**

Lymphatic Filariasis	
Annual LF UTG	21,560,743
Total LF Treatments	**21,560,743**

Schistosomiasis	
Annual SCH UTG	4,166,868
Total SCH Treatments	**4,166,868**

Soil-Transmitted Helminthiasis	
Annual STH UTG	7,387,888
Semiannual STH UTG(2)	3,934,098
Total STH Treatments	**11,321,986**

Training Objectives	
CDDs	303,795
Community Supervisors	86,174
Teachers	16,283
Health Workers	8,523

ONCHOCERCIASIS ELIMINATION PROGRAM FOR THE AMERICAS (OEPA)

Summary: The Onchocerciasis Elimination Program for the Americas (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. The highlight in 2017 was the successful completion of post-treatment surveillance (PTS) in the Northeast Focus of Venezuela; the focus is now considered to have eliminated transmission of onchocerciasis, and its population of 95,567 was moved from the category of 'at risk' to 'not at risk.' Ninety-four percent of Mectizan® treatments in the Region of the Americas have been halted, and the cross-border focus between Venezuela and Brazil called the Yanomami Focus Area (YFA) is now on the only remaining active transmission zone (O1).

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 ES3). 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), calling for the elimination or drastic reduction 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 (Figures ES19 and ES20).

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, MSD also known as Merck & Co., Inc., Kenilworth, N.J. USA (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.

Elimination of transmission in the Northeast Focus of Venezuela in 2017: *Note that the following report on the Northeast focus borrows heavily from the OEPA report to WHO "Progress towards eliminating onchocerciasis in the WHO Region of the Americas: elimination of transmission in the north-east focus of the Bolivarian Republic of Venezuela." Wkly Epidemiol Rec. 2017; 92:617-23.*

There are two foci of onchocerciasis in northern Venezuela (O2) and one focus in the south that is actually a sub-focus of the Yanomami Focus Area.

Transmission of onchocerciasis in the Northcentral Focus was interrupted in 2010 when MDA was halted after 20 rounds of treatment. After completing PTS, transmission was declared eliminated in 2013 and its population of 14,385 in 45 communities was declared to be no longer at risk for onchocerciasis.

The Northeast Focus is the largest focus in Venezuela with a population of 95,567 distributed in 465 communities, 233 of which were hypo-endemic (designated by having a baseline mf prevalence 1-20%), 197 meso-endemic (21-59%) and 35 hyper-endemic (>60%). Semiannual MDA was launched in 2001 (O3), but in an effort to hasten interruption of transmission, quarterly MDA was provided in 2010 in all hyper-endemic and 5 meso-endemic communities. From 2011-2012, another 100 meso-endemic communities were added to the quarterly treatment approach. Epidemiological, entomological and ophthalmological assessments (O4) conducted in 2012 indicated that transmission had been interrupted, and MDA was stopped and PTS launched in 2013. From 2015-2017, a PTS entomological assessment of the main vector (*Simulium metallicum* s.l.) was conducted. Results of this assessment showed that the transmission of the parasite had reached the elimination phase according to WHO 2016 guidelines. However, while the overall focus's Infectivity Rate [0.38/2000, (95% CI 0.22-0.73/2000)] and Seasonal Transmission Potential [1.87 (95% CI 1.08 – 3.6)] were below the WHO threshold transmission indicators (Infectivity <1/2000 and Seasonal Transmission Potential <20), the OEPA PCC was concerned that three of the eight sentinel communities assessed had Infectivity Rates whose 95% confidence intervals were above the threshold (all Seasonal Transmission Potentials were below threshold, however). As a result, the PCC strongly recommended an entomological assessment be conducted beginning in September 2019 as part of Post Elimination Surveillance activities.

The elimination of the Northeast focus of Venezuela in 2017 represents an important advance toward the regional goal of eliminating onchocerciasis transmission. The population of this focus represents 76% of the overall Venezuelan endemic population and nearly 17% of the entire endemic population in the Americas. In fact, the Northeast focus of Venezuela was the third largest in the Region of the Americas, after Guatemala's Central Endemic Zone and Mexico's South Chiapas focus. Elimination in the Northeast focus reduces the regional number of persons still at risk for contracting onchocerciasis from 125,102 to 32,371.

The 'Yanomami Focus Area (YFA): The YFA is a Special Intervention Zone (SIZ), the remaining active onchocerciasis transmission zone in the Americas, and the only area that will be under treatment in 2018. It is shared by Brazil and Venezuela (Figure O1, O5, and O6).

The YFA is comprised of the South focus of Venezuela and the Amazonas focus of Brazil. The YFA is named after the approximately 32,000 nomadic indigenous Yanomami people who live in onchocerciasis endemic communities scattered throughout approximately 168,000 square kilometers of savannah and Amazon rainforest along the border between those two countries. (Figure O5) The 602 very small (usually under 75 persons) villages (called "shabonos" or "malocas") are targeted for twice- or four-times-per-year MDA. 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 (twice or four times per year), availability of areal transport, weather conditions, and government support with permits and helicopter flights. Given the Yanomami mobility, communities often are (permanently or temporarily) empty when the program staff visits.

For the YFA as a whole, a total of 67,292 Mectizan® treatments were delivered in 2017 (17,409 in the twice-per-year scheme and 49,883 in the four-times-per-year scheme). Details of 2017 treatments are provided in Figure O7. The twice-per-year MDA scheme reached a coverage of 90% (8,688 treatments) during the first six months and 91% (8,721 treatments) during the second. Coverage in the four-times-per-year approach steadily increased during the year but never reached the $\geq$85% goal: 73% (11,669 treatments) during the first quarter, 76% (12,173 treatments) during the second, 82% (13,042 treatments) during the third, and 81% (12,999 treatments) during the fourth. For this reason, in 2018 Brazil has elected to only use the twice-per-year scheme in an attempt to reach $\geq$85% coverage in all villages.

Figure O8 shows treatment plans for 2018 in the YFA. A total of 65,090 treatments are planned, 38,918 in Venezuela and 26,172 in Brazil. For the twice-per-year approach the UTG(2) is 43,570 treatments, which include the populations of all communities of the Brazilian Amazonas Focus and all hypo-endemic communities of the Venezuelan South Focus. The four-times-per-year scheme will aim to provide a total of 21,520—the UTG(4)—for meso and hyper-endemic communities in Venezuela.

The Venezuela South focus team has continued in its efforts to rehabilitate old landing strips that have fallen into disrepair due to jungle overgrowth (O9). In some cases, the team parachuted in (tethered to Venezuelan army paratroopers) with the tools required to clear off the strip! Accessing landing strips increases the program's reach and improves treatment coverage. A total of eight landing strips have been recovered (three in 2017) and at least two more are slated for recovery in the coming year.

As noted above, the YFA is being tackled by national teams working largely independently from each other, each staying on their own side of the border. The OEPA

program has pressed the idea that the YFA is a single epidemiological transmission unit where onchocerciasis must be eliminated on both sides in a coordinated manner. The WHO 2015 onchocerciasis elimination guidelines state that WHO will not grant a country verification if transmission continues in areas immediately bordering the country. Therefore, OEPA assumes that future verification of the YFA will certainly be a joint IVT verification exercise moving back and forth across the Venezuela-Brazil border. To prepare for this eventuality, OEPA is supporting meetings between the two technical teams to improve mapping of the entire cross-border YFA focus so that it can be pictured as a single unit for the IVT.

The 27th Annual InterAmerican Conference on Onchocerciasis (IACO'17) in Guatemala: The 27th InterAmerican Conference on Onchocerciasis (IACO) was held October 31 – November 1, 2017, in Antigua Guatemala. OEPA partners gathered to review progress and challenges of the elimination initiative. A major part of the 2017 agenda was dedicated to Venezuela's announcement that its Northeast focus had successfully completed PTS. However, the theme of IACO related to the Yanomami Focus Area: "Improving health access in the Yanomami area with ingenuity and indigenous empowerment." The meeting sought to better understand the culture of the people who remain to be reached with Mectizan® treatments two or four times per year. Two anthropologists (Dr. Johanna Gonçalves and Dr. Alejandro Reig) gave in-depth reports on the Yanomami cultural mindset regarding health and disease, and Yanomami migratory movements across the border between Brazil and Venezuela. Brazilian and Venezuelan technical staff attending the meeting pledged to work together to increase involvement of Yanomami health agents in the provision of Mectizan® treatment in their communities and shared examples where this has led to improved treatment coverage in Brazil and Venezuela.

2018 RECOMMENDATIONS FOR THE ONCHOCERCIASIS ELIMINATION PROGRAM FOR THE AMERICAS (OEPA)

By the end of 2018, identify, and make progress in the epidemiological assessment and treatment of all new Yanomami communities in the South Venezuela Focus of the Yanomami Area. This 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.

Focus implementation of treatment in villages prioritized by the scoring system Venezuela is using. High priority for four-times-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, and 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 twice-per-year approach. OEPA should continue to encourage Brazil to use this scoring system in 2019 to stratify their endemic communities and identify those where four-times-per-year treatment might be given.

Programs should monitor coverage success by reporting coverage in each round as well as by UTG(2) and UTG(4).

Promote the highest level of political support from Venezuela and Brazil for the elimination of onchocerciasis from the Yanomami Area.

Fulfill the Program's plan to recover and maintain 14 airstrips and build landing strips in Venezuela, as accessing remote, hard to reach communities and having fully operational airstrips ready would greatly facilitate achieving the program's treatment and assessment goals, and construct two new strips, including one 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 work with anthropologists to help the program understand Yanomami

movements, cultural outlooks pertinent to the treatment program, and further improve the training approach for IHAs.

Support and develop the geographical information system (QGIS) agreed to by the two technical teams in 2017 to be the common platform for mapping and tracking community treatment performance and epidemiological indicators and keeping coordinates as current as possible.

Seek antimalarial commodities [especially malaria rapid diagnostic tests (RDTs) and artemisinin combination therapy (ACTs)] for the medical teams visiting the Yanomami area to allow them to treat the many people afflicted by the malaria epidemic.

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

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

Encourage Colombia and Ecuador to publish the results supporting the declaration of elimination of transmission of onchocerciasis, in peer-reviewed journals, by the end of 2018.

2018 Treatment Objectives:

River Blindness	
UTG(2)	43,570
UTG(4) [Venezuela only]	21,520
Total Treatments	65,090

Figure O1

Brazil and Venezuela: the Yanomami Focus Area (YFA)

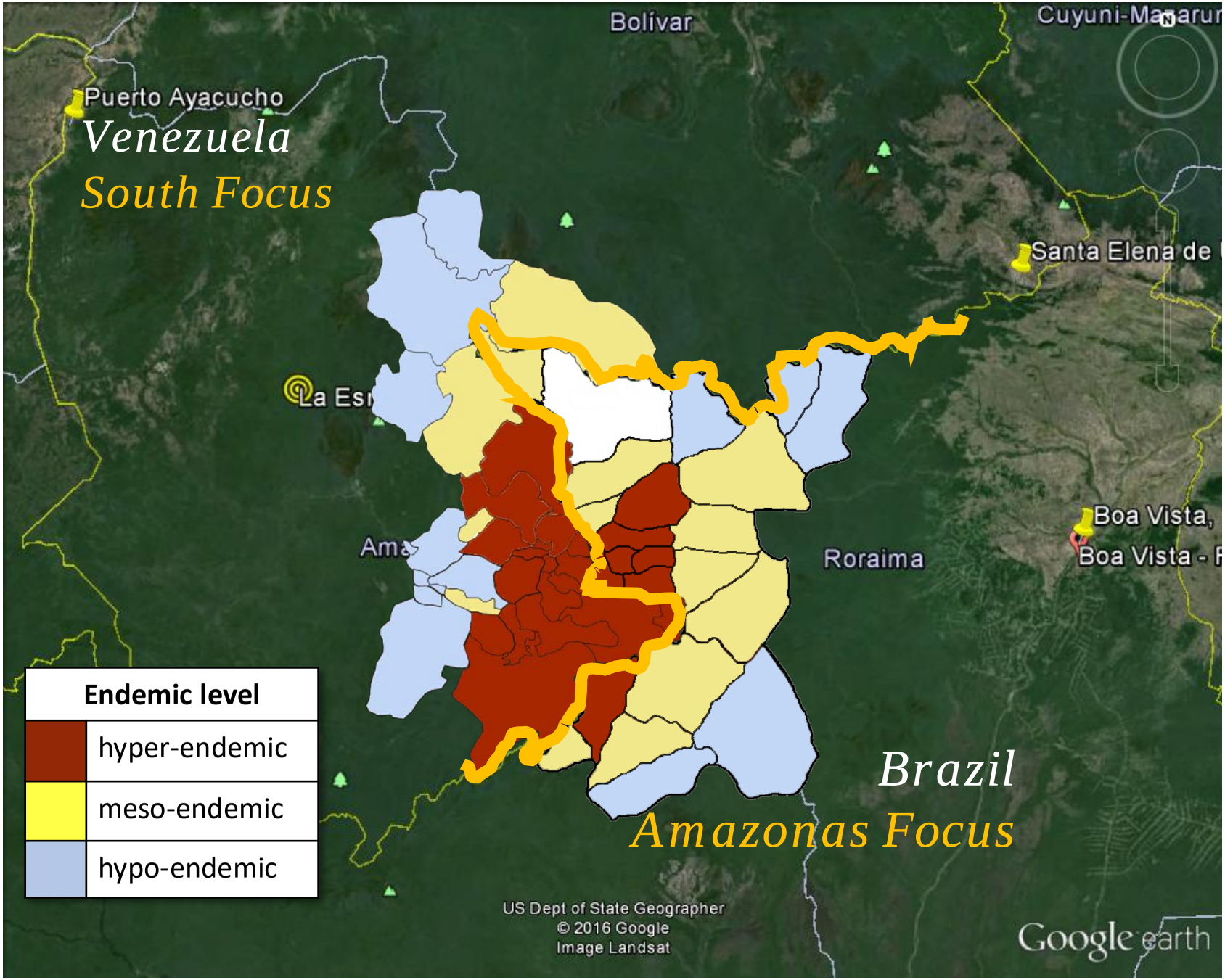


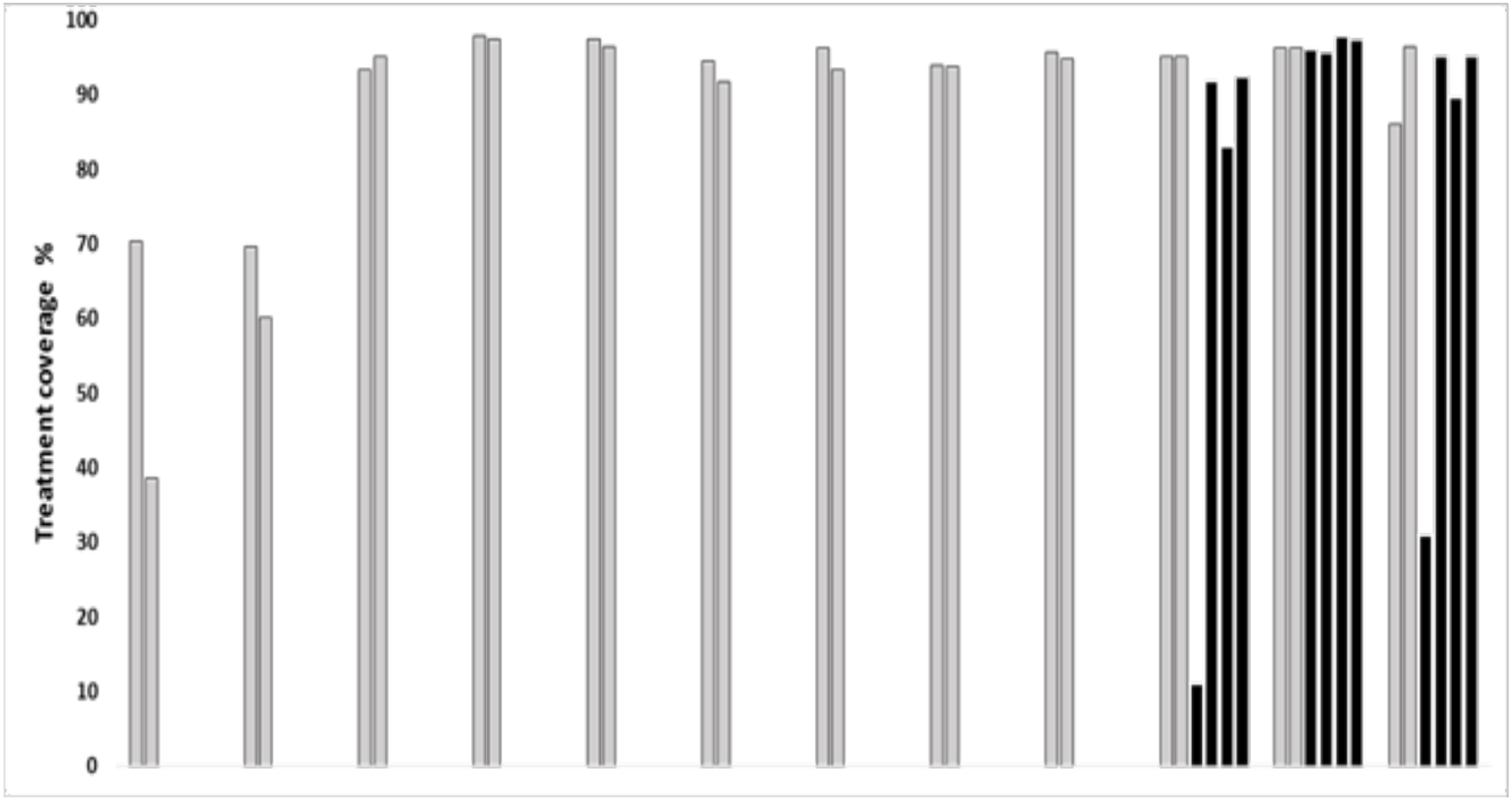
Figure O2

Onchocerciasis distribution in the Bolivarian Republic of Venezuela

1. Northeast Focus 2. Northcentral Focus 3. South Focus (Part of the YFA)

Figure O3

Ivermectin Treatment History in the Venezuelan Northeast Focus 2001-2012



Treatment approach	Treatment Round	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
		Population treated											
2x/year	1st Round	48,597	50,008	74,884	79,288	79,106	78,079	79,437	78,647	80,600	81,726	83,278	77,840
	2nd Round	26,634	43,138	76,369	78,934	78,257	75,797	77,015	78,471	79,848	81,635	83,642	83,644
4x/year	1st Round										489	19,383	5,830
	2nd Round										4,126	19,292	19,755
	3rd Round										3,732	19,722	18,566
	4th Round										4,154	19,656	19,753

Figure O4

Northeast Focus of Venezuela: Fact Sheet

POPULATION AT RISK	95,567 IN 465 COMMUNITIES
Main vector:	Simulium metallicum s. l.
Onchocerciasis Transmission status:	Eliminated in 2017
MDA years:	2001 - 2012
2 times-per-year treatment rounds since 2001:	24 (20 rounds >85%)
4 times-per-year treatment rounds (in selected areas) since 2010:	12 (9 rounds >85%)
Treatment approaches:	2 and 4 times-per-year
Hyper-endemic communities	35 (all treated 4x/year since 2010)
Meso-endemic communities	197 (5 treated 4x/year since 2010)
Hypo-endemic communities	233
Sentinel communities	5 (hyper-endemic)
Extra-sentinel communities	8 (3 hyper-endemic and 5 meso-endemic)
2012 Parasitology	Microfilariae in skin: 0.3%
	Nodules: 0%
2012 Ophthalmology	Microfilariae in the Anterior Chamber (MfAC): 0.2%
	Microfilariae in Cornea (MfC): 0.8%
2012 Serology in children (Ov16 IgG4 Antibodies by ELISA)	0% (Upper 95% CI* <0.1%)
2012 Entomology	Infectivity Rate: 0/2000 (95% CI* 0-0.4)
	Seasonal Transmission Potential: 0 (95% CI* 0-2.2)
Post-Treatment surveillance (PTS)	2013-2017
2015-2017 Post PTS Entomology	Infectivity Rate: 0.38/2000 (95% CI* 0.22-0.73/2000)
	Seasonal Transmission Potential: 1.87 (95% CI* 1.08-3.6)

*** CI = Confidence Interval**

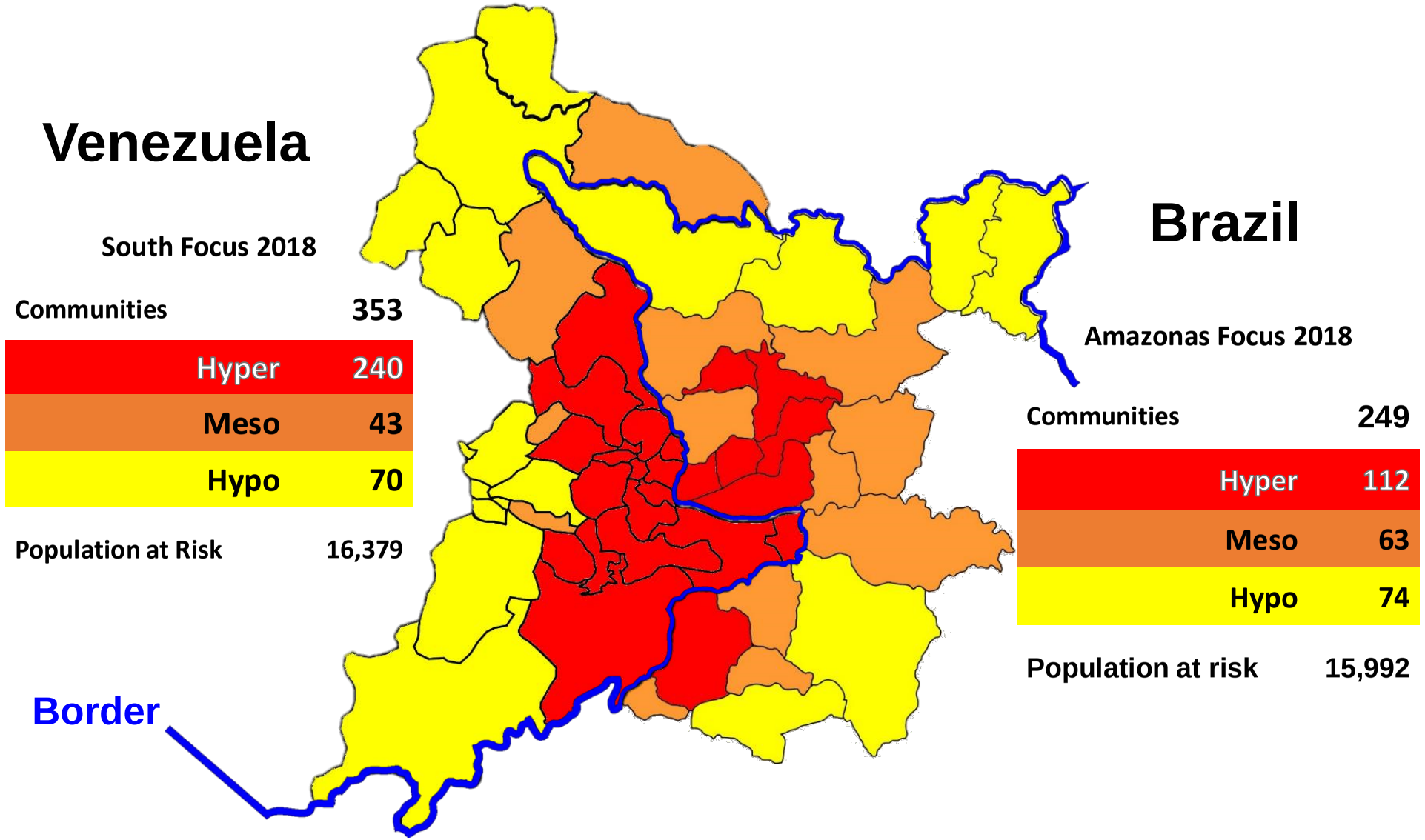
Figure O5

The Yanomami focus area: 2018 Statistics by Country

	Brazil	Venezuela	Total
Territory km^2	94,191	74,095	168,286
Population at risk	15,992	16,379	32,371
Communities	249	353	602

Figure O6

The Yanomami Focus Area: Community Endemicity Statistics



Updated: 02/28/2018

Figure O7

OEPA Treatment Report 2017

Twice-Per-Year

Focus	Communities			Pop @ Risk 2x/year	Eligible for Tx	Treated Rd 1	Cov Rd 1 %	Treated Rd 2	Cov Rd 2 %	UTG2	Treated UTG2	Cov UTG2 %
	Total	Meso	Hypo									
Amazonas-BRA	116	43	73	7,115	5,872	5,328	91%	5,092	87%	11,744	10,420	89%
South-VEN	66		66	4,248	3,744	3,360	90%	3,629	97%	7,488	6,989	93%
TOTAL	182	43	139	11,363	9,616	8,688	90%	8,721	91%	19,232	17,409	91%

Four Times-Per-Year

Focus	Communities			Pop. @ Risk 4x/year	Eligible for Tx	Tx Rd 1	Cov Rd 1 %	Tx Rd 2	Cov Rd 2 %	Tx Rd 3	Cov Rd 3 %	Tx Rd 4	Cov Rd 4 %	UTG4	Tx UTG4	Cov UTG4 %
Amazonas-BRA	123	103	20	8,360	6,716	4,569	68%	5,113	76%	5,475	82%	6,180	92%	26,864	21,337	79%
South-VEN	236	193	43	10,838	9,273	7,100	77%	7,060	76%	7,567	82%	6,819	74%	37,092	28,546	77%
TOTAL	359	296	63	19,198	15,989	11,669	73%	12,173	76%	13,042	82%	12,999	81%	63,956	49,883	78%

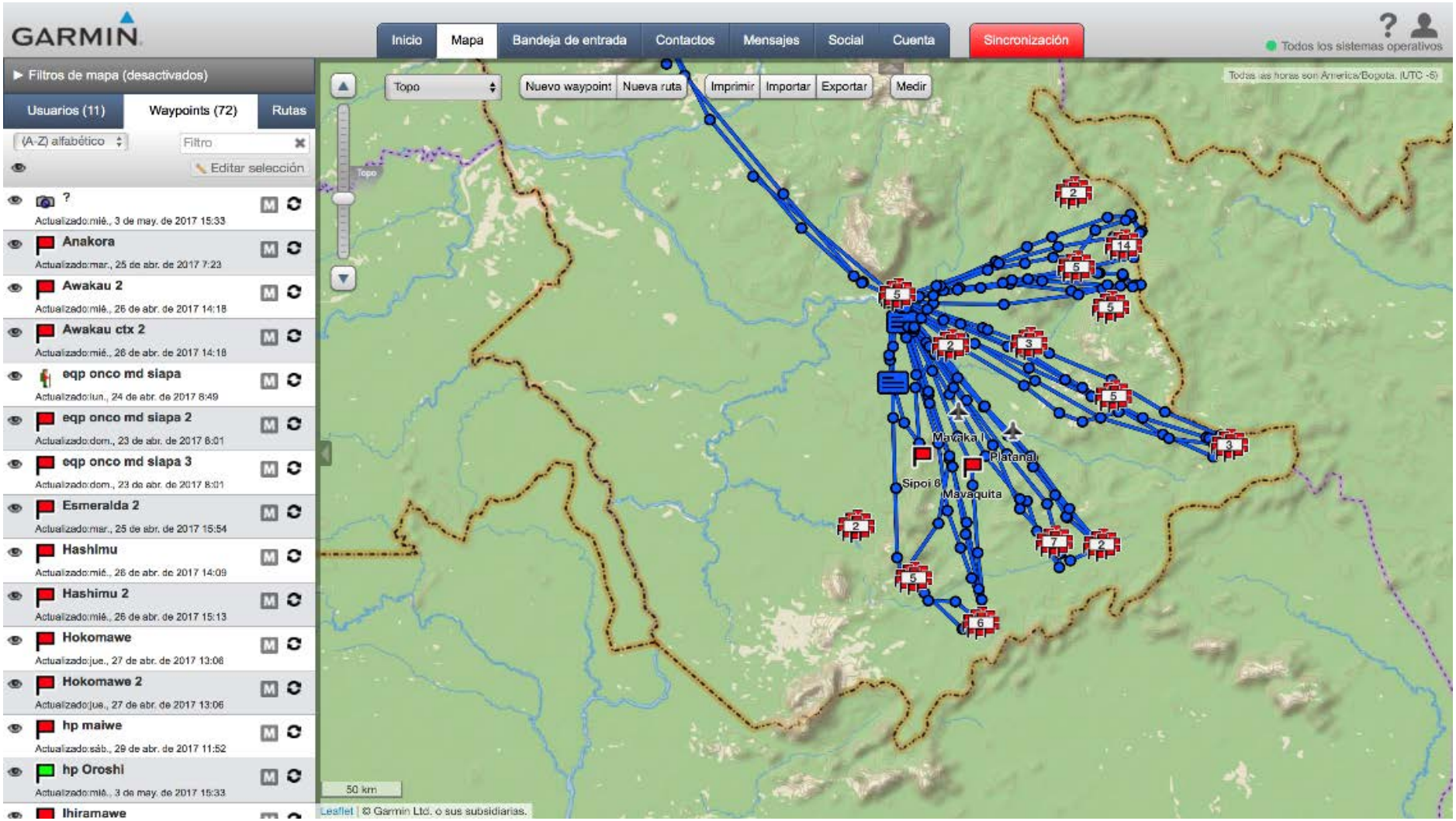
Figure O8

Plans for 2018 Treatments in the Yanomami Focus Area (YFA)

Country	Treatment approach	Rounds >85% In 2017	Number of Communities	Population at Risk	Eligible Population for Treatment	Treatments	Transmission Status
Venezuela	2x/year	18	187	9,948	8,699	17,398	Ongoing
	4x/year	9	166	6,431	5,380	21,520	
	Total VZ	**27**	**353**	***16,379***	***14,079***	***38,918***	
Brazil	2x/year	42	262	16,088	13,086	26,172	Ongoing
	Total BZ	**42**	**262**	***16,088***	***13,086***	***26,172***	
YFA Total			**615**	**32,467**	**27,165**	**65,090**	

Figure O9

Aerial Routes into the Yanomami Focus Areas (for the Venezuelan Team)



Note: Routes traced by InReach device

UGANDA

Summary: Since Uganda declared elimination of onchocerciasis transmission as a goal in 2007, the country has classified 11 foci as either 'transmission interrupted', or 'transmission eliminated' (Figures U1 and ES17). In 2017, two new foci (Kashoya-Kitomi and Wambabya-Rwamarongo) were classified as having eliminated onchocerciasis after completing post treatment surveillance. A twelfth focus (the Victoria Nile focus) was eliminated in the early 1970's. Excluding Victoria Nile, this translates into about 1.9 million treatments for onchocerciasis no longer being required in Uganda. Transmission interruption is suspected in three foci where treatment is still ongoing. Transmission is still active in two foci: the small Lhubiliha focus on the border with DRC, and large Madi/Mid-North focus on the border with RSS. Both of these foci have potential cross border transmission and so are considered Special Intervention Zones (SIZs). Both of these areas reached their targeted treatment coverage for 2017, which is a remarkable improvement over the past years.

Figure U1 shows the current status of onchocerciasis endemicity in Uganda. Figure U2 shows that 1,215,826 people are no longer at risk for oncho (e.g., they are living in areas that have completed PTS) and another 715,099 reside in areas where MDA has stopped but PTS is not completed.

Background: Onchocerciasis was initially endemic in 17 transmission zones (foci), in 36 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 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 ivermectin program received financial support from The River Blindness Foundation (RBF), GTZ/Bernhard Nocht Institute for Tropical Medicine, Hamburg, AVSI, 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 approach to Mectizan® distribution. 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 MSD, also known as Merck & Co., Inc., Kenilworth, N.J. USA (Merck) (and administered through the NGDO Coalition for Onchocerciasis Control). Wadelai showed that twice per year treatment could be provided by the CDTI approach**.**

The Uganda Ministry of Health (MOH) announced a nationwide elimination policy in 2007 based on a 'flexible' strategy of twice-per-year treatment (where necessary) and (where 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 activities and community-directed treatment with ivermectin (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) technically assists in all foci (and in all 38 of the 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 reagents for the MOH laboratory that offers state-of-the-art 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 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 2017, the lab analyzed 14,453 blood spots for OV16 antibodies and 1,483 *Simulium* flies by PCR.

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 tenth meeting the UOEEAC recommended reclassification of two foci (Kashoya-Kitomi and Wambabya-Rwamarongo) as having completed PTS and eliminated onchocerciasis; 311,436 Ugandans living in these two foci are no longer at risk of onchocerciasis. Two other foci (Wadelai and West Nile) were classified as transmission interrupted (Figure U2). Treatment for LF continued in these foci, however and PTS cannot begin until LF treatments are stopped. Three foci (Budongo, Bwindi and Nyagak-Bondo) remain under treatment for onchocerciasis but UOEEAC suspects interruption of transmission has occurred there. In Bwindi and Nyagak-Bondo, the uncertainty regarding interruption of transmission is due to potential cross border transmission with DRC. Interventions cannot be halted unless the RB transmission status across the border in DRC is known. UOEEAC recommended that the Ministry of Health work alongside DRC MOH personnel to conduct joint cross-border SIZ assessments. DRC cross-border assessments were conducted in 2017 and the UOEEAC will receive a report of those findings in 2018. If this model

[1]38 oncho endemic districts: Bushenyi, 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).

is successful, it will offer a way forward in other foci with possible ongoing cross-border transmission such as Lhubiliha and (with RSS) Madi/Mid-North.

Treatments: The Carter Center-assisted treatments achieved 95% of their 2017 treatment target of 4,070,215. All the treatments were delivered on a semiannual basis. In 2017, the Uganda RBEP assisted in 3,950,170 MDA treatments including 130,365 passive and visitor treatments, totaling 4,080,535 treatments (Figure U3). The Carter Center assisted 3,676,747 treatments in Bwindi, Lhubiliha, Madi/Mid-North and Nyagak-Bondo foci, while Sightsavers assisted 273,423 in the Budongo focus (Figures U3 and U4). The Uganda RBEP reached 100% of the 3,846 villages targeted for treatment. The kinship/neighborhood-based CDTI approach in northern Uganda (called the "Rwot Kweri" system) allowed most districts in Madi/Mid-North to reach or exceed the desired treatment coverage of 90%. Two districts (Omoro and Lamwo) attained 88% UTG coverage (Figure U5).

Training and Health Education: Uganda trained or retrained 26,784 Community-Directed Distributors (CDDs) and 8,730 Community-Directed Health Supervisors (CDHSs) in 2017.

Of those trained in 2017, 44% of the CDDs and 34% of the CDHSs were female. The current ratio of CDDs to population served is 1 CDD to 92 persons served, and the supervisor-to-CDD ratio was 1:3.

Integration: The RBEP-assisted CDTI program actively co-implements with the national lymphatic filariasis elimination effort 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.

2018 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, UGANDA

Improve treatment coverage in Omoro and Lamwo districts in the Madi/Mid-North focus and report specifically on those districts at next year's Program Review.

Intensify training of new Community Directed Distributors (CDDs) in Lubirihia and the Madi/Mid-North Foci. Efforts should be made to reach a ratio of 1 CDD: 80 persons and 1 CS:5 CDDs indices in Lamwo district.

Provide financial and administrative support for the 2018 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 of such activities at the 2018 UOEEAC and Program Review.

In the Ituri cross-border focus, compare Uganda lab ELISA based OV16 results with OV16 RDT results from a Task Force survey conducted in the same area to confirm reported discordant results by these two tests in the same area. Report results at the 2018 UOEEAC and Program Review.

MOH Uganda should help DRC to launch twice-per-year MDA in area opposite Nyagak-Bondo focus.

Continue to publish on the Uganda country experience with onchocerciasis elimination in peer reviewed journals.

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 HQ, conduct a new study to determine what the former RB CDDs in these foci are doing now that onchocerciasis interventions have been halted.

Monitor the results of research in Dr. Tom Unnasch's vegetation clearing study to determine if communities will do this work in a sustainable way. Continue vector control feasibility pilot studies of vector control study Professor Rory Post's dry season larviciding approach against vector *refugia*.

2018 Treatment and Training Objectives:

River Blindness	
Semiannual UTG (2)	4,580,695
Training Objectives	
CDDs	31,386
CSs	10,018
HWs	149
Parish	1,257

Figure U1

Uganda's Progress towards Elimination of Onchocerciasis 2017

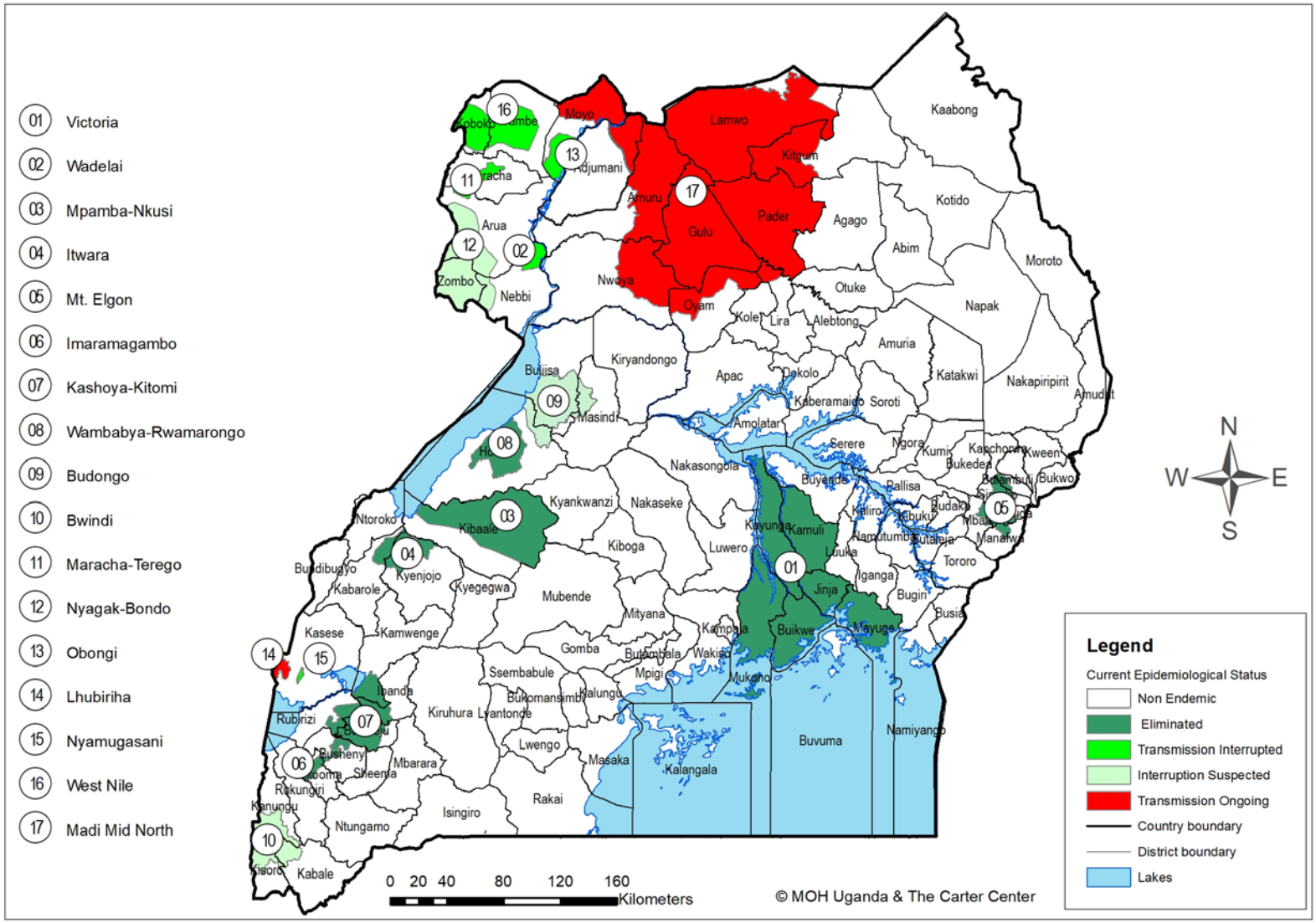


Figure U2

Foci Under Transmission Eliminated or Transmission Interrupted: Treatments Stopped (2011-2017)

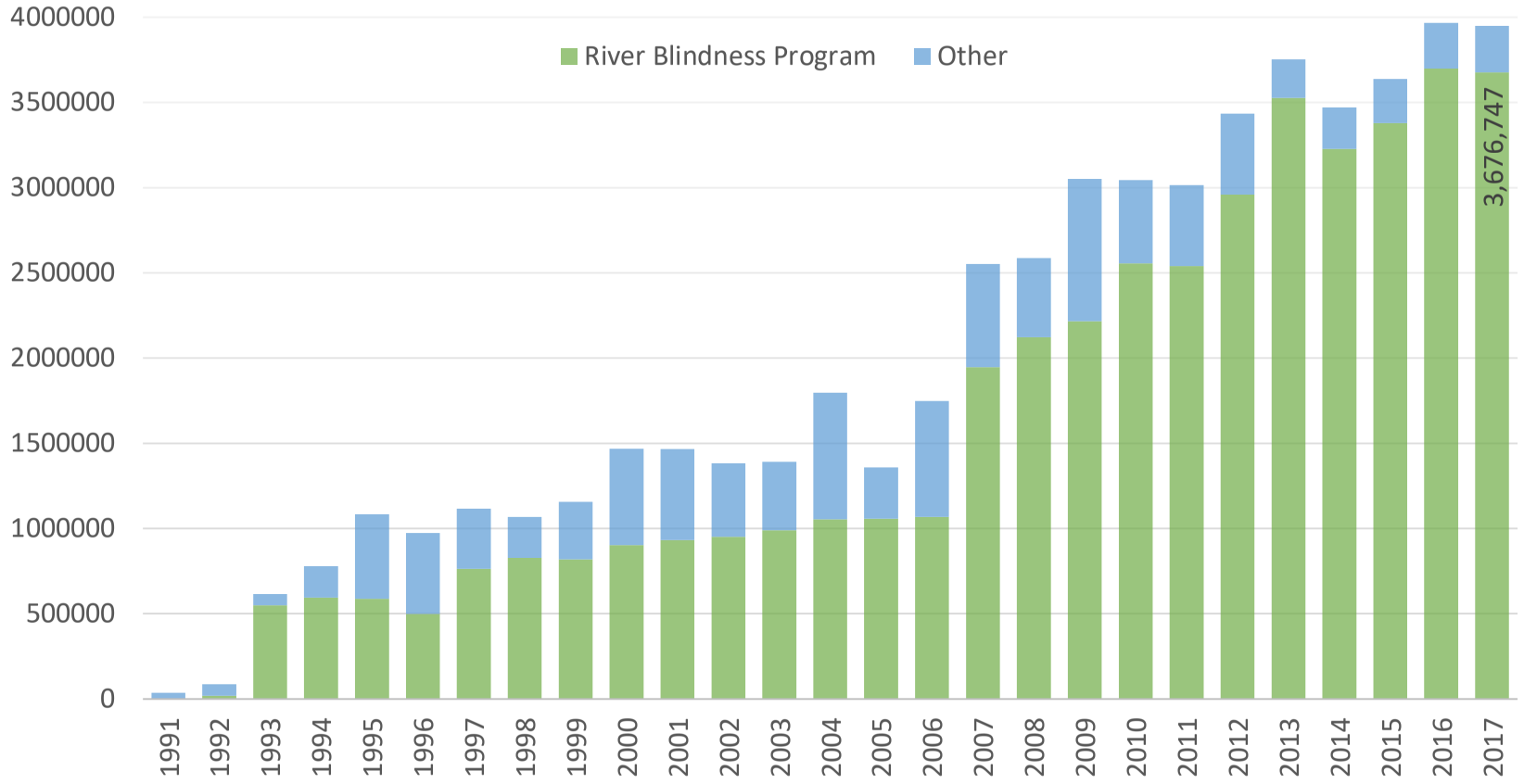
Focus	District	Transmission Interrupted	Total Popn (time of interruption)	UTG1	UTG2	Projected Popn	Treatments Stopped	Communities	PTS Status
Itwara	Kabarole	2011	31,763	26,999		38,482	32,710	49	
	Kyenjojo	2011	66,085	56,172		80,063	68,054	83	
Mt. Elgon	Manafwa	2011	40,604	33,698	67,396	47,529	80,800	98	
	Mbale	2011	50,253	40,781	81,562	58,824	100,001	131	
	Sironko	2011	76,375	64,396	128,792	89,401	151,982	179	
	Bududa	2011	161,630	139,656	279,312	189,197	321,635	412	
Mpamba-Nkusi	Kibale	2012	194,045	160,062	320124	222,763	378,697	330	
Imaramagambo	Bushenyi	2012	112,633	95,738		119,607	101,666	212	
Kashoya-Kitomi	Buhweju	2013	60,255	49,512	99024	65,842	111,932	97	PES
	Rubirizi	2013	77,250	63,676	127,352	84,413	143,502	170	PES
	Ibanda	2013	26,144	21,805	43,610	28,568	48,566	60	PES
	Kamwenge	2013	45,626	37,173	74346	49,857	84,756	58	PES
Wambabya-Rwamarongo	Hoima	2013	75,733	62,654	125,308	82,755	140,684	70	PES
Sub Total			*1,018,396*	*852,322*	*1,346,826*	***1,157,303***	*1,764,985*	*1,949*	
Wadelai	Pakwach	2010	17,979	14,727	29,454	23,022	39,137	34	PTS
Maracha-Terego	Maracha	2012	171,222	145,539		199,389	169,481	307	No PTS
Obongi / Moyo	Moyo	2014	37,539	30,848		41,020	69,734	61	PTS
Nyamugasani	Kasese	2015	11,368	10,237		12,060	20,503	7	PTS
West Nile	Yumbe	2017	313,192	266,213		313,192	266,213	284	PTS
	Koboko	2017	182,568	155,183		182,568	155,183	394	PTS
Sub Total			*733,868*	*622,747*	*29,454*	***771,252***	*720,251*	*1,087*	
Total			**1,752,264**	**1,475,069**	**1,376,280**	**1,928,555**	**2,485,236**	**3,036**	

Eliminated | Transmission interrupted

Note: 1. PTS is not yet done in Maracha Terego focus due to co-endemicity with LF. TAS will be done in 2018.
2. Itwara, Imaramagambo, Maracha-Terego & West Nile remained on Annual Treatments - thus their UTG2 = UTG1

Figure U3

Uganda: Carter Center-Assisted Treatments and Total Mectizan® RB Treatments Provided, 1991-2017



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

Figure U4

Uganda - Transmission Interruption Suspected: Semiannual Treatments 2017

Focus	District	Transmission Suspected	Total Popn	Ultimate TX Goal (UTG 1)	UTG RD1/RD2	No. Treated		Popn Treated (UTG 2)	% UTG Coverage		% UTG RD1/RD2	Active Villages UTG	LF Endemicity
						RD1	RD2		RD1	RD2			
Bwindi	Rubanda	2013	33,282	26,520	53,041	25,778	25,001	50,779	97.2	94.3	95.7	59	No LF
	Kanungu	2013	64,166	51,953	103,906	50,187	50,715	100,902	96.6	97.6	97.1	107	No LF
	Kisoro	2013	41,024	33,086	66,171	30,758	31,724	62,482	93	95.9	94.4	47	No LF
Nyagak-Bondo	Nebbi	2014	142,850	130,457	260,914	122,295	128,255	250,550	93.7	98.3	96	171	No LF
	Zombo	2014	252,098	208,169	416,338	188,222	200,270	388,492	90.4	96.2	93.3	730	No LF
	Arua	2014	186,294	158,312	316,624	150,972	143,420	294,392	95.4	90.6	93	325	LF
Budongo (Supported by TCC & Sightsavers)	Hoima	2014	82,518	68,282	136,564	65,303	62,797	128,100	95.6	92	93.8	70	No LF
	Buliisa	2014	34,376	29,716	59,431	29,325	29,299	58,624	98.7	98.6	98.6	54	No LF
	Masindi	2014	54,001	44,141	88,281	43,799	42,900	86,699	99.2	97.2	98.2	60	No LF
Total			**890,609**	**750,635**	**1,501,271**	**706,639**	**714,381**	**1,421,020**	**94.1**	**95.2**	**94.7**	**1,623**	

Figure U5

Uganda: Transmission Ongoing- Semiannual Treatments 2017

Focus	District	Total Population	Ultimate Tx Goal (UTG 1)	Ultimate Tx Goal (UTG 2)	Popn Treated		Popn Treated RDS 1&2	% UTG Cov		% TX Cov RDS 1&2	Active Villages UTG	LF Endemicity
					Rd1	Rd2		Rd1	Rd2			
Lubilia	Kasese	135,046	111,559	223,117	107,986	110,423	218,409	97%	99%	98%	124	
Madi Mid North	Adjumani	28,589	23,609	47,217	22,260	21,250	43,510	94%	90%	92%	43	LF
	Moyo	90,729	79,204	158,408	77,903	74,779	152,682	98%	94%	96%	165	LF
	Gulu	149,990	128,655	257,310	124,209	124,237	248,446	97%	97%	97%	83	LF
	Omoro	192,557	165,185	330,370	142,142	149,652	291,794	86%	91%	88%	149	LF
	Amuru	242,538	206,158	412,315	191,669	195,820	387,489	93%	95%	94%	67	LF
	Pader	194,828	167,407	334,814	160,649	159,328	319,977	96%	95%	96%	617	LF
	Kitgum	107,765	90,622	181,243	84,680	86,909	171,589	93%	96%	95%	234	LF
	Lamwo	153,001	129,708	259,416	114,194	113,742	227,936	88%	88%	88%	427	LF
	Lira	73,110	61,376	122,752	61,037	61,136	122,173	99%	100%	100%	225	LF
	Oyam	23,841	20,425	40,850	19,955	19,795	39,750	98%	97%	97%	35	LF
	Nwoya	180,617	161,300	322,600	122,723	182,672	305,395	76%	113%	95%	54	LF
Total		**1,572,611**	**1,345,206**	**2,690,412**	**1,229,407**	**1,299,743**	**2,529,150**	**91%**	**97%**	**94%**	**2,223**	

SUDAN

Summary: Sudan had four known river blindness foci: Abu Hamad (River Nile state), Galabat (Gedaref state), Radom (South Darfur state), and Khor Yabus (Blue Nile state) (Figure S1). In 2015, the Abu Hamad focus completed Post Treatment Surveillance (PTS) and was declared eliminated by the Federal Ministry of Health (FMOH). Assessments in Galabat in 2015 indicated that transmission had been interrupted in accord with WHO Stop MDA guidelines. Galabat is recognized to be a part (sub-focus) of the larger cross-border focus with Ethiopia known as the Galabat/Metema focus, so Sudan (in consultation with Ethiopia) agreed to continue (annual) Mectizan® treatments in Galabat until the Metema sub-focus in Ethiopia also satisfied WHO's Stop MDA guidelines. The civil conflict in South Darfur rendered treatments in Radom difficult, although security there is improving. Conflict in Blue Nile has for many years prevented the assessment of the Khor Yabus focus, where the current status of onchocerciasis transmission remains unknown. No treatments in Khor Yabus have ever been provided.

During the program review, there was discussion of a possible fifth focus in Sudan in Blue Nile State (Geissan District) contiguous with recognized transmission on the Ethiopian side of the border.

Background: The Republic of Sudan was the first African country to declare a nationwide onchocerciasis elimination policy, in December 2006. In recent years, the RBEP has supported Sudan in this effort only technically, since all programmatic support is provided by Sudan itself (an example for the rest of Africa to emulate).

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, a national meeting was held, with the support of The Carter Center, to review the entomological and serological data from Abu Hamad transmission zone and at that time 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 to 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 2018.

The recent epidemiological status of the Khor Yabus focus in Blue Nile state is still unknown due to ongoing conflict there. Plans to reach displaced populations from this area (who are now in relatively secure government-controlled camps) for OV16 surveys can hopefully be conducted in 2018.

Radom and Blue Nile are on international borders. Assessments are needed there to determine if there is ongoing transmission and if so if these are areas where Special Intervention Zones (SIZs) need to be established with Ethiopia, South Sudan and the Central African Republic (Figure ES14).

Treatments: The Sudan program provided a total of 174,781 treatments in 2017: in Galabat there were 128,569 treatments in one round (Figure S2) and 46,212 treatments in Radom in one round (Figure S3). Due to the conflict in Radom and an influx of agricultural laborers, it was difficult to determine the ultimate treatment goal (UTG).

Training and Health Education: During 2017, the program trained a total of 1,441 Community-directed distributors (CDDs) (Figure S4). Galabat trained 1,341 (60% male). Radom trained an estimated 100 male CDDs. The ratio of CDDs:population in Radom was about 1:500.

2018 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, SUDAN

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

Galabat Focus in Gedaref State

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

Radom

An OV-16 assessment in 2017 confirmed that Radom needs a full elimination effort with twice-per-year MDA. The Sudan NOTF has recommended such a Radom program given reports of an improved security situation there. However, International SOS continues to report to TCC HQ a high degree of insecurity in Radom. It is suggested that TCC/RBEP work with the Peace Program at The Carter Center to determine if an enhanced MDA program is feasible in Radom. This decision should involve discussions with HQ. In addition to twice-per-year MDA the program should:

- Provide further information on infection rates and treatment plans for the large RSS refugee population.
- If security permits, determine if this is a cross-border focus with Central African Republic and RSS.

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

In collaboration with the Peace Program of The Carter Center, conduct an assessment of the security situation in Blue Nile with the purpose of establishing a temporary opportunity to rapidly assess the onchocerciasis transmission in Khor Yabus, Wad Elmahi and Geissan districts of Blue Nile state. These are adjacent to known RB transmission zones in Ethiopia (Guba in Metekel zone of Ethiopia). Serological (OV-16) surveys are proposed to establish if MDA is required in these areas.

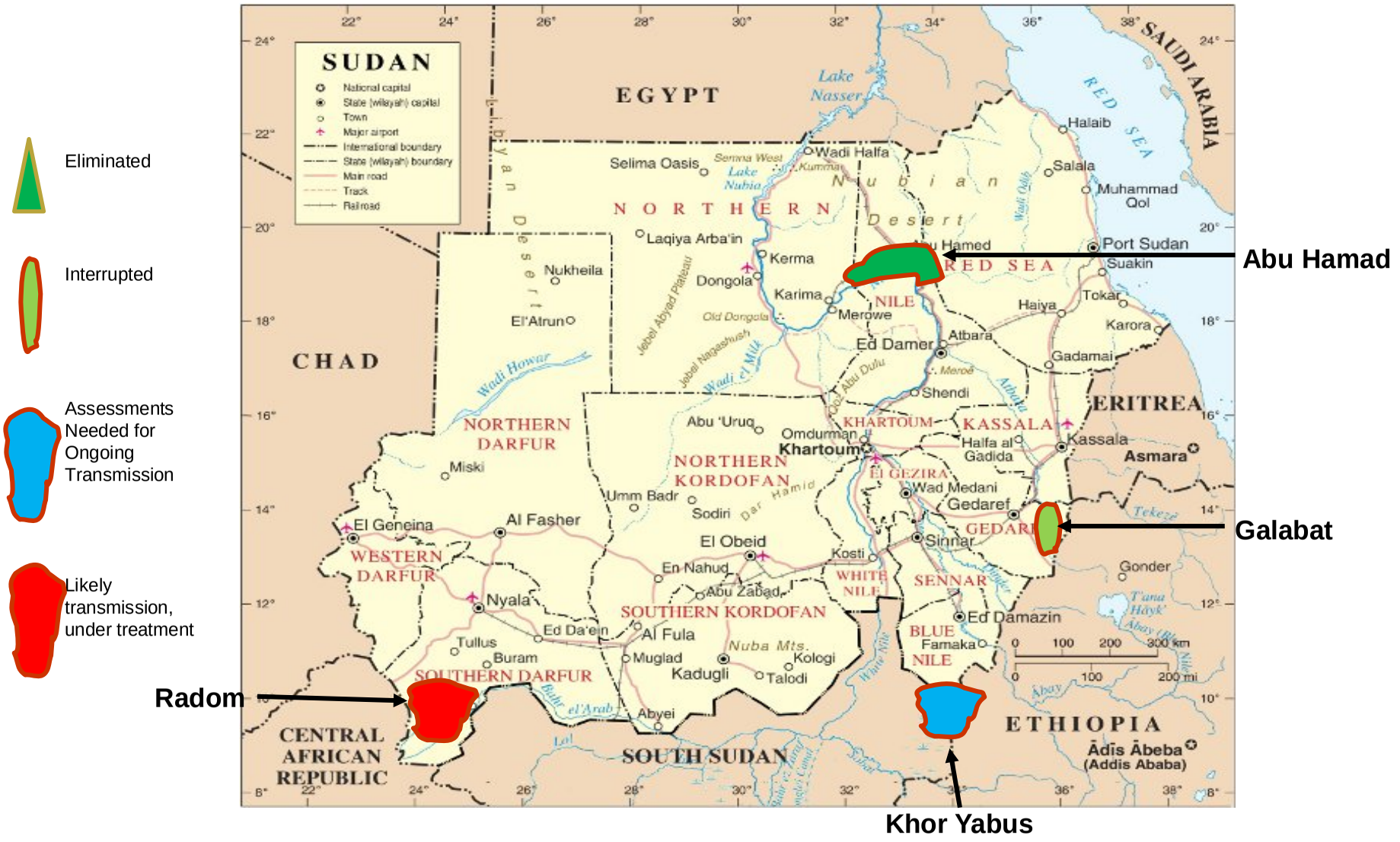
If these areas are shown to be endemic for onchocerciasis, then it is recommended that TCC/RBEP work with the Peace Program at The Carter Center to determine if an enhanced MDA program is feasible in Blue Nile state. In addition to twice-per-year MDA, the program should determine whether a SIZ is needed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

2018 Treatment and Training Objectives:

River Blindness	
Annual UTG	69,200
Semiannual UTG(2)	139,400
Refugees UTG(2)	46,000
Training Objectives	
CDDs	692
CSs	138

Figure S1

Map of Sudan Onchocerciasis Program Areas



Note: Galabat has cross-border transmission with Ethiopia. Status in previously recognized Foci of Radom and Khor Yabus is unknown at this time.

Figure S2

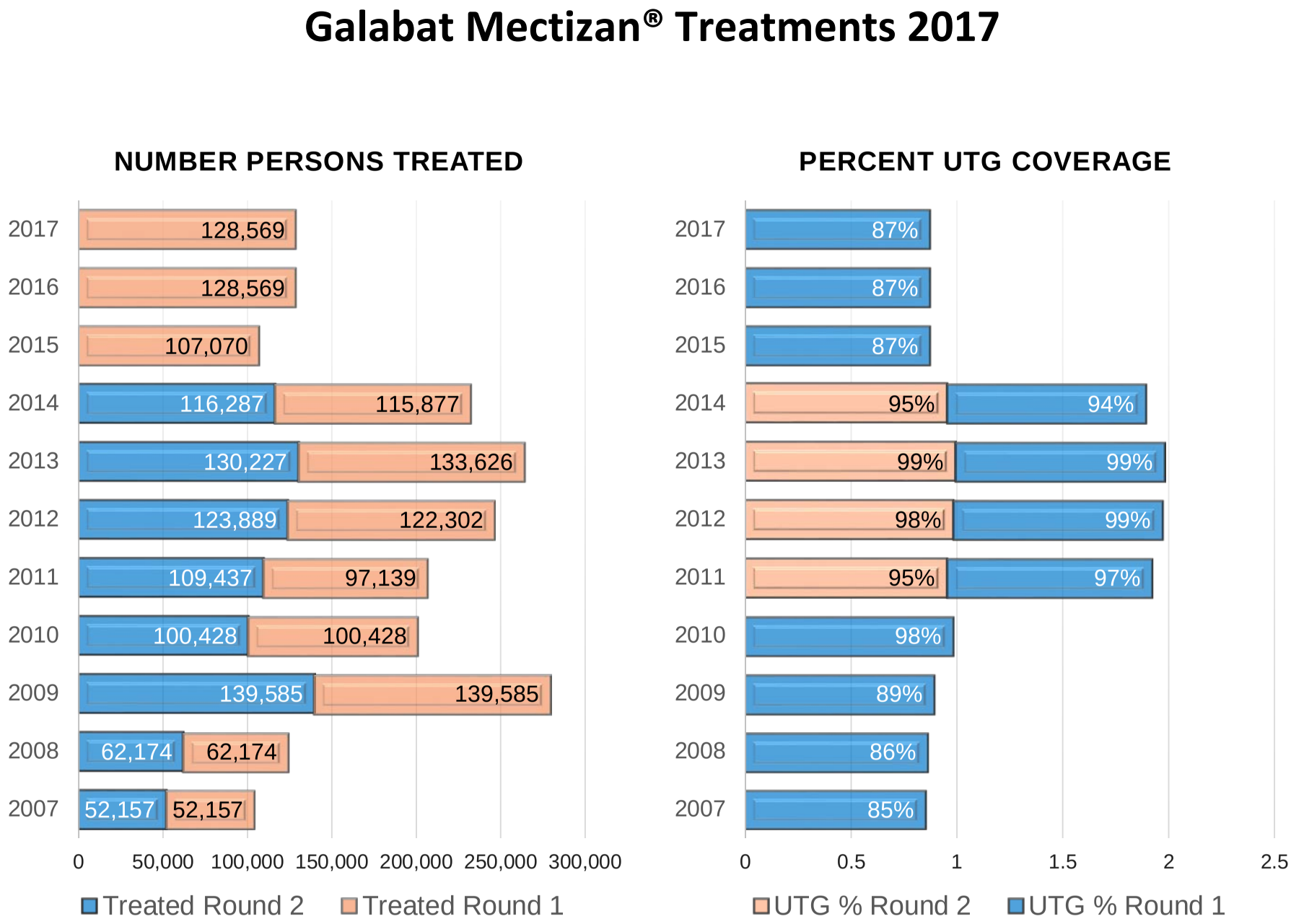
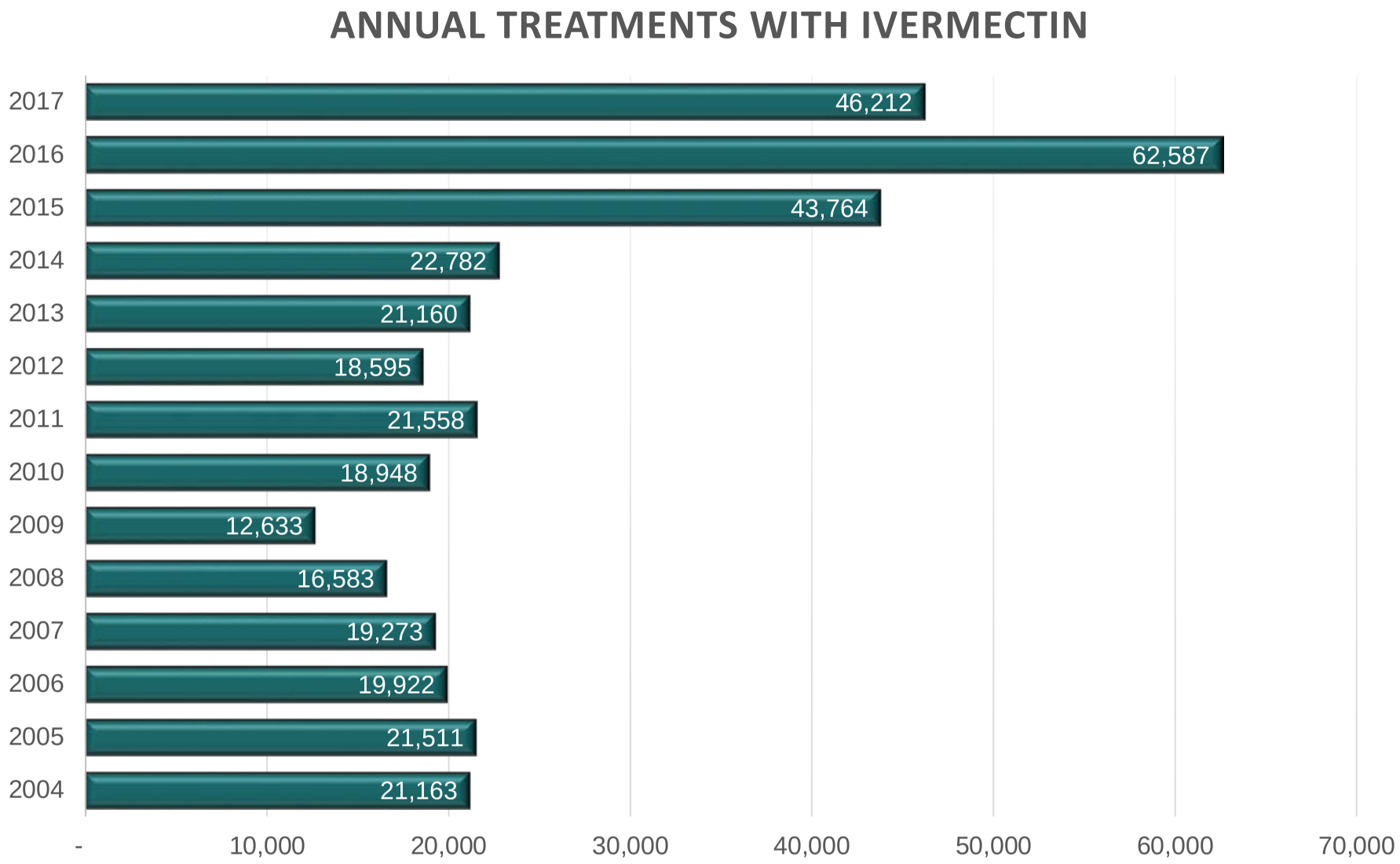
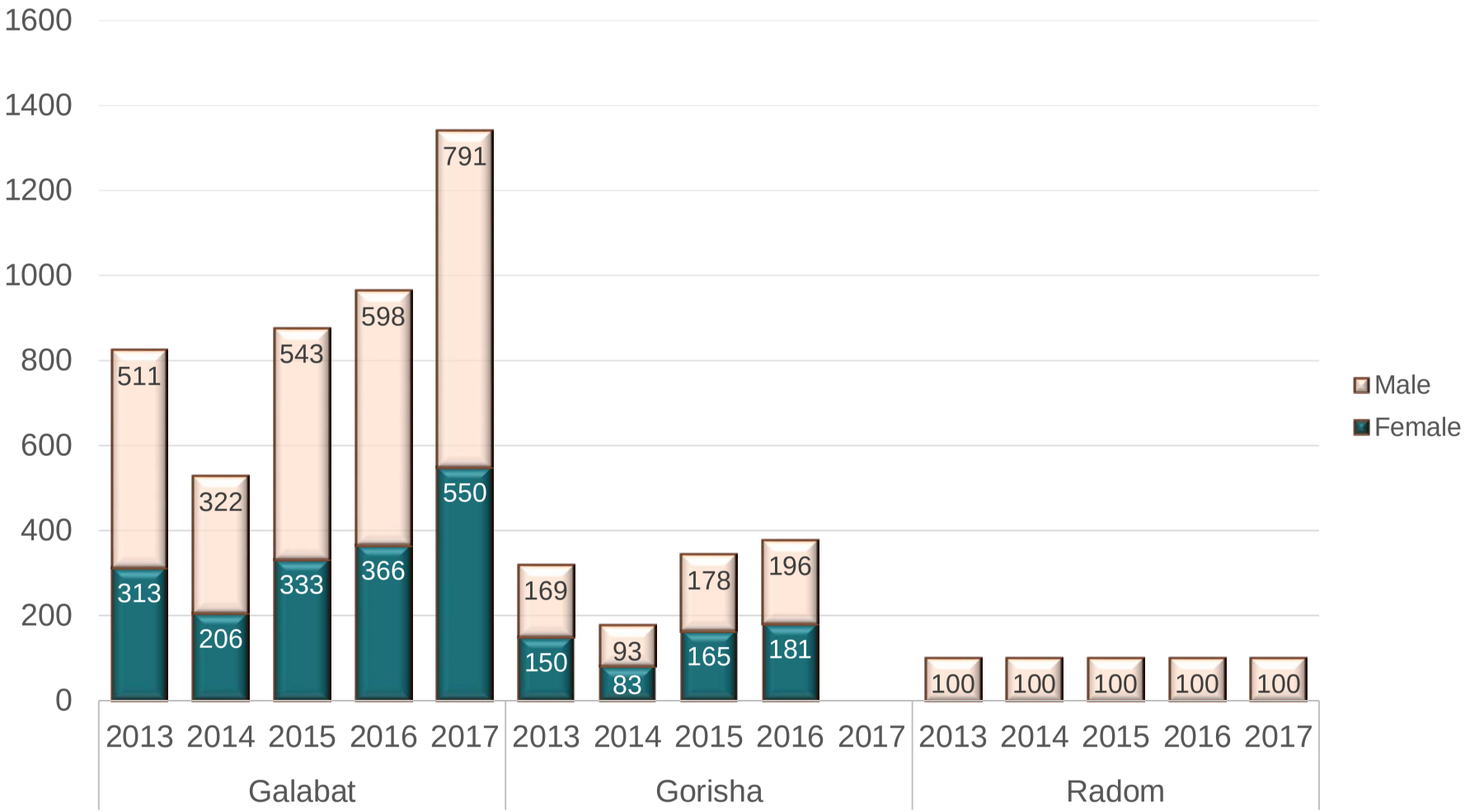

Galabat Mectizan® Treatments 2017
NUMBER PERSONS TREATED
2017
2016
2015
2014
2013
2012
2011
2010
2009
2008
2007
128,569
128,569
107,070
116,287
115,877
130,227
133,626
123,889
122,302
109,437
97,139
100,428
100,428
139,585
139,585
62,174
62,174
52,157
52,157
0
50,000
100,000
150,000
200,000
250,000
300,000
Treated Round 2
Treated Round 1
PERCENT UTG COVERAGE
87%
87%
87%
95%
94%
99%
99%
98%
99%
95%
97%
98%
89%
86%
85%
0
0.5
1
1.5
2
2.5
UTG % Round 2
UTG % Round 1

Figure S3

Radom Mectizan® Treatments 2017



Number of CDDs Trained in Galabat, Gorisha and Radom Foci By Gender, 2013-2017



Note: Training numbers in Radom are estimates

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 2022, in accord with the Federal Ministry of Health's plan for onchocerciasis elimination. In 2017, 32,976,792 Mectizan® mass treatments (with health education) for onchocerciasis were distributed (Figures N2 – N3) with assistance from The Carter Center (TCC) in those states. While this was approximately 69% of all RB treatments in Nigeria (Figure N4) according to available figures, national reports for 2017 were still incomplete at the time of the Review. Twice-per-year treatments for onchocerciasis were massively scaled up from about 1.5 million in part of Edo state in 2016 (in a special intervention zone bordering Ondo state) to 22 million in five of the seven Southeast zone and South South zone ('southern') states[1] we assist in 2017.

The Carter Center and its ministry of health partners stopped MDA for lymphatic filariasis (LF) in Plateau and Nasarawa in 2013. After the two states stopped nearly four million albendazole-Mectizan® treatments (Figure N5) TCC helped the states maintain good coverage with long lasting insecticidal bed nets (LLIN). In 2017, a transmission assessment survey confirmed that LF had been eliminated as a public health problem in Plateau and Nasawara states; a historic milestone for Nigeria. The seven southern RBEP-assisted states launched their own LF programs in 2014, and quickly scaled up treatments (Figures N5 - N6). The Nigeria program also pioneered twice-per-year MDA (using albendazole alone) for LF in the country, starting with Imo state in 2015 and expanding to six of the seven states in 2016 (Figure N6). TCC's LF program saw 17,426,794 LF treatments in 2017.

In 2017, TCC assisted in providing 2,211,319 praziquantel treatments with health education for schistosomiasis (Figure N7). The oscillation of treatments observed between years in our assisted states is due to the WHO-recommended alternating year treatment strategy in many Local Government Areas (LGAs) (Figure N8).

The Carter Center also supported 8,150,501 treatments for soil-transmitted helminths (STH) in 2017; this is a decrease from 2016 as some areas treat every other year based on WHO guidelines. (Figures N9 - N11).

The 2017 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. Of course, these programs would not be possible without donated products and coordination from many different partners (including MSD, also known as Merck & Co., Inc., Kenilworth, N.J. USA (Merck & Co., Inc.), Merck KGaA, Darmstadt, Germany (E-Merck), GSK, Johnson & Johnson, The Task Force for Global Health, the World Health Organization, and Clarke Cares Foundation/Clarke Mosquito Control).

[1] Abia, Anambra, Delta, Ebonyi, Edo, Enugu, and Imo are collectively referred to in this document as "SE/SS."

River Blindness in Nigeria

***Background*:** Nigeria is home to about 40% 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, 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 RBEP in Nigeria is headquartered in Jos, Plateau state, with supporting sub-offices in Benin City, Enugu, Lagos, and Owerri. Active in nine states (Figure N1) since 1996, the TCC RBEP enjoyed LCIF support from 1999 to 2008, and core APOC support from 2000 to 2005. It currently receives funding from the Margaret A. Cargill Foundation and USAID's ENVISION project, led by RTI International.

Treatments: In 2017, the TCC-assisted RBEP program in Nigeria provided 32,976,792 Mectizan® treatments along with health education (Figures N2 and N3), achieving 90% of the treatment target. This year, an incredible expansion of semi-annual treatments took place, reaching about 11 million people with two doses of Mectizan; as a result, twice per year treatments now far surpass annual treatments in the RBEP Nigeria program. This expansion is in accordance with NOEC guidelines that call for twice per year treatment in states 'not on track' to reach interruption of transmission by 2022. 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 states in Nigeria in 2017, despite close monitoring for adverse reactions is carried out in the south because of the presence of *Loa loa.* 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 a risk factor for SAEs (Emukah et al 2018).

Training, health education, and financial contributions are discussed in the Integrated Programs sections below, as well as treatments for LF, schistosomiasis, and STH.

The Integrated 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 to 'piggy-back' launching of LF elimination and SCH control activities by sharing costs and infrastructure across several programs (Hopkins 2001, Dean 2003). The integrated RB program began in 1999 with onchocerciasis and 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 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) (Eigege et al. 2013, Evans et al. 2011).

Training and Health Education: There were 68,979 health personnel and volunteers involved in drug distribution in TCC-assisted states for the various programs in 2017: 7,596 community supervisors and 61,383 CDDs. The ratio of CDDs to persons served increased in 2017 to an average 587 to 1. The goal in Nigeria is to have one CDD per 250 persons, and the program is working in several creative ways to improve the ratio. Over half (57%) of CDDs were female. One community supervisor managed about nine CDDs, 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, and distribution and use of LLIN. However, TCC is also interested in gathering additional evidence to demonstrate elimination of LF transmission. The TCC LF program in Plateau and Nasarawa was the first to be launched in Nigeria, in 2000. An in-depth history of the TCC LF campaign in these two states 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 transmission remained interrupted in LGAs that stopped LF MDA in 2010, while TAS surveys conducted in 2015 and 2017 confirmed transmission interruption in all other LGAs. Plateau and Nasarawa are the first two Nigerian states to eliminate LF as a public health problem.

In the seven TCC-assisted states in the SE/SS, LF MDA was launched in 2014 with support from USAID's ENVISION project, led by RTI International. Following the 'piggy-back' approach, the program began in LGAs with an existing river blindness program (Figure N4), then expanding rapidly into LGAs without river blindness. Treatments in 2017 totaled 17,426,794, and in all but two LGAs these were annual treatment with

ivermectin and albendazole. For several years however, the program's expansion was 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 program therefore followed the WHO strategy for twice-per-year MDA with albendazole alone, together with LLINs. The FMOH and Carter Center began to target twice-per-year albendazole-only treatments in these areas in 2015, but late drug arrival precluded the second round in all but a few areas in Imo State. However, in 2016 the program successfully delivered about 9 million twice-per-year treatments to over 4 million people. The Carter Center, in partnership with the Federal and local governments of Nigeria, conducted a large 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 stats. Thus, after two years of albendazole-alone monotherapy MDA, the program switched to annual treatment with ivermectin and albendazole in 2017.

Fighting Malaria and Lymphatic Filariasis with LLINs: In Nigeria, LF is transmitted by the same mosquitoes that transmit malaria (*Anopheles gambiae* sl and *An 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. 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 11.5 million LLINs in Nigeria since 2004. As noted above, Eigege et al. (2013) demonstrated in an entomological longitudinal study that LLIN were synergistic with MDA in halting transmission of LF. The Carter Center continues to support the FMOH policy of integrated malaria LF field operations in Nigeria.

Schistosomiasis/STH Control: The SCH program is our oldest program after RB. It was launched in Plateau and Nasarawa states in 1999 with a focus on *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, SCH/STH treatments have been able to expand in a largely integrated fashion to all endemic areas in the nine states we assist (Figure N7). In 2017, we assisted in providing 2,211,319 praziquantel treatments (Figures N7 and N8). The SCH treatment numbers change dramatically from year to year given the WHO recommendations which FMOH and ENVISION follow religiously. For SCH, adults and children are treated for schistosomiasis in LGAs that had average baseline prevalence exceeded 50%, and school-aged children alone were treated where LGA prevalence exceeded 10%. Areas where prevalence is lower than 10% alternate treatment years. As none of our assisted LGAs have schistosomiasis prevalence exceeding 50%, treatment is offered to school-aged children only, and we frequently alternate years. As a result, the SCH program is very complicated to

implement, driving us to design training and strategies tailor-made for each district, which may change for a given district from year to year. In a similar fashion, the STH treatments are given through schools but with an algorithm that differs from that SCH (adults are not targeted). This further complicates the district by district variance of program execution. In TCC-assisted areas treatments occur twice-per-year in the most highly endemic areas (Figures N9 and N10). In 2017, 6,518,674 treatments were given. Of these, 1,859,801 were given in areas targeted for twice-per-year treatments; however, only about a quarter of these (426,655) were second-round treatments. Two well-spaced rounds of treatments are not always compatible with the school year; treatments depend on the timing of the arrival of drugs.

As LF and RB programs stop MDA, we will observe in 2018 a complete transition in Plateau and Nasarawa States from community-based to school-based treatment, and from Ministry of Health toward the Ministry of Education. It is important to study this transition and implications it might have (see below) to reaching children not in school, girls, and preschool children who could be more easily reached in community-based programs.

Combination MDA in Community based (CDTI) programs: As noted above, WHO promotes, the FMOH supports, and ENVISION requires school-based MDA for STH and SCH. In contrast these partners promote community-based MDA for RB, LF and Trachoma. We have worked to economize our programs by adding SCH and STH MDA to our RB and LF programs. Double drug administration (ivermectin and praziquantel, mebendazole and praziquantel, or albendazole and praziquantel) or triple (ivermectin, albendazole and praziquantel) drug administration is used when possible, and with considerable cost savings (Evans et. al., 2013). However, in Plateau and Nasarawa our combined drug administration activities in our community based CDTI platforms will begin to transition in 2018.

2018 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, NIGERIA

Overarching for the three programs:

Establish specialized teams to undertake rolling treatment coverage surveys, in close consultation with HQ. Explore the feasibility of having only one or two dedicated teams (in two vehicles) operating separately and serving to rapidly and continually assess the entire TCC program.

Whenever possible, we should 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, 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.

Conduct (in consultation with HQ) a quantitative CDD attrition study (see Kaplan-Meier survival methodology) and attempt to determine causes of CDD attrition. Develop with HQ 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.

All TCC assisted states should try the Benin and Owerri field offices' approach to help frontline health facilities more accurately tally data from the CDD treatment registers. Report results at the next Program Review.

Lymphatic Filariasis/Malaria:

Publish the 2016 study that showed no high-density *Loa loa* microfilaremia (despite high RAPLOA findings). As a result of this study the LF MDA strategy in the SE/SS moved in 2017 from twice- per- year albendazole monotherapy to once per year ivermectin and albendazole in all TCC assisted states except two LGAs in Ebonyi state. In 2018 these two LGAs should also change to the once per year strategy as well.

Improve treatment efforts in urban centers using approaches suitable for highly populous areas (utilizing central gathering points like churches, mosques and schools, as well as other community groups). Determine innovative ways to monitor urban treatment coverage, in consultation with HQ.

LF Malaria FMOH guidelines: Work to scale up and operationalize these guidelines in

TCC-assisted areas, especially with regard to LLIN use, care, and resupply.

Complete the analysis of specimens (Wb123 and Ov-16) from the research funded by Task Force for Global Health on post MDA surveillance in suspected LF transmission hotspots in Plateau and Nasarawa states. Based on the epidemiological findings of 'hot spots,' follow-up with entomological and epidemiological assessments as indicated.

Continue entomological collections in LF sentinel villages in Plateau and Nasarawa, but store (rather than dissect) specimens for later molecular testing for kdr genes.

Conduct pre-TAS in 19 LGAs in Anambra, Ebonyi and Imo with FTS. Where these LGAs are oncho-endemic, also collect blood spots for OV-16 to determine onchocerciasis transmission status (see below in Onchocerciasis section).

Publish TAS2 and TAS3 results.

Onchocerciasis:

Stop MDA and develop a Post Treatment Surveillance (PTS) plan for Plateau and Nasarawa states. The plan should include establishing Special Intervention Zones (SIZs) with states that have apparently active transmission zones 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. Sightsavers has agreed to conduct an assessment in an area in Bauchi posing the greatest threat for infected vector reinvasion into Plateau and Nasarawa. Publish the results from the 2017 Plateau and Nasarawa Stop MDA studies in a peer reviewed journal.

Analyze and publish the hypodendemic mapping data (from the 2016 Loa loa study) that used OV-16 RDTs.

Provide lab support for halting MDA for RB in Kebbi, Zamfara, and Kaduna states (states assisted by SightSavers). If specimens are provided in time, have results available for the December 2018 NOEC meeting so that a decision to halt MDA in 2018 might be made. Offer technical support to these states for entomological collections via trapping.

All SE/SS states should begin prospecting the entomological sites preselected by the NOEC for future stop MDA entomological assessments. Those sites that are not productive of 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.

Encourage FMOH, WHO, and partner NGDOs to consider state cross-border foci as SIZs. One of these is the Edo-Ondo SIZ, where we will work in collaboration with

MITOSATH and surveyed treatment coverage in 2016 has been very poor. A KAP survey should be conducted in the Edo/Ondo border LGAs to learn more to improve treatment coverage, and to enable the TCC team to understand the cultural differences and their influence on disease and health-seeking behaviors. Twice-per-year Mectizan® treatment is recommended on both sides of the Edo-Ondo border.

Conduct a reclassification survey in Edo, Delta, and Ebonyi using OV-16 prevalence to determine whether these states need to go to twice-per-year treatment and receive a new status on the NOEC map.

Assess the remaining six hypoendemic onchocerciasis local government areas in SE/SS that are not yet slated for ivermectin treatment either for RB or LF.

An effort should be made to identify the next TCC-assisted states ready to propose to NEOC for stop MDA surveys. To rapidly assess onchocerciasis transmission status, take a DBS for OV-16 ELISA in the 29 LF pre-TAS LGA surveys that are also RB endemic.

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

Provide financial and administrative support for the 2018 NOEC meetings.

Schistosomiasis (SCH) and Soil Transmitted Helminthiasis (STH):
Conduct a statewide STH/SCH (urinary and intestinal) impact assessment in Plateau and Nasarawa that includes intensity of infection determinations. The survey should be conducted in the same villages that were visited in the original 2013 mapping exercise. Locate the lost baseline intensity data for Plateau from the 2013 ENVISION-supported survey (this data is present in the other states' files).

Consider an SCH/STH evaluation in Izumi Foundation supported areas in Edo and Delta.

Consider multiple studies/publications: 1) The results of the impact analysis of baseline (2013) and impact 2018; 2) An analysis of maximum values versus averages for STH and schistosomiasis from the 2013 and 2018 surveys; 3) Comparison of 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).

2018 Treatment and Training Objectives: NIGERIA

River Blindness	
Annual UTG:	8,922,109
Semiannual UTG:	25,142,700
Lymphatic Filariasis	
Annual UTG:	20,125,329
Schistosomiasis	
Annual UTG:	4,166,868
Soil-Transmitted Helminths	
Annual UTG:	7,387,888
Semiannual UTG:	3,934,098
Training Objectives:	
CDDs:	67,225
CSs:	9,459
Teachers:	15,026
FLHWs:	8,374

Figure N1

Nigeria: Carter Center-Assisted States

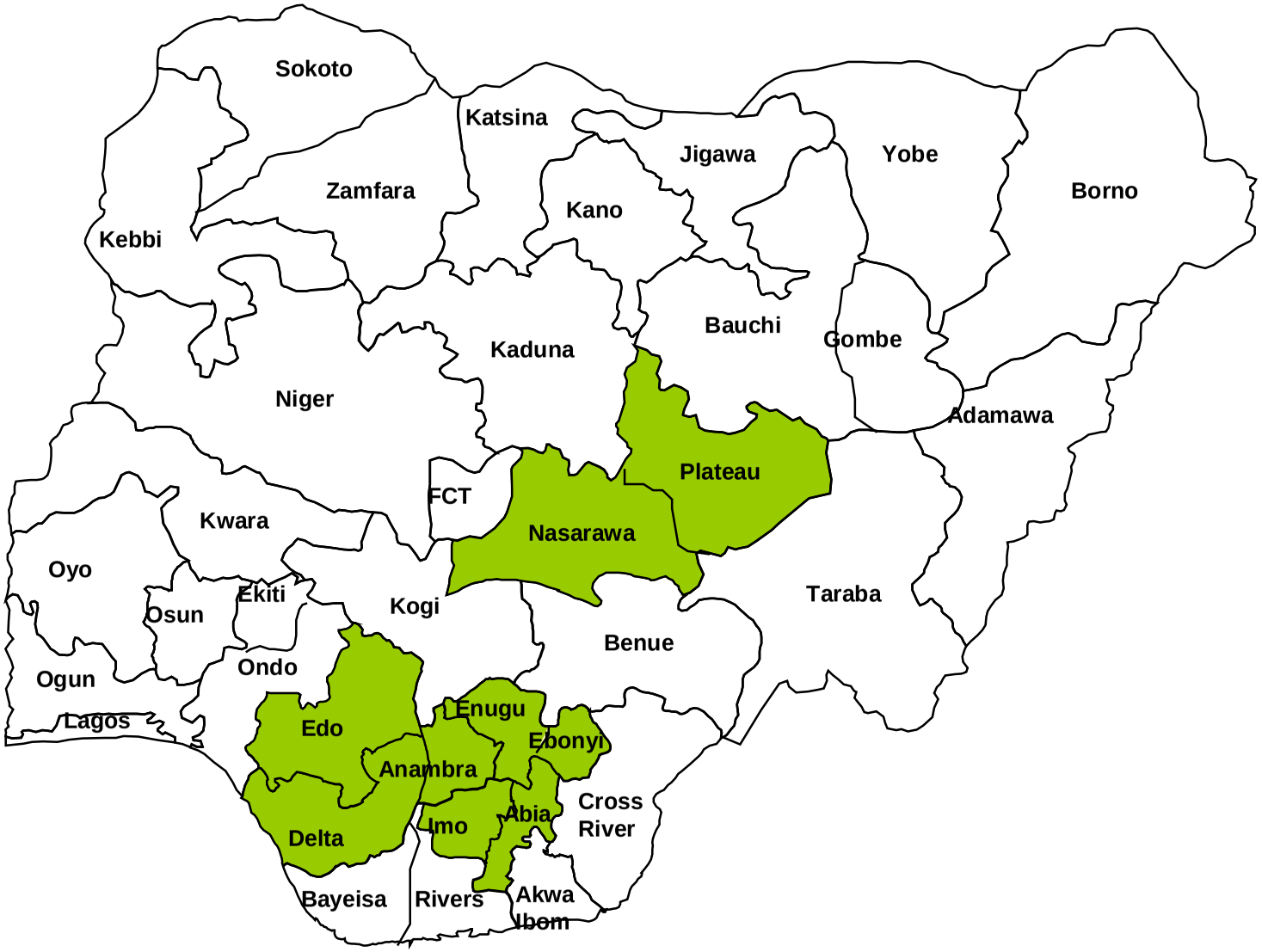


Figure N2

Nigeria: Carter Center-Assisted Areas
2017 River Blindness Semiannual Treatments

State	Number of LGAs Targeted	Total population in targeted LGAs	UTG2	Round 1 Treatments	Round 2 Treatments	Total Treatments	% UTG2 reached	Village Goal	Villages Reached	Percent of Village Goal Reached
Enugu	15	3,691,848	5,906,834	2,762,481	2,758,481	5,520,962	93%	5,913	5,899	100%
Anambra	16	4,431,970	7,091,152	3,458,924	2,777,982	6,236,906	88%	2,109	2,104	100%
Edo	5	1,129,972	1,807,956	818,819	852,441	1,671,260	92%	1,016	1,016	100%
Imo	18	3,629,523	5,807,242	2,824,222	2,349,864	5,174,086	89%	3,646	3,646	100%
Abia	12	2,386,673	3,818,634	1,852,839	1,723,466	3,576,305	94%	2,541	2,541	100%
Total	**66**	**15,269,986**	**24,431,818**	**11,770,647**	**10,408,872**	**22,179,519**	**91%**	**15,225**	**15,206**	**100%**

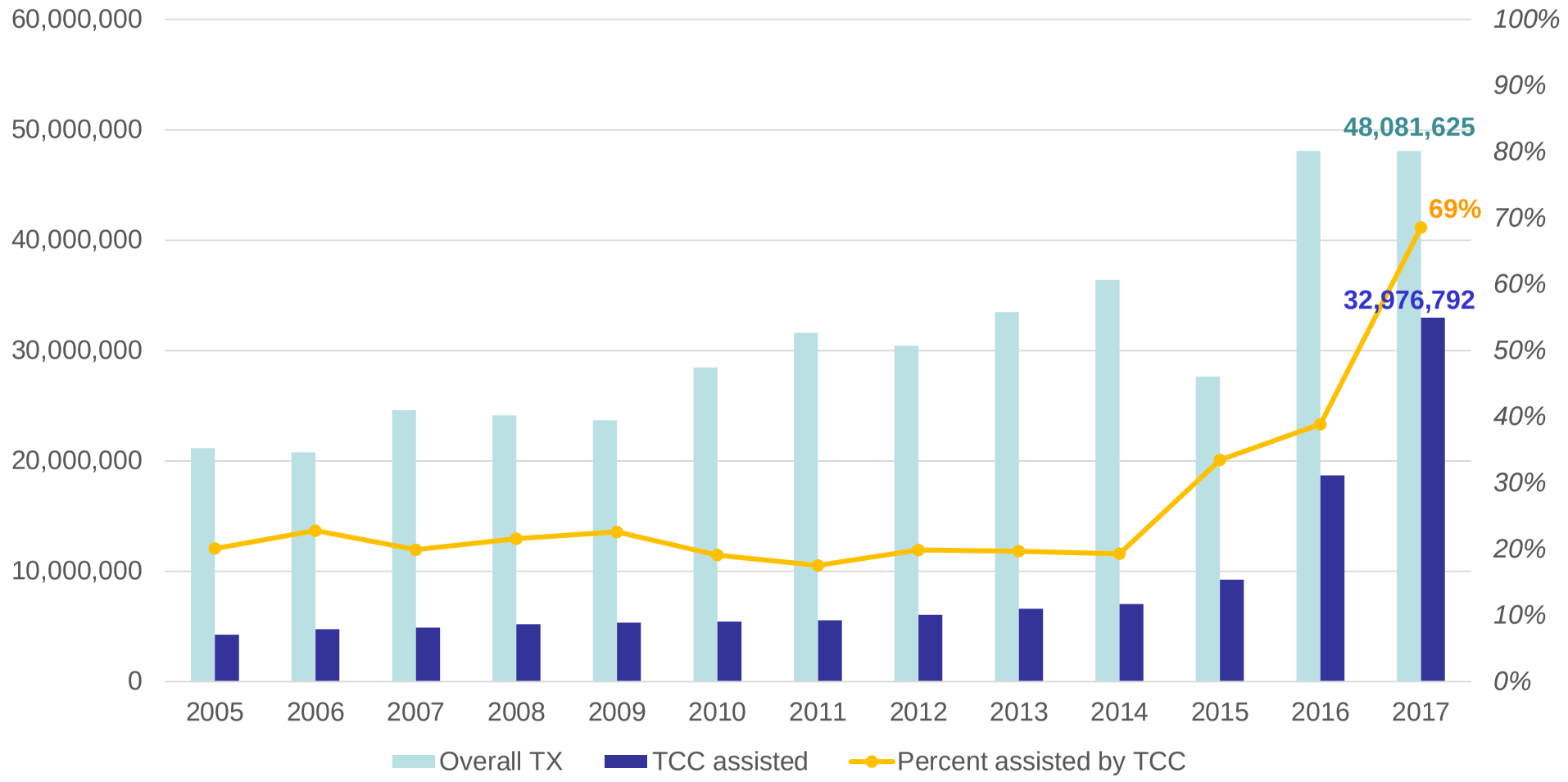
Figure N3

Nigeria: Carter Center-Assisted Areas
2017 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	2	582,009	465,607	445,415	96%	341	341	100%
Ebonyi	10	2,189,045	1,751,235	1,743,889	100%	2,357	2,357	100%
Edo	16	3,488,121	1,886,519	1,688,546	90%	1,256	1,256	100%
Delta	22	4,570,885	3,656,708	2,876,169	79%	2,932	2,932	100%
Imo	9	1,533,404	1,226,721	1,072,598	87%	1,679	1,651	98%
Abia	5	1,331,806	1,065,445	909,232	85%	1,009	1,009	100%
Plateau	5	1,073,297	858,637	833,104	97%	573	573	100%
Nasarawa	7	1,545,564	1,236,451	1,228,320	99%	589	589	100%
TOTAL	**76**	**16,314,131**	**12,147,323**	**10,797,273**	**89%**	**10,736**	**10,708**	**100%**

Figure N4

Nigeria: Carter Center-Assisted Treatments and Total Mectizan® Treatments for RB Provided 1992-2017*



*** The 2017 Total (Overall) TX figure for Nigeria is provisional.**

Figure N5

Nigeria: Carter Center-Assisted Lymphatic Filariasis Treatments (with Mectizan® and Albendazole) 2000-2017, and 2018 Target

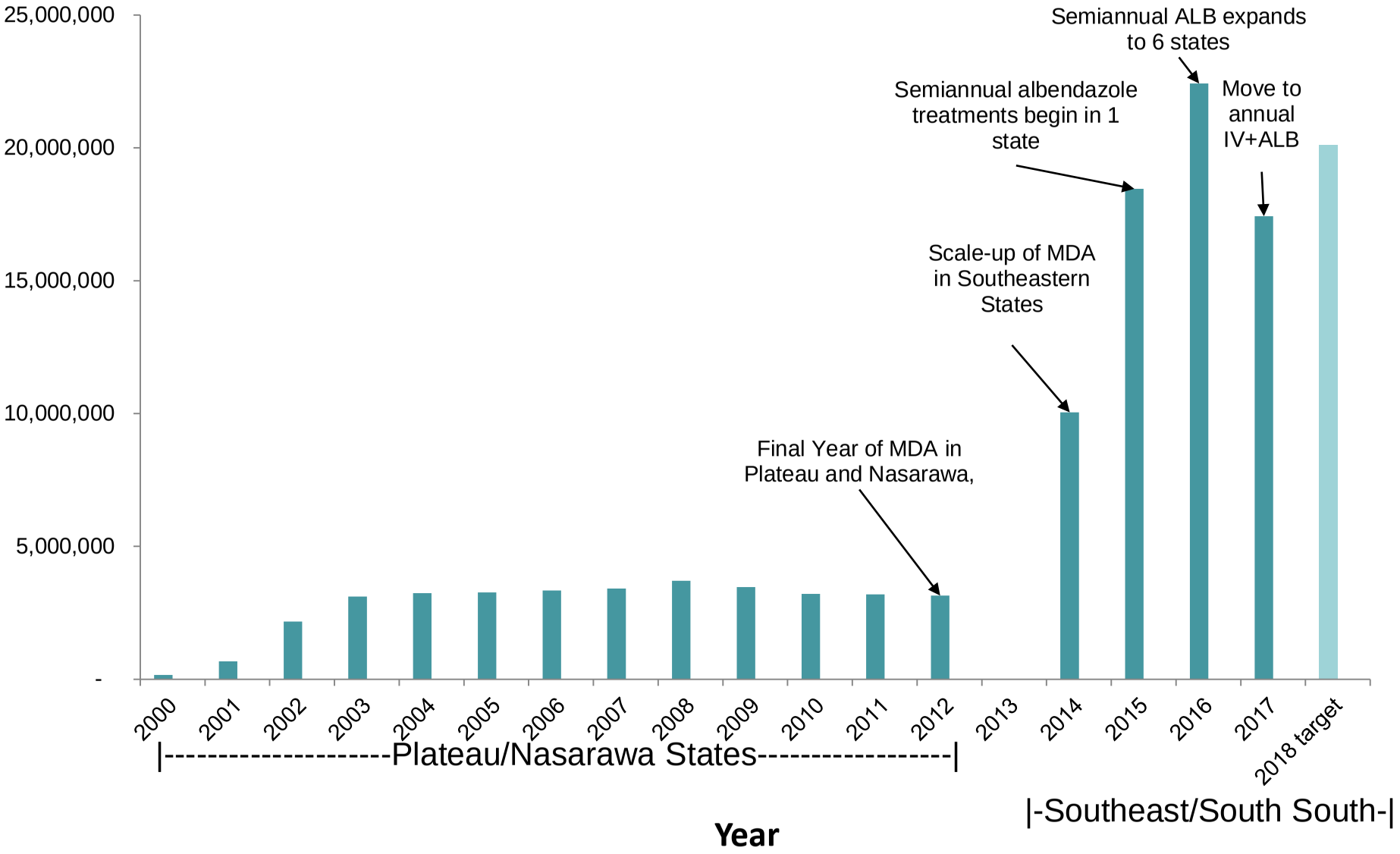


Figure N6

Nigeria: Carter Center-Assisted Areas
2017 Lymphatic Filariasis Treatments

Annual Treatments with Mectizan and ALB

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	3,594,676	2,875,741	2,717,562	94%	4,970	5,242	105%
Anambra	21	5,487,190	4,389,752	3,645,687	83%	2,935	3,200	109%
Ebonyi	7	1,544,873	1,235,898	1,229,101	99%	1,739	1,919	110%
Edo	7	1,484,103	1,187,282	1,117,371	94%	1,187	1,187	100%
Delta	16	3,094,178	2,475,342	1,976,370	80%	2,392	2,392	100%
Imo	27	5,162,927	4,130,342	3,445,319	83%	5,325	5,299	100%
Abia	17	3,718,479	2,974,762	2,566,744	86%	3,550	3,550	100%
Total	**109**	**24,086,426**	**19,269,119**	**16,698,154**	**87%**	**22,098**	**22,789**	**103%**

Semi-annual Treatments with ALB alone

State	Number of LGAs targeted	Total population in targeted LGAs	UTG2	Round 1 Treatments	Round 2 Treatments	Total Treatments	Percent of UTG2 Reached	Village Goal	Villages reached	Percent Village Goal reached
Ebonyi	2	456,685	730,696	364,622	364,018	728,640	100%	802	1,313	164%

Figure N7

Nigeria: 2017 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	4	900,178	252,050	220,261	87%	1,008	1,181	117%
Anambra	2	417,586	116,924	96,987	83%	352	352	100%
Ebonyi	4	782,109	218,991	217,218	99%	1,294	1,094	85%
Edo	14	3,405,577	953,562	815,993	86%	2,091	2,091	100%
Delta	12	1,959,835	649,807	400,343	62%	1,568	321	20%
Imo	3	48,739	13,647	11,894	87%	480	33	7%
Abia	3	84,018	23,525	20,938	89%	563	83	15%
Plateau	4	1,229,129	344,156	318,264	92%	290	290	100%
Nasarawa	2	390,964	117,290	109,421	93%	184	184	100%
Total	**48**	**9,218,135**	**2,689,952**	**2,211,319**	**82%**	**7,830**	**5,629**	**72%**

Figure N8

Scale up of Carter Center-Assisted Schistosomiasis Treatments in Nigeria and 2018 Target

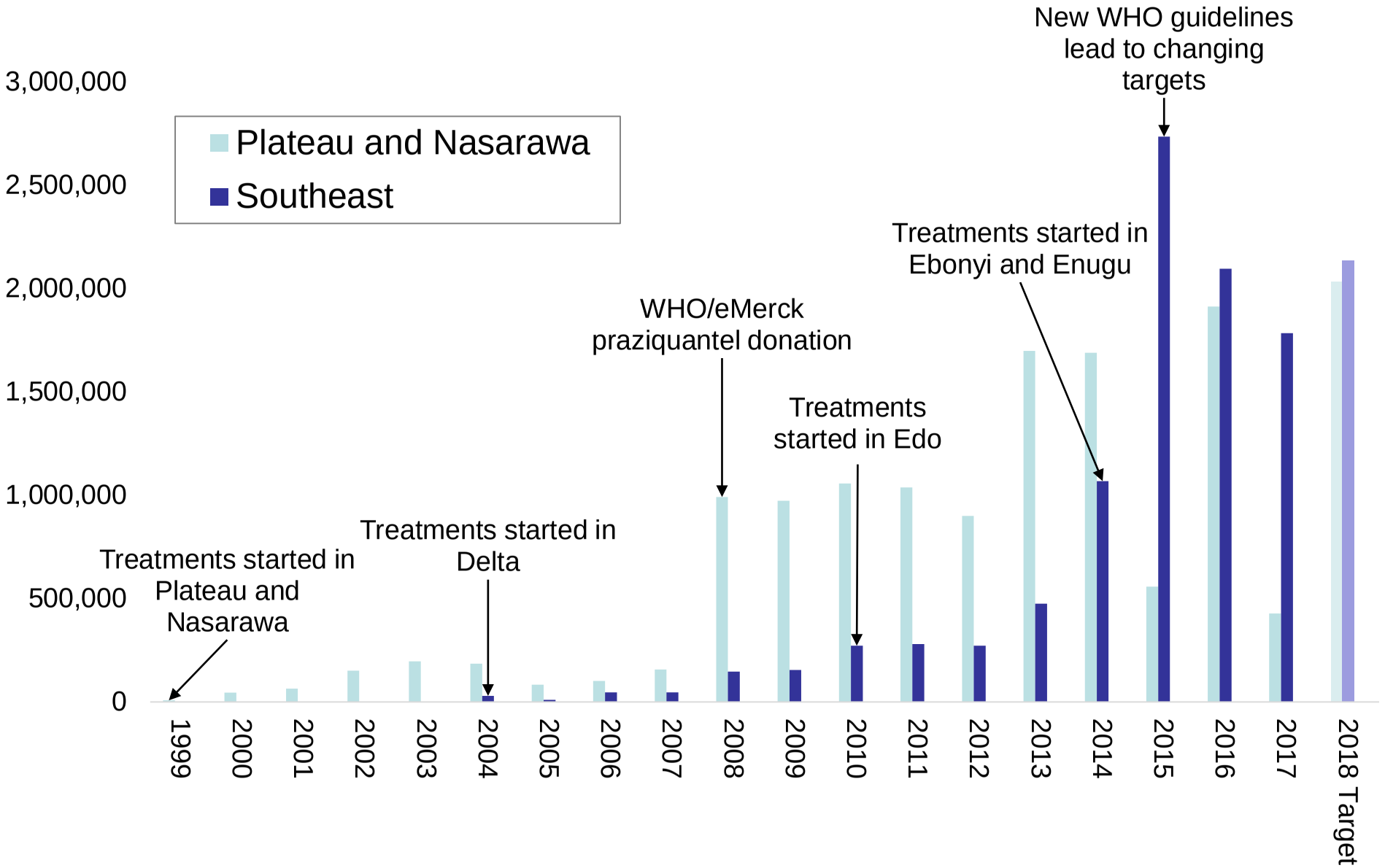


Figure N9

Nigeria: 2017 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
Anambra	9	2,386,160	827,369	706,703	85%	1,564	1,677	107%
Ebonyi	12	2,994,090	838,345	548,664	65%	1,409	2,027	144%
Edo	7	1,572,758	547,691	378,200	69%	1,134	1,134	100%
Delta	18	4,425,699	440,372	527,945	120%	1,268	1,268	100%
Imo	25	5,377,443	704,245	606,177	86%	4,943	4,719	95%
Abia	24	4,708,557	668,125	591,441	89%	3,299	3,019	92%
Nasarawa	14	3,430,302	1,274,309	1,033,049	81%	920	494	54%
Plateau	6	1,357,214	559,918	513,067	92%	1,244	1,253	101%
Nasarawa	9	1,999,707	380,020	347,139	91%	416	382	92%
Total	**124**	**28,251,930**	**6,240,394**	**5,252,385**	**84%**	**16,197**	**15,973**	**99%**

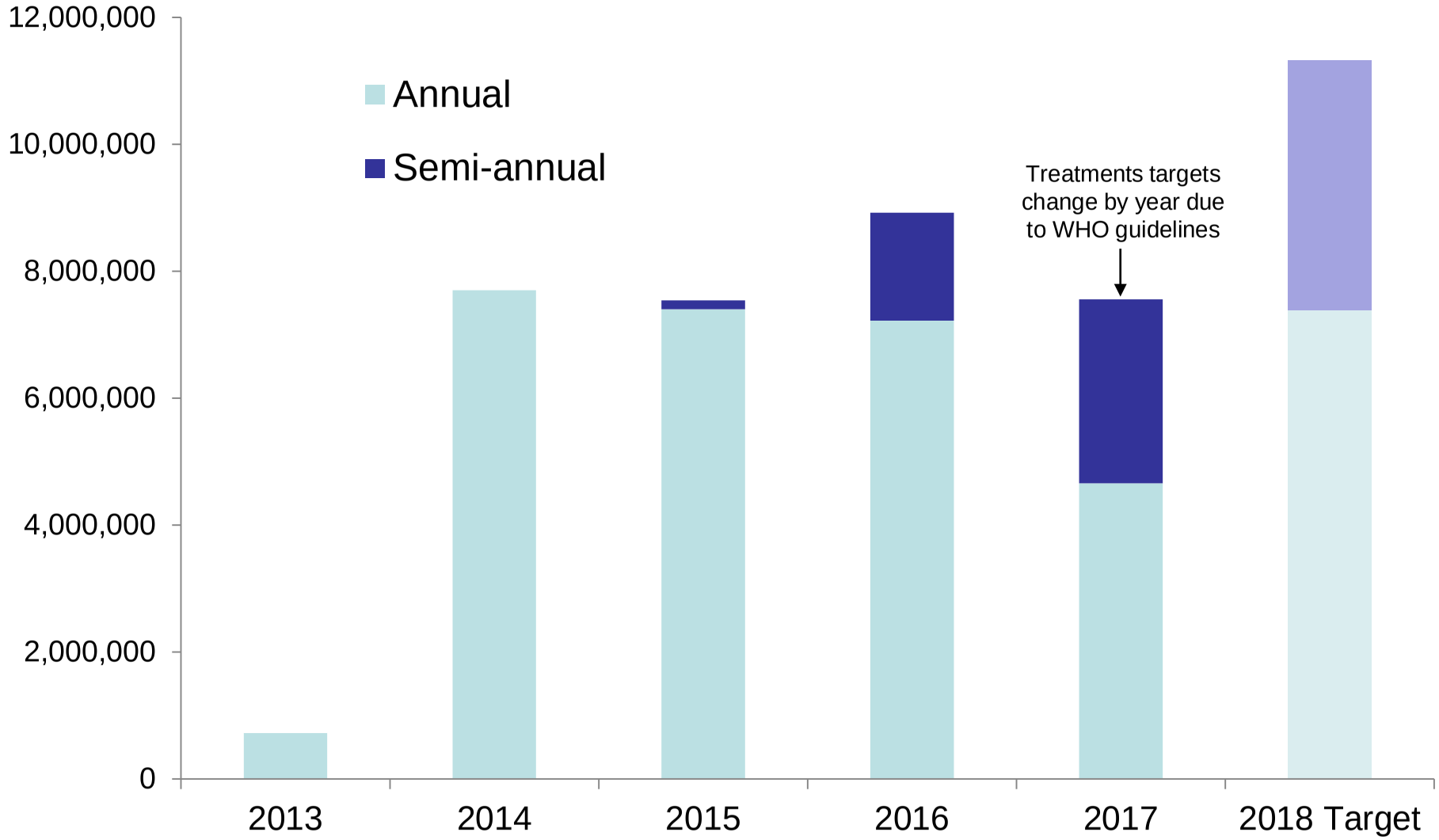
Figure N10

Nigeria: 2017 Carter Center-Assisted Semiannual Soil-Transmitted Helminthiasis Treatments

State	Number of LGAs targeted	Total population in targeted LGAs	UTG2	Round 1 Treatments	Round 2 Treatments	Total Treatments	Percent of UTG2 Reached	Village Goal	Villages Reached	Percent of Village Goal Reached
Enugu	1	175,456	98,256	47,602	49,335	96,937	99%	174	174	100%
Ebonyi	3	646,864	362,244	180,027	174,348	354,375	98%	1,292	1,292	100%
Edo	8	1,910,538	1,069,902	439,396	409,214	848,610	79%	1,393	1,393	100%
Delta	19	3,077,300	1,915,986	670,277	629,101	1,299,378	68%	2,101	2,101	100%
Imo	1	157,454	88,174	37,280	28,456	65,736	75%	228	228	100%
Abia	2	475,416	266,218	129,922	103,158	233,080	88%	280	280	100%
Total	**34**	**6,443,028**	**3,800,780**	**1,504,504**	**1,393,612**	**2,898,116**	**76%**	**5,468**	**5,468**	**100%**

Figure N11

Soil Transmitted Helminthiasis Treatments, 2013 – 2017 and 2018 Target



Note: Treatments are with either Albendazole or Mebendazole

ETHIOPIA

Summary: In 2017, the RBEP assisted five regions in Ethiopia (Amhara, Benshangul-Gumuz, Gambella, Oromia, and SNNPR, see Figure E1). The program provided 17,780,204 river blindness treatments under the twice-per-year approach, 22% more than the 14,467,640 treatments given in 2016 (Figure E2). A remaining challenge is to refine onchocerciasis mapping in areas formally deemed hypo-endemic as well as such areas deemed ecologically conducive for onchocerciasis transmission in the eastern part of Ethiopia.

Cross-border coordination between Ethiopia and Sudan in the Special Intervention Zone of Galabat (Sudan) and Metema (Ethiopia) culminated with the demonstration (in accord with WHO guidelines) that transmission had been interrupted on both sides of the border. MDA ended in most of the Metema, with the exception of a small area of localized transmission of the Wudi Gemzu locality. This entomologically positive 'hot spot' is now being treated with Mectizan® every three months. Staff from both ministries will keep each other informed as new results come in.

The TCC Lymphatic Filariasis program continued assisting Ethiopia in its work toward eliminating that infection by providing 809,783 treatments in 2017 (Figure E6). The program also successfully completed TAS assessments in the Metema area, so that there was coordinated stop MDA between the LF and onchocerciasis programs in that part of western Amhara. Three woredas in Bench Maji zone (SNNPR) also passed their first TAS.

Background: Rapid Epidemiological Mapping of Onchocerciasis (REMO) was conducted in Ethiopia in 2001 with support from the African Programme for Onchocerciasis. REMO identified and initially targeted 10 areas for treatment, primarily in the western part of the country, where the overall prevalence of onchocerciasis was estimated to be more than 40% (≥20% nodule rate). 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 hypo-endemic zones).

Key 2017 elimination program partners with The Carter Center (TCC) in Ethiopia include the Federal Ministry of Health, The Lions Clubs International Foundation and the Lions Clubs of Ethiopia. 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 project areas of Ethiopia.

The Ethiopia Onchocerciasis Elimination Expert Advisory Committee (EOEEAC): With the declaration of an elimination strategy in 2012, the EOEEAC was launched to provide recommendations to the FMOH on their national program. The committee is

composed of national and international experts. EOEEAC Chair Dr. Mark Eberhard (former director of the Division of Parasitic Diseases and Malaria at the CDC) stepped down at the end of 2017 and will be replaced in 2018 by Prof. Rory Post of Liverpool John Moores University. Dr. Zerihun Tadesse (Ethiopia Country Representative of The Carter Center) serves as EOEEAC co-secretary with Mr. Nebiyu Negussu (FMOH NTD 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 several occasions. MDA will continue in Wudi Gemzu on a four-times-per year schedule.

Treatments: The total number of treatments provided in 2017 was 17,780,204, which were all delivered semi-annually (Figure E2). Coverage of the UTG(2) reached 97%, considerably higher than the 80% reached in 2016. Geographic coverage was 100% of targeted villages (Figure E3). Carter Center-assisted treatments represented 77% of all ivermectin treatments given in Ethiopia in 2016.

Training and Health Education: In accord with the terminology of the Ethiopian health system, CDDs are referred to as members of the Health Development Army (HDA) and CSs are grouped with Health Extension Workers (HEWs). Training was provided to 225,094 community-directed distributors (HDA) in 2017, slightly less than 2016 (Figure E4). The percent of female members of the HDA was 59% in 2017, continuing the trend of increasing female participation that began in 2012 (Figure ES5). The average population per HDA was a remarkable 59 to 1, and all zones reached ratios below the target of 1 CDD per 100 population.

A total of 76,686 community supervisors (HEW) were trained in 2017, overseeing an average of 3 HDAs each, on par with the preceding year. The proportion of community supervisors who are women dropped to 47% from 60% in 2016. The reason for this change was not explained.

Lymphatic Filariasis (LF): 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 where possible, in those zones where RB is also endemic. Thus, as the RB program expands eastward with mapping activities into new, co-endemic areas, the LF program will likewise continue to grow in scope. The LF efforts began in the Gambella region and have expanded to LF/RB co-endemic zones in SNNPR, Beneshangul-Gumuz, and Amhara regions, increasing the UTG nearly tenfold. There were 809,783 treatments in 2017 (Figures E6 and E7). Transmission Assessment Surveys (TAS-1) for stop LF MDA decisions were successfully conducted in portions of North Gondar and Bench Maji zones during 2017; a resulting nearly 350,000 LF treatments will be halted there in 2018.

Other Integration Activities: In the North Gondar zone (Amhara region) the RB-LF integrated program works with Carter Center-assisted trachoma control activities.

2018 RECOMMENDATIONS FOR THE CARTER CENTER RBEP, ETHIOPIA

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

Onchocerciasis

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

Conduct epidemiological and entomological studies in the Wadi Gemzu 'hot spot' in the Metema sub-focus in accord with the recommendations of the EOEEAC. Results should be presented at the 2018 EOEEAC meeting.

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

In the mapping protocol to districts in potential eastern expansion zones, switch focus from children to resident adults with an MDA threshold ≥ 2%, in accord with 2017 WHO OTS recommendations. If treatments are needed in any new area these should be twice-per-year. Interim mapping results should be reviewed at the October 2018 EOEEAC meeting. Expand mapping activities as resources allow and in consultation with HQ and FMOH.

Establish twice-yearly MDA in the 31 untreated 'hypo-endemic' districts identified by EOEEAC at its last meeting if additional data supports that those districts meet the threshold recommended by the WHO OTS of ≥ 2% OV-16 prevalence in adult residents.

Complete PCR assessment of *S. ethiopiense* vectors in the laboratory in time for presentation at the 2018 EOEEAC meeting.

Provide financial and administrative support for the 2018 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 address the 200,000 refugees from RSS in Gambella.

Lymphatic Filariasis

In consultation with HQ and FMOH- NTD secretariat, conduct pre-TAS and TAS studies in 2018. Pre-TAS studies should use only filarial antigen testing and not nocturnal mf assessments. Consider obtaining DBS for OV-16 testing during pre-TAS and TAS studies, if indicated.

2018 Treatment and Training Objectives:

River Blindness	
Semiannual UTG(2)	17,896, 759
Lymphatic Filariasis	
Annual UTG	1,435,414
Training Objectives	
CDDs	204,492
CSs	66,559

Figure E1

Map of RB & LF Areas Assisted by The Carter Center

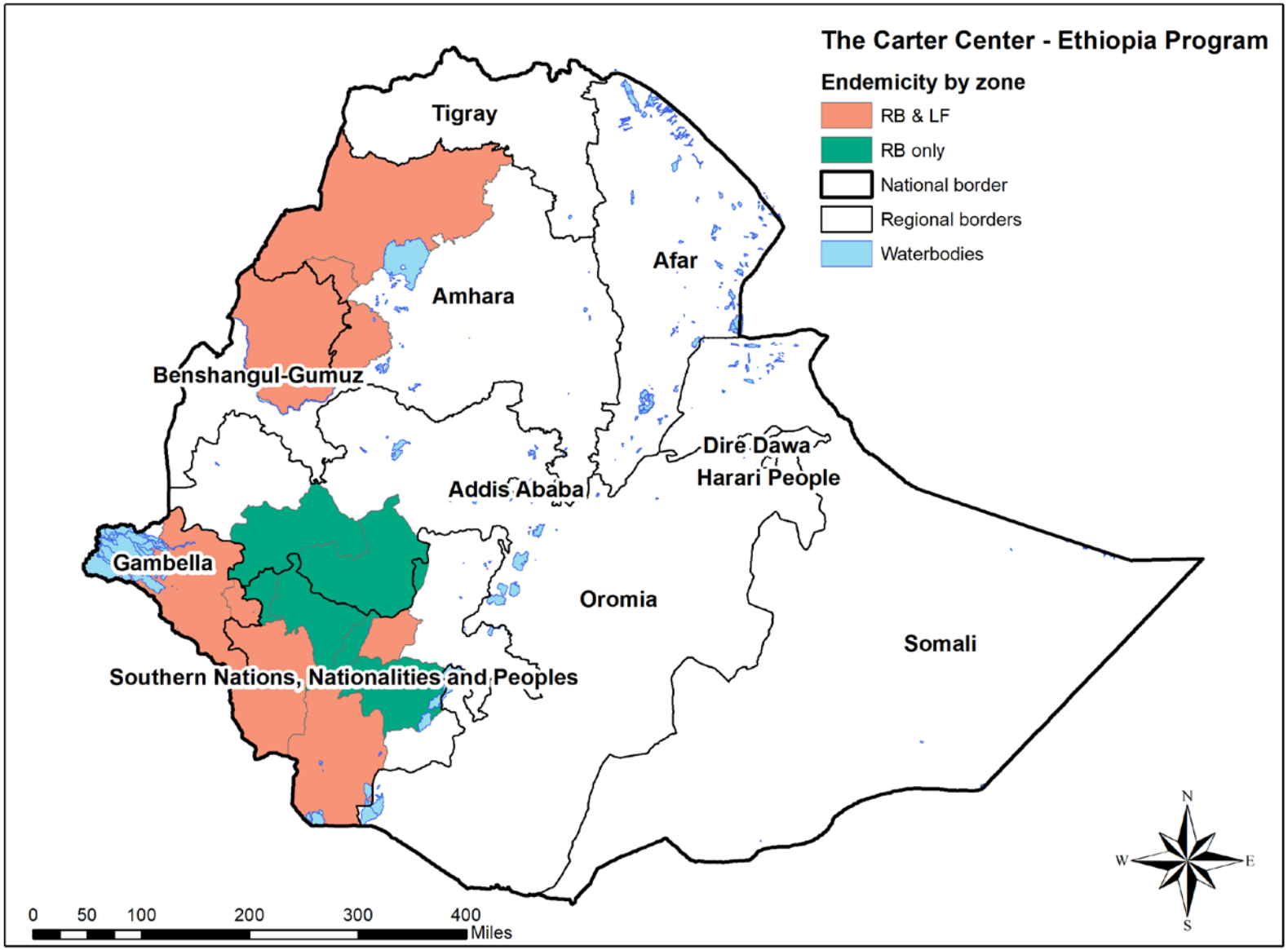


Figure E2

Ethiopia: History of TCC-Supported Mectizan® Treatments by Treatment Regimen

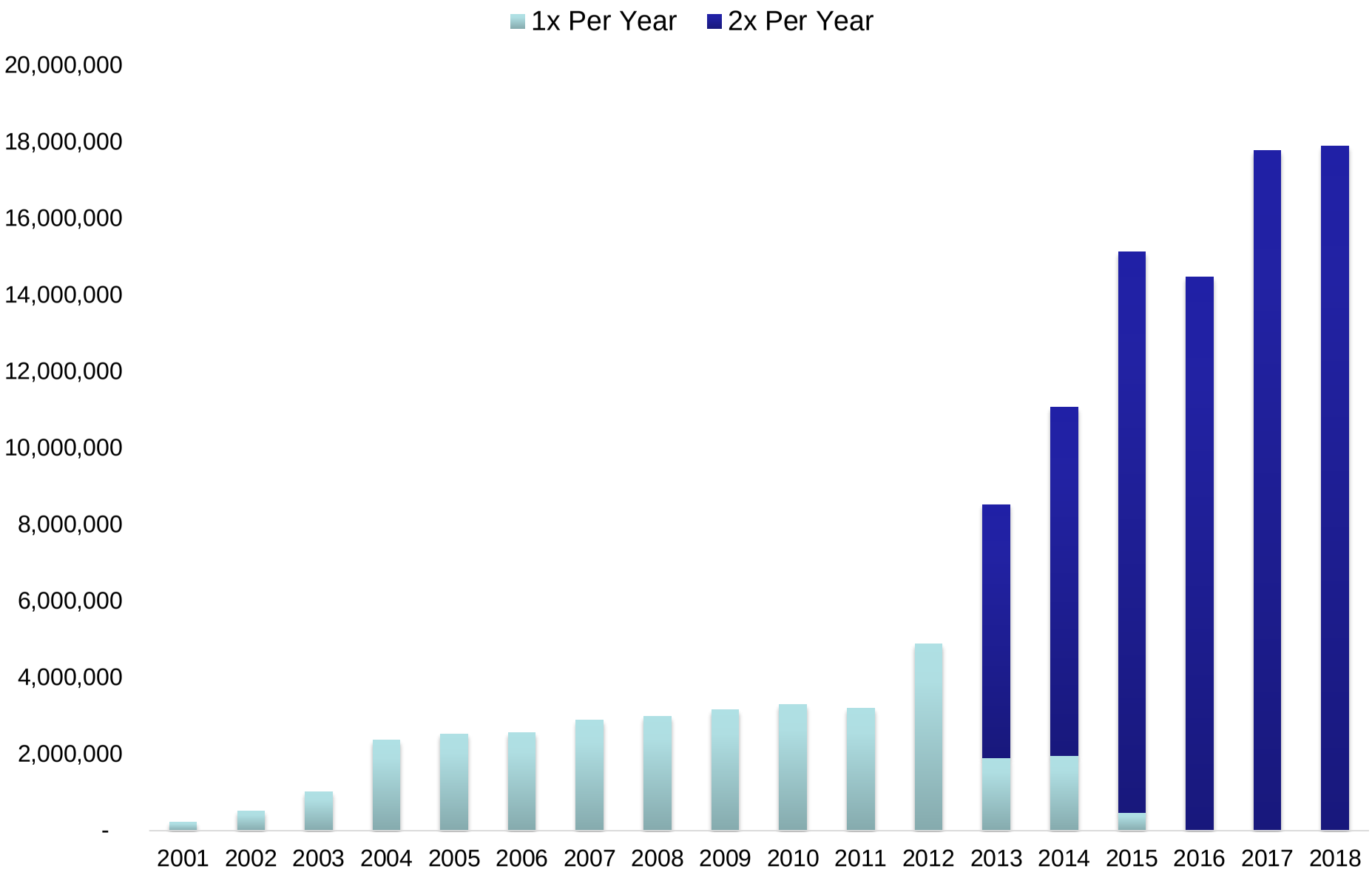


Figure E3

River Blindness: Semi-Annual Treatments, 2017

Region	Zone	No. of Districts	Total Pop	UTG 1	UTG 2	Treatments UTG1	Treatments UTG2	Treatments UTG 1 & 2	% UTG 1	% UTG 2	No. Comm	% Comm Treated
SNNPR	Kaffa	11	1,151,228	967,032	1,934,063	939,177	990,267	1,929,444	97	100	4,718	100
	Sheka	5	229,013	192,371	384,742	203,792	205,229	409,021	106	106	1,391	104
	Bench-Maji	11	841,433	706,804	1,413,607	686,127	729,482	1,415,609	97	100	3,028	100
	Dawuro	6	521,138	437,756	875,512	445,735	478,762	924,497	102	106	2,029	100
	Konta	1	124,163	104,297	208,594	98,665	104,858	203,523	95	98	499	100
	Yem Spe.	1	86,475	72,639	145,278	68,384	72,459	140,843	94	97	523	100
Oromia	Illubabor	24	1,627,161	1,366,815	2,733,630	1,384,057	1,414,733	2,798,790	101	102	8,357	100
	Jimma	19	3,414,507	2,868,186	5,736,372	2,947,726	3,022,583	5,970,309	103	104	15,834	100
Amhara	North Gondar	8	998,521	838,758	937,737	869,540	98,352	967,892	104	103	6,378	100
	Awi	11	1,090,439	915,969	1,831,938	968,232	992,984	1,961,216	106	107	6,436	100
Benshanghul G.	Metekel	7	397,037	333,511	667,022	351,058	360,044	711,102	105	107	2,548	100
Gambella	Agnuwa	5	115,318	96,867	193,734	108,930	108,094	217,024	112	112	273	105
	Mezheng	2	84,364	70,866	141,732	66,111	63,640	129,751	93	92	198	100
	Itang	1	48,114	40,416	80,832	41,445	43,842	85,287	103	106	90	100
Total	**14**	**112**	**10,728,911**	**9,012,285**	**17,284,792**	**9,178,979**	**8,685,329**	**17,864,308**	**102**	**103**	**52,302**	**100**

Gambella Refugees Rx: 193, 112

Figure E4

Ethiopia: Community Directed Distributors (CDDs*) and Community Supervisors (CSs*) Trained (2005 – 2017) in Carter Center-Assisted Areas

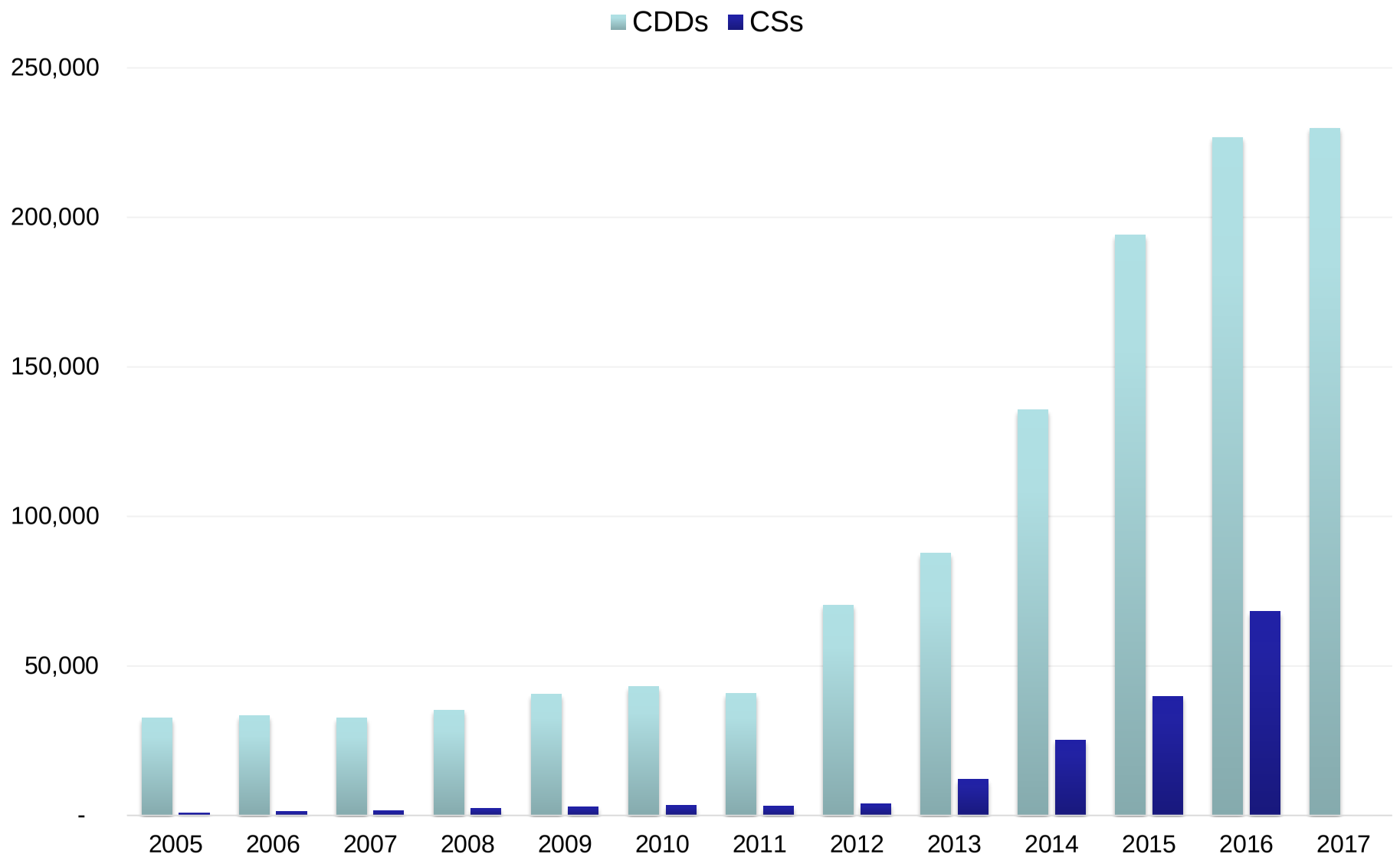


Figure E5

Ethiopia: Training of Community Directed Drug Distributors: 2001 – 2017 and Percentage Female

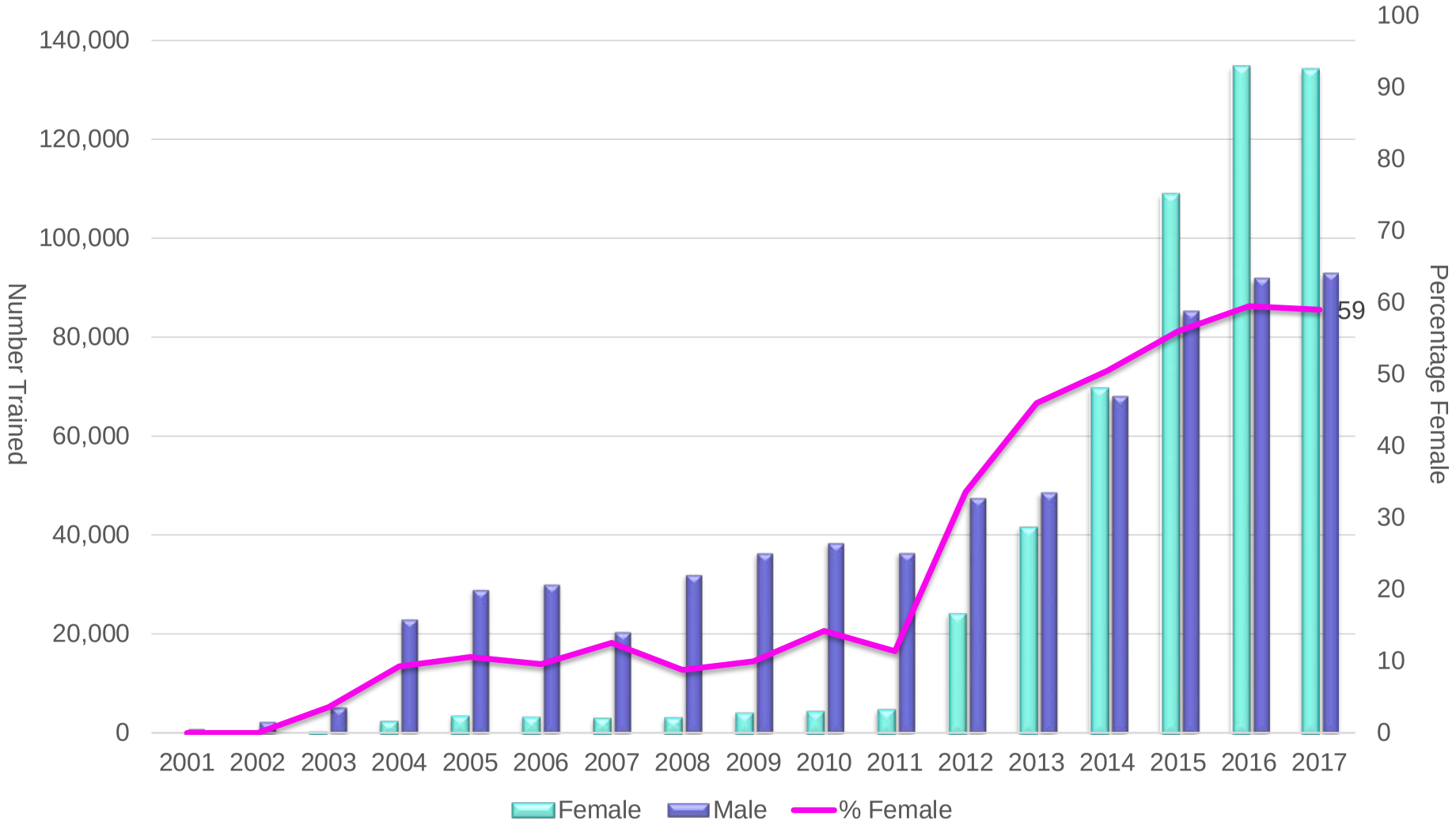


Figure E6

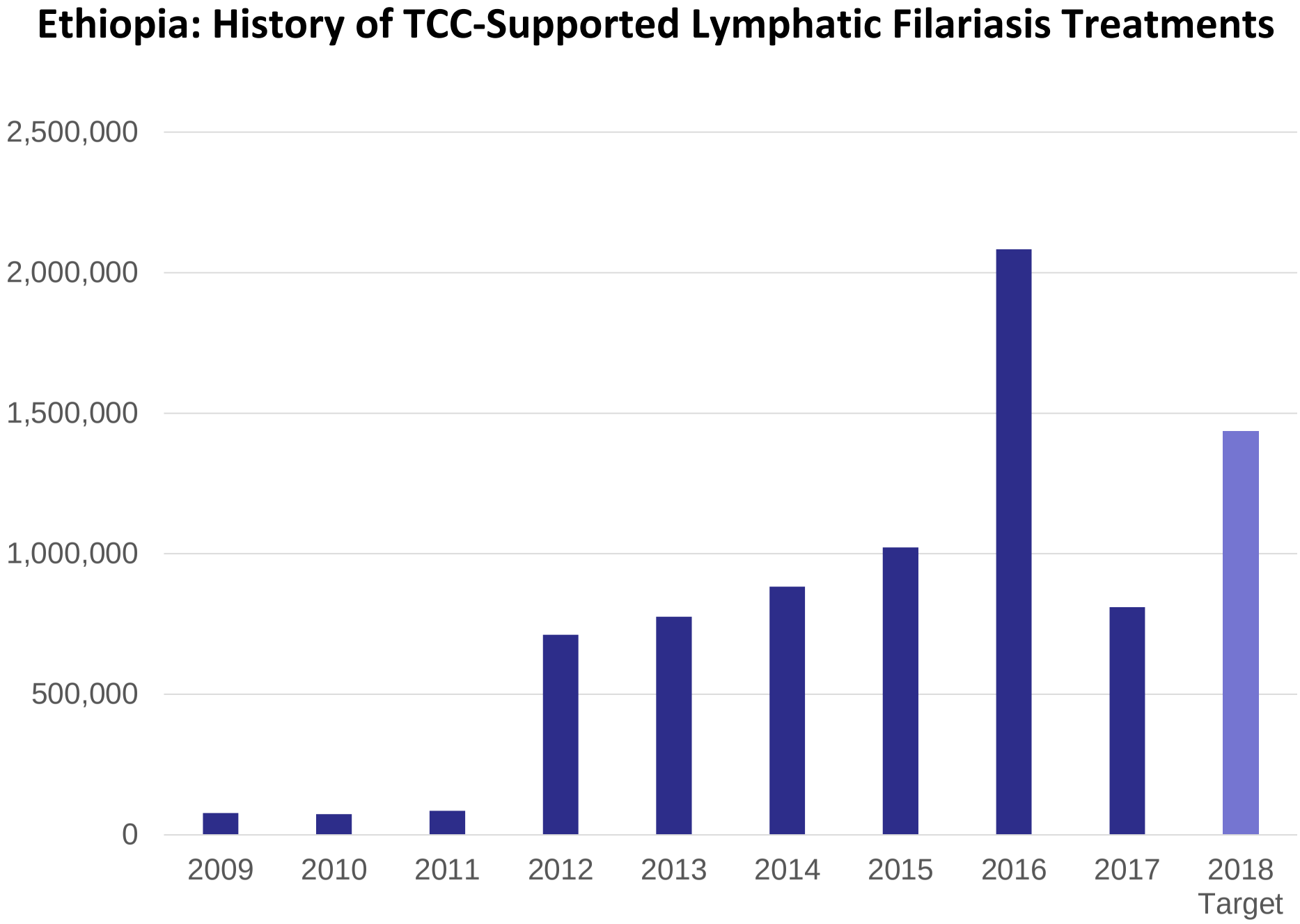

Ethiopia: History of TCC-Supported Lymphatic Filariasis Treatments
2,500,000
2,000,000
1,500,000
1,000,000
500,000
0
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018 Target

Figure E7

Lymphatic Filariasis Treatments - 2017

Region	Zone	# of Districts	# of Comm-unities	Total Population 2017	Eligible Pop	# people treated	% treated (UTG)	No. of Comm-unities treated	% of Comm-unities treated
SNNPR	Bench-Maji	6	2,657	457,937	384,667	411,594	107%	2657	100%
	Dawuro	1	321	77,011	64,690	69,303	107%	321	100%
Amhara	Awi	3	1,504	287,781	241,736	243,027	101%	1504	100%
Benshangul G.	Metekel	2	459	90,433	75,964	85,859	113%	459	100%
Gambella	Agnuwa	4	238	69,905	58,720	56,966	97%	238	100%
	Mezheng	2	198	86,304	72,496	63,640	88%	198	100%
	Itang Sp. Woreda	1	90	49,221	41,345	43,842	106%	90	100%
Total		**19**	**5,467**	**1,118,593**	**939,618**	**974,231**	**104%**	**5,467**	**100%**

Note: No. of treatments in North Gondar and B.Maji reduced due to the stop MDA following TAS.

ANNEX 1: BACKGROUND

Human onchocerciasis, an infection caused by the parasitic worm *Onchocerca volvulus,* causes chronic skin disease and severe itching, as well as eye lesions that can progress to visual loss or complete blindness. The worms live in fibrous 'nodules' that often can be felt just under the skin. Onchocerciasis is transmitted by small black flies that breed in rapidly flowing rivers and streams, thus leading to the common name for the disease, "river blindness." The World Health Organization (WHO) estimates that approximately 37.2 million people are infected and 770,000 are blinded or severely visually impaired in 31 endemic countries. Approximately 190 million people live in endemic areas worldwide and are therefore at risk of infection; more than 99.9% 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.

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 in areas where the eye and skin disease from the infection is greatest (the so-called meso/hyperendemic areas). 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' so that transmission can eventually be broken. 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. Of note, we advocate for our programs to cooperate and integrate, when possible, with the national Lymphatic Filariasis (LF) programs of these countries (in Africa), which also use MDA with Mectizan®. We also seek interruption of transmission of LF in all areas TCC assists.

A historical barrier to treatment in some parts of Nigeria where The Carter Center works has been co-endemicity of a parasite called *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 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 per ml blood). Our results (published in 2018 by Emukah *et al. in the AJTMH*) were reviewed by the Mectizan®

Expert Committee and the Federal Ministry of Health of Nigeria. Both gave their permission to use ivermectin MDA treatment in *Loa loa* areas in Nigeria that are ivermectin-naïve and hypoendemic for onchocerciasis as a result of our work.

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 total (program census-based) number of treatment-eligible people living in a program area (persons >5 years of age). **UTG(2) and UTG(4)** is 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).

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's) supported project areas throughout Africa in the late 1990's. In some areas, The Carter Center'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 treatments activities are handled at that 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 CDD 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 per 30 persons. Uganda is steadily increasing its concentration of CDDs with an ultimate goal of 1:34 persons.

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

- **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.
- **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 the 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.
- **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).
- **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.
- **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.
- **2003:** Richards co-authors a paper on mass treatment decision-making in *Loa loa* areas where onchocerciasis occurs (Addis 2003).
- **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).
- **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).

- **2007:** TCC's International Task Force for Disease Eradication reviews RB eradicability

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

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.

- **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.
- **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).
- **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.
- **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.
- **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.
- **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.

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

- **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.
- **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.
- **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, and 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. Unfortunately, the MacArthur money is not obtained.
- **2017:** This was the most successful year ever for numbers of RBEP-assisted Mectizan® treatments (over 55 million) delivered. It was also remarkable for 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). Sudan and Ethiopia jointly declared a stop ivermectin MDA decision for 1.2 million persons in the cross-border Galabat/Metema onchocerciasis transmission zone. Nigeria determined that MDA for river blindness could be halted among 2.2 million persons in Plateau and Nasarawa States. Uganda will halt MDA among 421 thousand persons in two foci. To the best of our knowledge, this is the largest number of persons in whom RB MDA has been stopped in a given year. Overall, our RB elimination partnership has enabled 6.5 million people in nine countries on two continents to reach a point where they no longer need Mectizan® treatment.

ANNEX 3: The Carter Center RBEP Reporting Processes

At-risk Villages (ARVs): 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, the survey villages are visited by field teams and a convenience sample of 30-50 adults are examined (by palpation) for characteristic onchocercal nodules. The mean nodule prevalence for each village sample was mapped using topographical maps and geographic information systems (GIS), and the map was used to define endemic zones called 'community directed treatment with ivermectin (CDTI) treatment zones.' These zones typically are defined by sample villages having nodule prevalence of ≥20%.

All villages within the CDTI treatment zone are initially offered mass Mectizan® treatment annually. The approach of REMO excludes some areas from CDTI where there is onchocerciasis, but nodules rates were 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) do not 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% prevalence of onchocerciasis when measured by microfilarial prevalence.

As the policy in Africa continues to shift towards elimination (all Carter Center-supported countries have an elimination policy), the role of hypoendemic areas in *O. volvulus* transmission is being critically re-examined. The River Blindness Elimination Program (RBEP) contributes to this area of investigation in our assisted areas. Based on evidence we have collected, we firmly believe that transmission occurs in many hypoendemic areas and that they must therefore be promptly reassessed and, if necessary, treated with CDTI under the elimination approach.

Any areas not yet mapped in the countries we support (and some of those where the mapping is outdated) have launched new field exercises based on the mapping guidelines of that country's national onchocerciasis elimination committee (typically serology in children). The WHO Onchocerciasis Technical Subcommittee (OTS) in 2017 suggests that Ov16 testing be used for such mapping, and that a seroprevalence > 2%

in adult residents be used as the indication for launching mass drug administration. There are as of yet no hard data to support this recommended threshold.

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 superficial skin biopsies to identify *O. volvulus* microfilaria in skin. Villages in which one or more persons are positive (sample prevalence ≥ 2%) are considered "at-risk" and are recommended for the mass treatment campaign. Thus, the cutoff prevalence for treatment is much lower for the Americas compared to Africa until recently, when elimination 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 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 originate from village-level records and are prepared during mass treatment activities and carried out by village distributors (Africa) or national Ministry of Health (MOH) personnel (Americas).

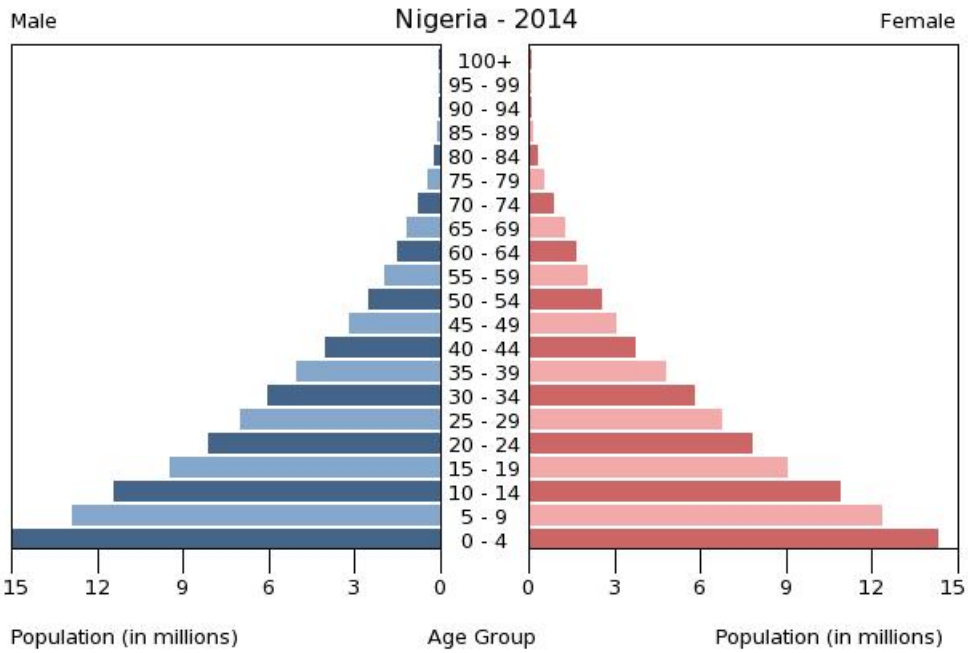
The accuracy of these reports is routinely confirmed with random spot checks performed primarily by Carter Center and MOH personnel, supplemented by a standardized treatment coverage monitoring surveys based on statistical sampling methods with household questionnaires administered by The Carter Center and MOH staff. Summary reports of numbers of villages and persons treated are compiled at the district level and forwarded (whenever possible through MOH surveillance and reporting channels) to both headquarters of the national onchocerciasis programs and the national Carter Center offices. In the Americas, the MOHs of Venezuela and Brazil report their treatments quarterly to the OEPA office in Guatemala City, which then provides a combined regional report to The Carter Center and to the Program Coordination Committee (PCC), InterAmerican Conference on Onchocerciasis (IACO) and the Pan American Health Organization (PAHO)/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.

The data from monthly reports are supplemented with additional information at the annual Carter Center River Blindness Elimination Program 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 and establish new treatment

objectives for the coming year. Data on Mectizan® treatments provided by other programs/partners operating in other parts of Carter Center-assisted countries also are discussed (if these data are available), as well as results from research initiatives. The Carter Center reports its final treatment figures to the Mectizan Donation Program (MDP), Merck, and the NGDO Onchocerciasis Coordination Group. The countries report their results to WHO through their national Ministries of Health.

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 geographical stratification of the country. Cumulative treatment figures for the year are compared to Ultimate Treatment Goals (UTGs), i.e., the eligible at-risk population that is targeted. Treatment coverage is calculated with treatments as the numerator and UTG as the denominator. UTG figures typically increase by about five percent annually to account for normal population growth.

The eligible populations of at-risk villages (ARVs) targeted for active 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 (treatment may be given one week or more after parturition); therefore, all adult women are included in the UTG calculation. In practice, the UTG is established by ARV census 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. WHO uses total population as their treatment denominator, so RBEP routinely reports both coverage of eligible population (UTG) and coverage of total population ("therapeutic coverage") to satisfy those program's 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 18-20% less than UTG (eligible) population coverage, in accord with population pyramids in areas being served, where approximately 20% of the population is under 5 years of age or otherwise (sick or pregnant) ineligible for Mectizan® treatment (see example below, Nigeria).



[1]

The UTG(2) and UTG(4) denominators are used by elimination programs where semiannual or quarterly treatments are delivered: 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) 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, where large sections of the population are highly mobile and are often from non-endemic areas.

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

ANNEX 4: List of Program Review Participants (*attendees of all 21 Reviews)

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Ms. Marsha Base
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Ms. Kelly Callahan
Ms. Kenya Casey
Dr. Yohannes Dawd
Mr. Don Denard
Ms. Janie French
Mr. Belachew Gebresadik
Ms. Emily Griswold
Ms. Shakia Guest
Ms. Madelle Hatch
Mr. Andrew Heacox
Dr. Rafe Henderson
Ms. Lauri Hudson-Davis
Dr. Moses Katabarwa
Mr. Curtis Kohlhaas
Ms. Nicole Kruse
Dr. Scott Nash
Ms. Anne Nguyen
Dr. Gregory Noland
Amb. Mary Ann Peters
Ms. Lindsay Rakers
Ms. Faith Randolph
Dr. Frank Richards
Dr. Ernesto Ruiz-Tiben
Ms. Lauren Shewmaker
Mrs. Janet Shin
Dr. Dean Sienko
Mr. Randall Slaven
Ms. Emily Staub
Ms. Aisha Stewart
Mr. Marc Tewari
Mr. Craig Withers
Ms. Zeldayah Wright
Ms. Eva Zamarripa

The Carter Center Field Office Staff

Dr. Nabil AwadAlla
Dr. Abel Eigege
Mr. Yemane Kejela Elill
Ms. Maymoona Eltayeb
Dr. Emmanuel Emukah
Ms. Peace Habomugisha
Dr. Cephas Ityonzughul
Mr. Tewodros Mehamed
Dr. Emmanuel Miri
Mr. Aderajew Mohammed
Ms. Alba Lucía Morales
Mr. Julius Musigire
Dr. Adamu Sallau
Dr. Mauricio Sauerbrey
Ms. Harriet Sengendo
Mr. Fetene Mihretu Sheta
Dr. Zerihun Tadesse

Country Representatives

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Dr. Chukwuma Anyaike
Mr. Christopher Katongole
Mr. Makoy Samuel Yibi
Dr. Edridah Muheki Tukahebwa
Mr. Nebiyu Negussu
Dr. Evelyn Ngige
Mr. Asam Zroug

University and NGDO Personnel & Special Guests

Capt. Stephanie Bialek – CDC
Dr. Vitaliano Cama – CDC
Dr. Paul Cantey – WHO
Dr. Stacy Dalvin – Children Without Worms
Dr. Christine Dubray – CDC
Dr. Katherine Gass – The Task Force for Global Health
Dr. Rafe Henderson
Mr. Paul Josephson – Huffington Post
Mr. Pascal Lutumba – The Task Force for Global Health
Dr. Barbara Marston – CDC
Dr. Deborah McFarland – Emory University
Prof. Edwin Michael – University of Notre Dame
Dr. Santiago Nicholls – PAHO
Dr. Gawrie Nirdoshi Lokue Galappaththy – WHO
Prof. B.E.B Nwoke – Imo State University Owerri
Dr. Kisito Ogoussan – The Task Force for Global Health
Dr. Eric Ottesen – The Task Force for Global Health
Capt. Monica Parise – CDC
Prof. Rory Post – LSHTM
Ms. Maria Rebollo Polo – WHO
Ms. Morgan Smith – University of Notre Dame
Dr. Yao Sodahlon – The Task Force for Global Health
Ms. Sarah Sullivan – The Task Force for Global Health
Dr. Thomas Unnasch – University of South Florida
Mr. Paul Weiss – Emory University
Dr. Stephen Yeh – Emory University
Mr. Phillip Albano – LCIF

ANNEX 4: List of Program Review Participants (*attendees of all 21 Reviews) - *continued*

University and NGDO Personnel & Special Guests

Hon. Tebebe Y. Berhan – LCIF
Mr. Benjamin Binagwa – RTI International
Mr. Daniel Cohn – RTI International
Ms. Amy Doherty – RTI International
Mr. Philip Downs – Sightsavers
Ms. Lora du Moulin – The ELMA Philanthropies
Ms. Minne Iwamoto – GSK
Ms. Juno Lawrence Jaffer – USAID
Dr. CarriAyne Jones – British Consulate General
Dr. Kayode Laro – Consulate General of Nigeria
Mr. Warren Lancaster – The END Fund
Ms. Theresa McCoy – Merck & Co. Inc.
Mr. Aryc Mosher – USAID
Mr. Johnson Ngorok – Sightsavers
Mr. Bolivar Pou – FHI360
Dr. David Ross – The Task Force for Global Health
Ms. Gretchen Stoddard – IZUMI Foundation
Ms. Jamie Tallant –The END Fund
Dr. Jordan Tappero – BMGF
Ms. Wangeci Thuo – RTI International
Ms. Yuko Yoshida – IZUMI Foundation
Mr. Abrahams Okoliko – Consulate of Nigeria

ANNEX 5: AGENDA

Twenty-Second Annual Carter Center River Blindness Elimination
Program Review Agenda
Wednesday, March 14 - Friday, March 16, 2018
The Carter Center, Atlanta GA

Day 1: Wednesday, March 14, 2018		
09:00	*Shuttle Pickup at Hotel*	
9:15-10:00	*Continental Breakfast*	
Chair: Dr. Frank Richards		
10:00-10:05 10:05-10:30	Welcome Overview and Introduction	Dr. Dean Sienko Dr. Frank Richards
10:30-10:55 10:55-11:05	Special Intervention Zones: Brazil-Venezuela Border (The Yanomami) *Discussion*	Ms. Alba Lucia Morales
11:05-11:35	*Group Photo and Coffee Break*	
11:35-12:05 12:05-12:15	Special Intervention Zones: Ethiopia and Sudan - Stop MDA *Discussion*	Dr. Zerihun Tadese Mr. Asam Zroug
12:15-12:30 12:30-12:40	Special Intervention Zones: Uganda and DRC *Discussion*	Dr. Moses Katabarwa
12:40-12:50	Huffington Post: Virtual Reality	Paul Josephson
12:50-2:20	*Lunch and Huffington Post Virtual Reality Viewing*	
2:20-2:50 2:50-3:00	Nigeria: Assessments to Stop RB MDA in Plateau & Nasarawa *Discussion*	Dr. Emmanuel Miri
3:00-3:40 3:40-3:50	Nigeria: Elimination of LF & Upcoming SCH/STH Assessments in Plateau/Nasarawa *Discussion*	Dr. Abel Eigege
3:50-4:00 4:00-4:10	Summary Table of Stop MDA for RB and LF in RBEP *Discussion*	Ms. Emily Griswold
04:10	*Session Adjourned*	
04:15	*Shuttle Departs for Hotel*	
05:30	*Atlantic Station Shopping Trip - Pickup from Hotel*	

Twenty-Second Annual Carter Center River Blindness Elimination
Program Review Agenda
Wednesday, March 14 - Friday, March 16, 2018
The Carter Center, Atlanta GA

Day 2: Thursday, March 15, 2018		
08:00	*Shuttle Pickup at Hotel*	
8:30-9:00	*Continental Breakfast*	
Morning Session Chair: Dr. Mauricio Sauerbrey		
9:00-9:30 9:30-9:45	Nigeria: Treatments-Southeast and Plateau/Nasarawa States *Discussion*	Dr. Cephas Ityonzughul
9:45-10:00 10:00-10:10	Comparison of Coverage Survey Methodologies *Discussion*	Ms. Emily Griswold
10:10-10:40	*Coffee Break*	
10:40-11:10 11:10-11:20	Nigeria: Training, Integration & Community Ownership *Discussion*	Dr. Adamu Sallau
11:20-11:35 11:35-11:45	Nigeria: LF Elimination: What's Next After Passing TAS-3? *Discussion*	Dr. Gregory Noland
11:45-12:00 12:00-12:10	Nigeria: Impact - LF Treatment on Hypo-endemic Onchocerciasis *Discussion*	Ms. Emily Griswold
12:10-1:40	*Lunch*	
Afternoon Session Chair: Ms. Peace Habomugisha		
1:40-1:55 1:55-2:00	Nigeria: OV16 Results - *Loa loa* Study *Discussion*	Ms. Lindsay Rakers
2:00-2:30 2:30-2:40	Ethiopia: Treatments and Impact *Discussion*	Mr. Aderajew Mohammed
2:40-3:10 3:10-3:25	Ethiopia: Training, Integration & Community Ownership *Discussion*	Dr. Zerihun Tadesse
3:25-3:55	*Coffee Break*	
3:55-4:25 4:25-4:35	Ethiopia: NTD Integration *Discussion*	Mr. Nebiyu Negussu
4:35-5:05 5:05-5:15	WHO: Onchocerciasis Update with Focus on Mapping *Discussion*	Dr. Paul Cantey
05:15	*Session Adjourned*	
05:15	*Reception: The Carter Center "Jimmy Carter Museum & Library" Lobby*	
07:15	*Shuttle Departs for Hotel*	

Twenty-Second Annual Carter Center River Blindness Elimination
Program Review Agenda
Wednesday, March 14 - Friday, March 16, 2018
The Carter Center, Atlanta GA

Day 3: Friday, March 16, 2018		
08:00	*Shuttle Pickup at Hotel*	
8:30-9:00	*Continental Breakfast*	
Morning Session Chair: Dr. Zerihun Tadesse		
9:00-9:30 9:30-9:45	Uganda: Treatments and Impact *Discussion*	Dr. Edridah Tukahebwa
9:45-10:15 10:15-10:30	Uganda: Training, Integration & Community Ownership *Discussion*	Ms. Peace Habomugisha
10:30-11:00	*Coffee Break*	
11:00-11:15 11:15-11:25	The Hot Spot in Ethiopia *Discussion*	Prof. Rory Post
11:25-11:55 11:55-12:10	Sudan: Treatments and South Darfur Challenges: Radom and Blue Nile *Discussion*	Dr. Nabil Aziz
12:10-1:40	*Lunch*	
Afternoon Session Chair: Dr. Emmanuel Miri		
1:40-2:10 2:10-2:30	OEPA: Overview 2017 *Discussion*	Dr. Mauricio Sauerbrey
2:30-3:00 3:00-3:20	Modeling update (with report on Gates Modeling Consortium) *Discussion*	Prof. Edwin Michael
3:20-3:50	*Coffee Break*	
3:50-4:20 4:20-4:40	Mectizan Donation Program: Update with Presentation on IDA *Discussion*	Dr. Yao Sodahlon
4:40-5:10	Summary and Closure of the Twenty-Second Session	Dr. Frank Richards
05:10	***2018 Carter Center River Blindness Elimination Program Review Adjourned***	
05:15	*Shuttle Departs for Hotel*	

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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 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) and albendazole (donated by GSK/The Task Force for Global Health), or diethylcarbamazine (DEC) 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 once- or 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 health education (HE) and annual drug combination therapy with albendazole and Mectizan®. The manufacturers of the drugs have global donation programs for LF: GSK donates albendazole and Merck donates Mectizan®. After disease mapping in 1998-99, The MDA program was launched in 2000. After years of high treatment coverage, LF transmission was broken in the two states in 2012. A TAS survey in 2017 confirmed that the five-year post-treatment surveillance period was successful and that LF had been eliminated as a public health problem. Seven million people are no longer at risk of LF as a result of this successful program. Post-elimination surveillance continues in the two states, which are surrounded by LF endemic areas (see Figure 1 below). LF morbidity work to help the state ministries strengthen referral networks for management of lymphedema and hydrocele surgery remains an important activity.

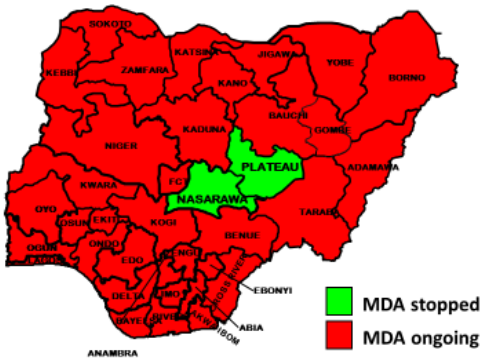


Figure 1: Elimination of LF in Plateau and Nasarawa states in 2017

***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 in 2014, 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 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 enough 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 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® is 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 mass distributed two per household throughout the majority of Nigeria for malaria prevention; this supplemented health education and drug combination therapy is one more way to fight LF. The national malaria and lymphatic filariasis programs are 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 the Center's Malaria Program closed in 2014.

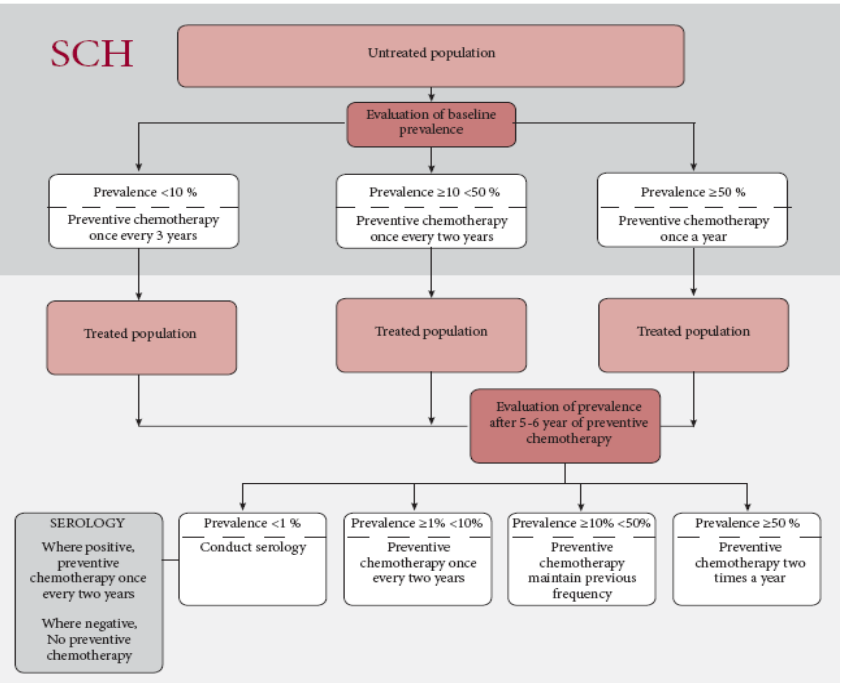
LF in Ethiopia: The much smaller LF program in Ethiopia was launched in 2008, in tandem with The Carter Center's Malaria Program, which was engaged in assisting the FMOH to distribute LLINs. The Ethiopian Malaria Program completed the mass distribution of LLINs throughout the malaria-endemic areas of 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 were one reason the FMOH was convinced to launch the LF MDA effort. LF antigenemia surveys were first conducted in several zones in western Ethiopia in areas where MDA for RB was ongoing (results reported in Shiferaw et al. *Trans Royal Soc Trop Med Hyg* 2011). With GSK support, The Carter Center assisted in the launching of a Ministry of Health 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 their first TAS (in 2018) and begun the five-year post-treatment surveillance period. Although LF mapping for Ethiopia has been completed, the Federal Ministry of Health identified the need for further surveys (Rebollo et al., *PLoS Negl Trop Dis* 2015).

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

SCHISTOSOMIASIS

Schistosomiasis (SCH) is a parasitic disease acquired from contact with infected fresh water in which infected snails live. The cercarial stages of the parasite leave the snails, penetrate the skin, and develop into adult male and female worms that reside in venules of the intestines (*Schistosoma mansoni*) or bladder and genitals (*S. haematobium*). It is important to note that in Africa where The Carter Center is working, SCH exists as two different infections with different geographical distributions, epidemiology, and disease patterns (morbidity). In both conditions, female worms lay thousands of eggs that exit the body in feces (*Schistosoma mansoni*) or urine (*S. haematobium*). 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 miracidae penetrate and infect the snails, and the miracidium transforms and multiplies, resulting in a single snail releasing thousands of cercariae, 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, school-aged children (ages 5 to 14) have the greatest number of adult worms and act as the main disseminators of this infection by passing large numbers of eggs in their urine and feces. 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. However, all age groups would need to be treated to have the greatest impact on transmission.



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

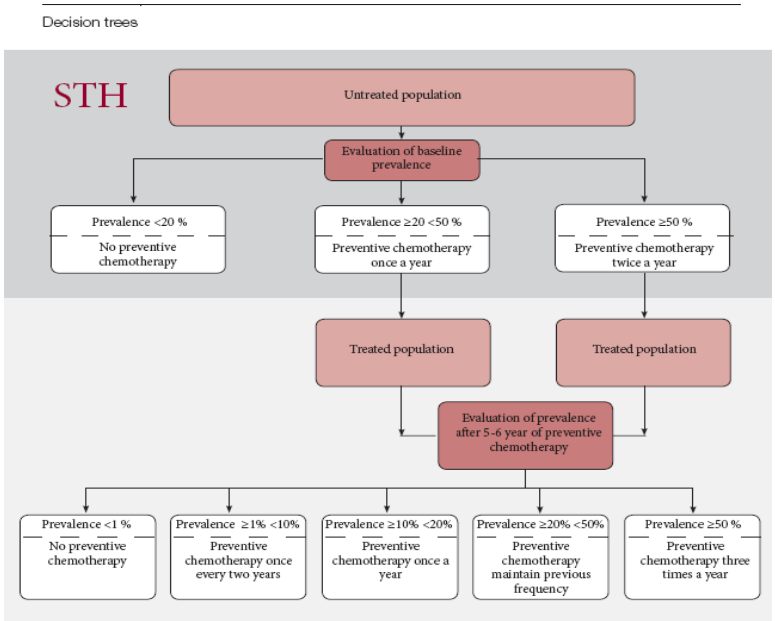
The Carter Center's SCH programs follow WHO guidelines for disease (morbidity) control; transmission is unlikely to be interrupted until open defecation and urination (or reduction of release of raw sewage into fresh water) are halted through deployment and use of sanitary systems. MDA with praziquantel under current WHO guidelines will have little to no impact on infected snails (which live for many months) or developing (pre-adult) worms in humans. In other words, persons treated are not cured of their developing infections, and/or become reinfected within hours/days of receiving their praziquantel treatment.

The current WHO guidelines for schistosomiasis treatment (above) focus on providing treatment to school-aged children and often call for praziquantel preventive chemotherapy once every two years. For this reason, treatment numbers in the same district can be very different from year-to-year.

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 often have their heaviest infections in adults.

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 eggs are passed to humans either by ingestion of fecally-contaminated food or water (*Ascaris* and *Trichuris*) or through penetration of the skin by larvae (the hookworms *Ancylostoma* and *Necator*). The infective eggs of the whipworm hatch, mature, mate, and lay eggs in the intestines within 70-90 days. Once hatched, both ascaris and hookworm larvae will 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.



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

Heavy infections result in blood loss which can lead to anemia and hypoproteinemia. In children, this can lead to poor physical and developmental growth causing stunting and decreased mental acuity. In adults, anemia reduces productivity and can be very dangerous in reproductive-aged (menstruating) women. In some cases, pulmonary complications can occur caused by the 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 (as we have seen for SCH) focus on providing treatment to school-aged children and often call for preventive chemotherapy once every two years. For this reason, treatment numbers in the same district can be very different from year-to-year. 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. However, because hookworm has a high prevalence in adults, the current WHO guidelines above (focused on STH control through MDA targeted at school-aged children) ought to target adults (especially adult women), as well.

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. *Ascaris* is most sensitive to treatment, while *Trichuris* is least sensitive. Hookworm is not sensitive to ivermectin. However, ivermectin/albendazole combinations given for LF are the best treatment for STH, including *Trichuris*.

The challenges in implementing schistosomiasis and STH programs in TCC Nigeria programs have included: 1) complex WHO guidelines (shown above); 2) unclear global goals (if this is for morbidity control, why are adults not treated for hookworm? Elimination of STH and SCH would require a major sanitation infrastructure investment); 3) alternating year treatment schedules for schistosomiasis (including treatment programs every third year); 4) twice-per-year treatment programs for STH; 5) a focus on ministry of education partners ('school-based') rather than ministry of health, which is more experienced at MDA activities and an effective, long-term partner of the integrated RBEP; 6) a focus on teachers (in schools) rather than community distributors (house to house); 7) exclusion of potentially infected preschool children, unenrolled children, girls, and adults (in most cases); 8) algorithms with thresholds statistically indistinguishable from one another; 9) mapping based on averages resulting in exclusion of communities that need interventions; 10) difficult calculations of coverage due to challenges with denominator determinations; 11) difficulty in justifying the closure of a long-standing distribution infrastructure that works well (community-based) to start a new approach (school-based); and 12) 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.

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

Jacob BG, Loum D, Lakwo TL, Katholi CR, Habomugisha P, Byamukama E, Tukahebwa E, Cupp EW, Unnasch TR. Community-directed vector control to supplement mass drug distribution for onchocerciasis elimination in the Madi mid-North focus of Northern Uganda. Published: 2018 Aug 27; https://doi.org/10.1371/journal.pntd.0006702

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