Supplementary Information

Modelling anti-Ov16 Seroprevalence for the Control and Elimination of Onchocerciasis

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Supplementary Tables and Figures

Table S1. Parameters used for calibrating EPIONCHO-IBM to observed microfilarial prevalence data from 4,257 individuals aged 5-90 years living in 58 onchocerciasis hypoendemic (treatment-naïve) communities in Gabon[1]

Annual biting rate (ABR, no. bites/person/uear) prior range	**Inter-individual exposure heterogeneity parameter, k_E**	**ABR best-fit value (range)[a]**
60 – 120	0.2	76 (74 – 76)
150 – 210	0.3	179 (177 – 180)

[a] Range of ABRs within 95% Wilson 95% confidence interval of observed prevalence estimate (7.1%-8.7%)[1].

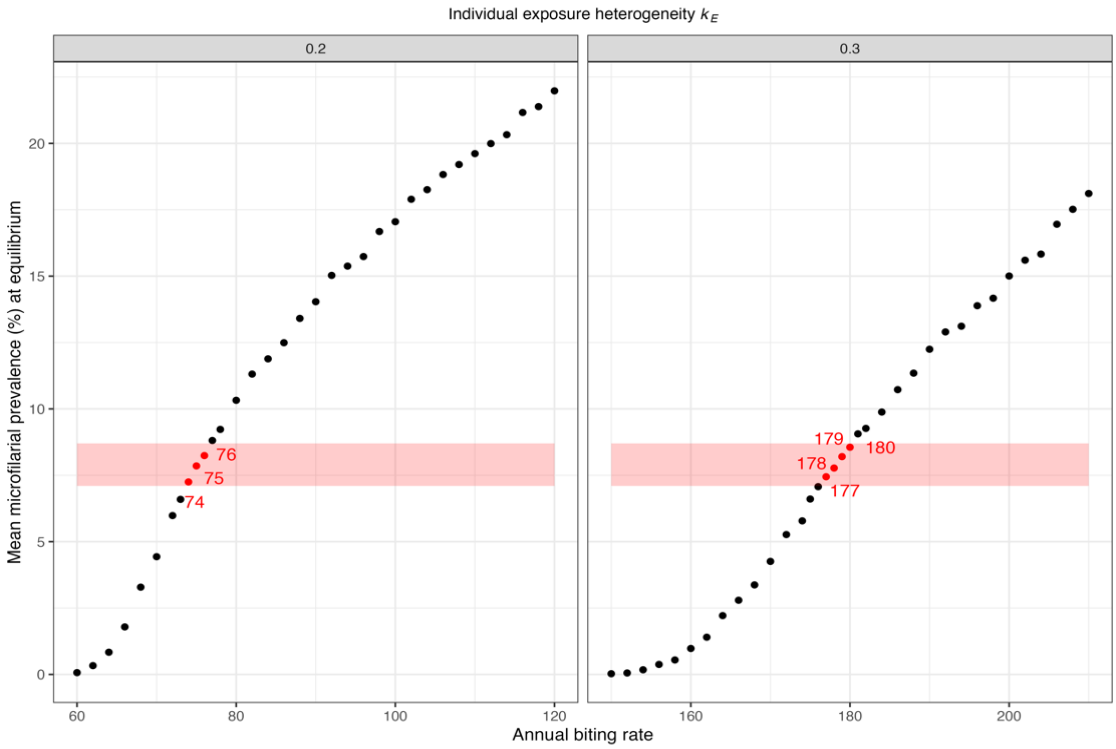

Figure S1. Observed and predicted microfilarial prevalence in individuals aged 5 years and older for different combinations of the annual biting rate (ABR) and inter-individual exposure heterogeneity parameter, k_E. The predicted microfilarial prevalence values (black circles) were generated using EPIONCHO-IBM after a 100-year burn-in period. The ABR-k_E values within the 95% confidence interval of the observed microfilarial prevalence estimate from 4,257 individuals from 58 hypoendemic treatment-naïve communities in Gabon are highlighted in red[1]. Left panel presents the results for k_E = 0.2; right panel presntes the results for k_E = 0.3. The best-fit ABR of 76 bites/person/year and k_E = 0.2 was selected.

Table S2. Parameters used for calibrating EPIONCHO-IBM to model-derived pre-intervention microfilarial prevalence estimates from 1,455 individuals aged 5-80 years living in four prefectures in Togo[2]

Prefecture	Number of individuals examined by skin-snip microscopy	Inferred pre-intervention microfilarial prevalence estimate (endemicity level)[a]	Annual biting rate range (no. bites/person/year)
Ôti/Kpendjal	324	70% (hyperendemic)	1,000 – 5,000
Kéran	539	85% (holoendemic)	6,000 – 60,000
Bassar	592	70% (hyperendemic)	1,000 – 5,000

[a] Inferred by aggregating model-derived village-level estimates presented in Amaral et al.[3]

Table S3. Sensitivity and specificity estimates for the SD BIOLINE Ov16 rapid diagnostic test (Ov16 RDT) using whole blood

Sensitivity	Specificity	Reference diagnostic	Sample size	Reference
51%	94.8%	Skin-snip microscopy	4,257	Atsame et al.[1]
60%	94%	Skin-snip microscopy	400	Nikièma et al.[4]
40%	98.9%	Ov16 ELISA (Tanzania)	931	Ogawa et al.[5]
28.4%	99.9%	Ov16 ELISA (Togo)	999	Ogawa et al.[5]
40% – 60%	–	Skin-snip microscopy	–	Ogunrinade et al.[6]

Table S4. Quantitative assessment of goodness-of-fit of EPIONCHO-IBM-predicted versus observed anti-Ov16 IgG4 seroprevalence from 4,257 individuals living in 58 hypoendemic communities in Gabon for each seroconversion-seroreversion hypothesis, assuming different sensitivity and specificity of the SD BIOLINE Ov16-RDT

Specificity	Sensitivity	Hypothesis	Unnormalised Mean Square Error (MSE)[a] (95% uncertainty interval)		
			No seroreversion (i)	Immediate seroreversion (ii)	Finite seroreversion (iii)
99%	40%	H1	63.54 (62.96 – 64.13)	74.76 (74.60 – 74.92)	16.20 (15.97 – 16.42)
		H2	62.49 (61.92 – 63.07)	74.76 (74.60 – 74.92)	15.13 (14.91 – 15.34)
		H3	61.43 (60.86 – 62.00)	14.23 (14.02 – 14.45)	14.12 (13.91 – 14.32)
		H4	**6.65 (6.52 – 6.77)[b, c]**	28.57 (28.30 – 28.85)	10.81 (10.62 – 10.99)
	50%	H1	141.41 (140.43 – 142.39)	74.81 (74.65 – 74.98)	38.50 (38.07 – 38.93)
		H2	139.51 (138.53 – 140.48)	74.80 (74.64 – 74.96)	35.91 (35.50 – 36.32)
		H3	137.49 (136.52 – 138.45)	33.33 (32.92 – 33.75)	33.41 (33.02 – 33.80)
		H4	13.76 (13.51 – 14.00)	21 (20.74 – 21.26)	**6.48 (6.35 – 6.61)[b, c]**
	60%	H1	252.21 (250.82 – 253.60)	74.84 (74.68 – 74.99)	76.13 (75.42 – 76.84)
		H2	249.08 (247.70 – 250.46)	74.84 (74.68 – 75.00)	71.52 (70.83 – 72.20)
		H3	245.79 (244.42 – 247.16)	66.49 (65.82 – 67.17)	67.03 (66.37 – 67.69)
		H4	30.67 (30.25 – 31.08)	14.86 (14.63 – 15.10)	**7.23 (7.08 – 7.37)[b]**
97%	40%	H1	81.74 (81.06 – 82.42)	47.89 (47.66 – 48.11)	26.7 (26.38 – 27.03)
		H2	80.54 (79.86 – 81.21)	47.89 (47.66 – 48.11)	25.18 (24.86 – 25.49)
		H3	79.26 (78.59 – 79.93)	23.79 (23.5 – 24.07)	23.68 (23.38 – 23.98)
		H4	9.25 (9.07 – 9.42)	16.41 (16.19 – 16.62)	**7.1 (6.96 – 7.24)[b]**
	50%	H1	168.60 (167.55 – 169.65)	47.56 (47.34 – 47.78)	57.13 (56.59 – 57.68)
		H2	166.41 (165.36 – 167.45)	47.56 (47.33 – 47.78)	53.98 (53.46 – 54.51)
		H3	164.14 (163.11 – 165.18)	50.50 (49.97 – 51.02)	50.91 (50.4 – 51.41)
		H4	22.19 (21.87 – 22.51)	11.56 (11.37 – 11.75)	**7.84 (7.69 – 7.98)[b]**
	60%	H1	288.30 (286.79 – 289.81)	47.49 (47.27 – 47.71)	102.40 (101.57 – 103.23)
		H2	284.93 (283.43 – 286.43)	47.49 (47.27 – 47.72)	97.13 (96.33 – 97.93)
		H3	281.32 (279.83 – 282.81)	91.67 (90.88 – 92.47)	91.99 (91.22 – 92.77)
		H4	45.54 (45.01 – 46.06)	**8.72 (8.56 – 8.89)[b]**	13.51 (13.27 – 13.74)
94%	40%	H1	115.75 (114.94 – 116.56)	21.94 (21.73 – 22.15)	50.37 (49.91 – 50.83)
		H2	114.30 (113.50 – 115.11)	21.95 (21.74 – 22.16)	48.22 (47.77 – 48.66)
		H3	112.76 (111.96 – 113.56)	46.06 (45.63 – 46.49)	46.11 (45.68 – 46.55)
		H4	22.63 (22.33 – 22.93)	**10.01 (9.86 – 10.17)[b]**	12.4 (12.21 – 12.58)
	50%	H1	215.29 (214.12 – 216.46)	22.11 (21.9 – 22.33)	92.52 (91.8 – 93.24)
		H2	212.81 (211.64 – 213.98)	22.13 (21.91 – 22.34)	88.68 (87.98 – 89.39)
		H3	210.21 (209.05 – 211.36)	84.36 (83.69 – 85.04)	84.91 (84.22 – 85.59)
		H4	44.92 (44.44 – 45.40)	**10.22 (10.06 – 10.38)[b]**	20.6 (20.32 – 20.88)
	60%	H1	349.15 (347.53 – 350.76)	22.04 (21.83 – 22.25)	149.65 (148.62 – 150.67)
		H2	345.36 (343.75 – 346.96)	22.04 (21.83 – 22.25)	143.49 (142.5 – 144.48)
		H3	341.37 (339.77 – 342.96)	136.90 (135.89 – 137.92)	137.46 (136.49 – 138.43)
		H4	77.05 (76.36 – 77.74)	**12.22 (12.03 – 12.4)[b]**	33.75 (33.34 – 34.16)

[a] Mean squared error (MSE) is calculated by weighting the squared error (residual) for each age group by the proportion of observations within the given age group for each of 1,500 model repeats (stochastic simulations) and calculating the arithmetic mean and 95% uncertainty interval (2.5^{th} – 97.5^{th} quantiles of MSEs).

[b] Best-fitting hypothesis (lowest MSE value) for each combination of sensitivity and specificity.

[c] Best-fitting (lowest MSE value) overall, uncertainty intervals overlap.

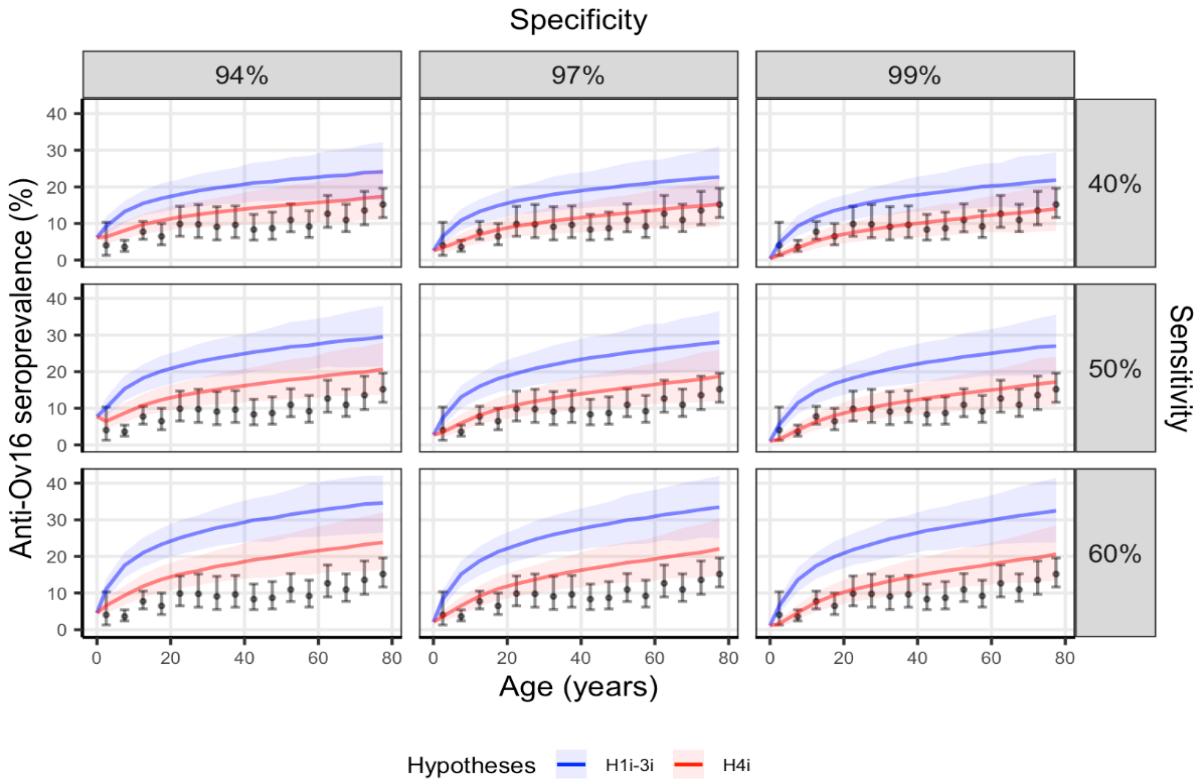

Figure S2. Observed and predicted anti-Ov16 IgG4 age-seroprevalence profiles for 4,257 individuals living in 58 ivermectin-naïve communities in Gabon, assuming no seroreversion. Solid coloured lines represent mean predicted age-seroprevalence profiles generated by EPIONCHO-IBM, calibrated to microfilarial prevalence estimates (Figure 1 of Main Text and Figure S1)[1] using an annual biting rate of 76 bites/person/year and an inter-individual exposure heterogeneity parameter of $k_E = 0.2$. Predictions were generated under different seroconversion hypotheses assuming no seroreversion and adjusted for varying diagnostic performance of the SD BIOLINE Ov16 rapid diagnostic test (Ov16 RDT) using whole blood. Blue lines represent seroconversion elicited by pre-patent infection (hypotheses H1i–H3i, aggregated); red lines represent seroconversion elicited by near-patent/patent infection (hypothesis H4i). Ov16 RDT specificity is varied by colum (94%, 97%, 99%), and sensitivity is varied by row (40%, 50%, 60%). Black circles show the observed seroprevalence estimates binned into 5-year age groups; the error bars are the associated 95% Wilson confidence intervals. For each hypothesis and diagnostic performance, the model-predicted means and 95% uncertainty intervals (2.5th to 97.5th quantiles of the simulated mean; shaded areas) were calculated from 1,500 stochastic repeats.

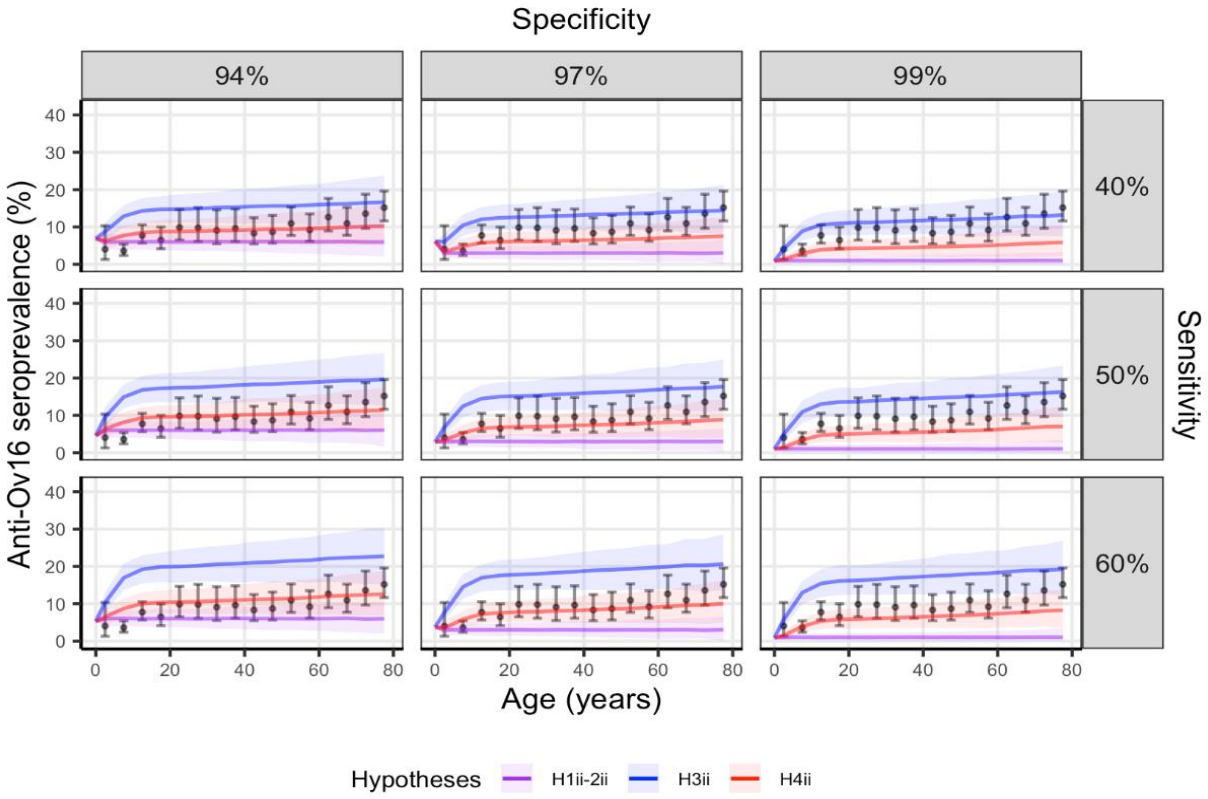

Figure S3. **Observed and predicted anti-Ov16 IgG4 age-seroprevalence profiles for 4,257 individuals living in 58 ivermectin-naïve communities in Gabon, assuming immediate seroreversion.** Solid coloured lines represent mean predicted age-seroprevalence profiles generated by EPIONCHO-IBM, calibrated to microfilarial prevalence estimates (Figure 1 of Main Text and Figure S1)[1] using an annual biting rate of 76 bites/person/year and an inter-individual exposure heterogeneity parameter of k_E = 0.2. Predictions were generated under different seroconversion hypotheses assuming immediate seroreversion and adjusted for varying diagnostic performance of the SD BIOLINE Ov16 rapid diagnostic test (Ov16 RDT) using whole blood. Purple lines represent seroconversion elicited by L3 larvae or L4-L5 moult (hypotheses H1ii–H2ii, aggregated); blue lines represent seroconversion elicited by any established worm of either sex (hypothesis H3ii); red lines represent seroconversion elicited by near-patent/patent infection (hypothesis H4ii). Ov16 RDT specificity is varied by colum (94%, 97%, 99%), and sensitivity is varied by row (40%, 50%, 60%). Black circles show the observed seroprevalence estimates binned into 5-year age groups; the error bars are the associated 95% Wilson confidence intervals. For each hypothesis and diagnostic performance, the model-predicted means and 95% uncertainty intervals (2.5th to 97.5th quantiles of the simulated mean; shaded areas) were calculated from 1,500 stochastic repeats.

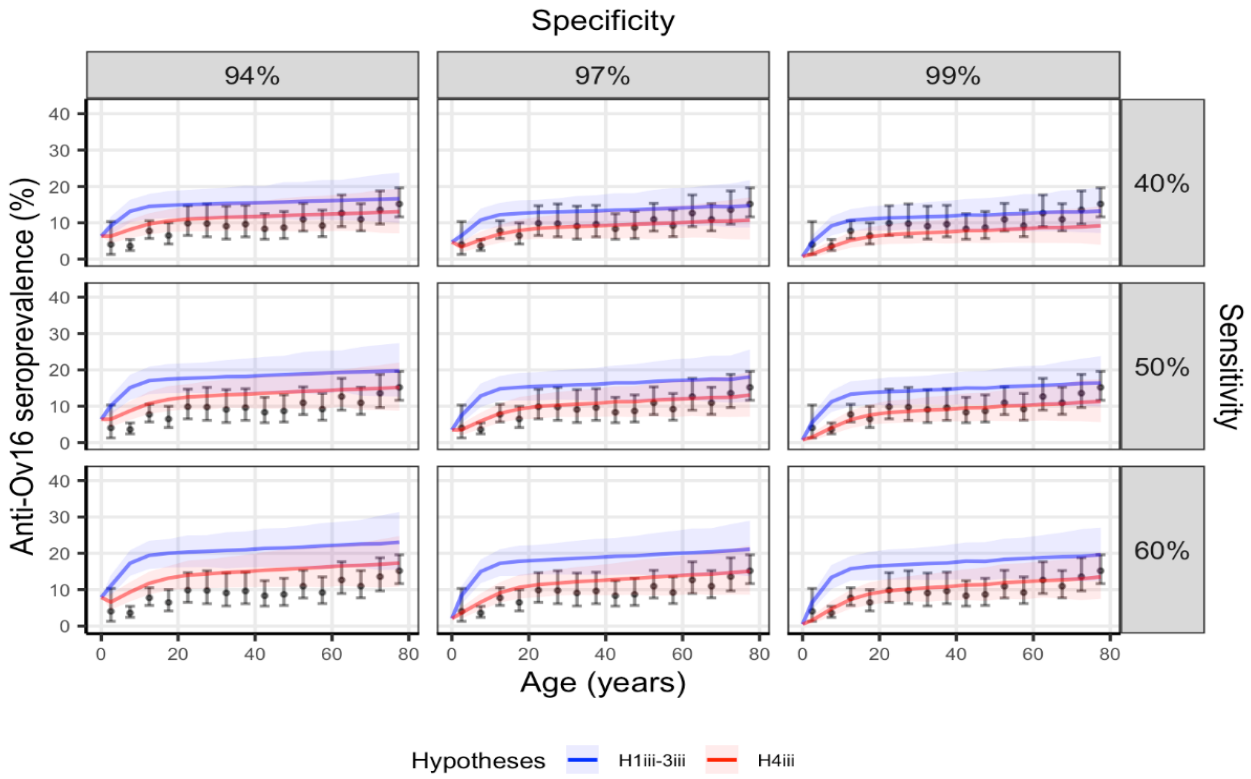

Figure S4. **Observed and predicted anti-Ov16 IgG4 age-seroprevalence profiles for 4,257 individuals living in 58 ivermectin-naïve communities in Gabon, assuming finite seroreversion.** Solid coloured lines represent mean predicted age-seroprevalence profiles generated by EPIONCHO-IBM, calibrated to microfilarial prevalence estimates (Figure 1 of Main Test and Figure S1)[1] using an annual biting rate of 76 bites/person/year and an inter-individual exposure heterogeneity parameter of k_E = 0.2. Predictions were generated under different seroconversion hypotheses assuming finite seroreversion and adjusted for varying diagnostic performance of the SD BIOLINE Ov16 rapid diagnostic test (Ov16 RDT) using whole blood. Blue lines represent seroconversion elicited by pre-patent infection (hypotheses H1iii–H3iii, aggregated); red lines represent seroconversion elicited by near-patent/patent infection (hypothesis H4iii). Ov16 RDT specificity is varied by colum (94%, 97%, 99%), and sensitivity is varied by row (40%, 50%, 60%). Black circles show the observed seroprevalence estimates binned into 5-year age groups; the error bars are the associated 95% Wilson confidence intervals. For each hypothesis and diagnostic performance, the model-predicted means and 95% uncertainty intervals (2.5th to 97.5th quantiles of the simulated mean; shaded areas) were calculated from 1,500 stochastic repeats.

Table S5. Categorizations and parameters defining the effectiveness of vector control (VC) and mass drug administration (MDA) in four prefectures of Togo for the period 1976-2015

Effectiveness categorization	Time period	Intervention	Frequency	Efficacy/coverage[a]	Systematic non-adherence[b]
Minimal	1976–2007[c]	VC	Continuous	60%	NA[d]
	1991–1995	MDA	Annual	50%	5%
	1996–2001	MDA	Annual	65%	5%
	2001–2003	MDA	Annual	65%	5%
	2003–2015	MDA	Biannual	65%	5%
Reference	1976–2007[c]	VC	Continuous	75%	NA[d]
	1991–1995	MDA	Annual	50%	2.5%
	1996–2001	MDA	Annual	65%	2.5%
	2001–2003	MDA	Annual	75%	2.5%
	2003–2015	MDA	Biannual	75%	2.5%
Enhanced	1976–2007[c]	VC	Continuous	90%	NA[d]
	1991–1995	MDA	Annual	65%	1%
	1996–2001	MDA	Annual	75%	1%
	2001–2003	MDA	Annual	80%	1%
	2003–2015	MDA	Biannual	80%	1%

[a] For vector control (VC), efficacy is the percentage reduction in the blackfly annual biting rate during the intervention; for mass drug administration (MDA), coverage is the percentage of the total population that receive ivermectin at each round.

[b] Systematic non-adherence is the percentage of the eligible population (aged ≥ 5 years) who never participate in ivermectin MDA.

[c] Vector control stopped in 1993 for Ôti/Kpendjal prefectures[3].

[d] Systematic non-adherence is not applicable to vector control.

Table S6. EPIONCHO-IBM-predicted and observed microfilarial prevalence estimates from 1,455 individuals living in four prefectures in Togo after 39 years of intervention[2]

Prefecture	**Intervention effectiveness[a]**	**Predicted microfilarial prevalence in 2015 (95% uncertainty interval)**	**Observed microfilarial prevalence in 2015 (95% confidence interval)[b]**
Ôti/Kpendjal	Mixed[c]	2.6% (0% – 9.0%)	2.5% (0% – 4.9%)
Kéran	Enhanced	11.8% (0% – 24.7%)	10.2% (8.3% – 12.1%)
Bassar	Minimal	3.3% (0.1% – 8.2%)	3.4% (1.5% – 5.2%)
Prefectures combined	–	5.8% (0.9% – 11.5%)	5.9% (4.6% – 7.1%)

[a] Parameters defining intervention effectiveness are given in Table S5.

[b] Mean and 95% (Wilson score) confidence interval calculated from data for three villages in Ôti/Kpendjal (Pancérys, Boutchakou and Koukoumbou); four villages in Kéran (Goulbi, Tchitchira, Koutougou Solla and Kpantiiyagou), and four villages in Bassar (Bawlesi, Mô-village, Katcha-Konkomba and Saboundi), from Komlan et al.[2]

[c] Each of the three villages in Ôti/Kpendjal were identified as having different intervention effectiveness, with simulations integrating this variability (see Supplementary Methods S2).

Table S7. Estimates of sensitivity and specificity for the horseradish peroxidase (HRP) Ov16 ELISA

Age range (yr)	Sensitivity	Specificity	Reference diagnostic	Reference
≥10	81%	–	Skin-snip microscopy or nodule palpation	Ogunrinade et al.[6]
≥10	95%	–	Skin-snip microscopy or or nodule palpation	Ogunrinade et al.[6]
All ages	84%	94%	Skin-snip microscopy	Golden et al.[7]
All ages	60%	75%	Skin-snip microscopy or skin-snip PCR positive	Golden et al.[7]
<11	80%	97%	Laboratory-confirmed active infection	Golden et al.[8]
All Ages	71.4%	71.1%	Skin-snip microscopy	Komlan et al.[2]
–	53%	>99%	Skin-snip microscopy	NTDSC, TFGH[9]
–	78%	>99%	Skin-snip microscopy	NTDSC, TFGH[9]
15 – 30 (IQR)[a]	83%	84.8%	Skin-snip microscopy/serostatus (concordant Ov16 ELISA & Ov16 RDT)	Hotterbeekx et al.[10]
All ages	82.5%	55.7%	Skin-snip microscopy	Djune-Yemeli et al.[11]

[a] IQR = Interquartile range.

Table S8. Prefecture-specific predictive performance of EPIONCHO-IBM-projected versus observed anti-Ov16 IgG4 seroprevalence from 576 individuals living in four prefectures in Togo after 39 years of intervention, assuming different sensitivity and specificity of the horseradish peroxidase (HRP) Ov16 ELISA

Specificity	Sensitivity	Unnormalised Mean Squared Error (MSE) (95% uncertainty interval)[a]					
		Ôti/Kpendjal		Kéran		Bassar	
		No seroreversion (H4i)	Finite seroreversion (H4iii)	No seroreversion (H4i)	Finite seroreversion (H4iii)	No seroreversion (H4i)	Finite seroreversion (H4iii)
95%	70%	565.20 (553.09 – 577.31)	**212.59 (203.03 – 222.15)[b]**	41.41 (37.80 – 45.02)	241.11 (222.44 – 259.78)	72.17 (69.34 – 74.99)	60.32 (56.32 – 64.32)
	80%	820.08 (803.84 – 836.31)	317.75 (304.05 – 331.44)	54.29 (51.50 – 57.07)	178.11 (160.43 – 195.79)	174.46 (169.45 – 179.47)	47.55 (44.07 – 51.04)
	85%	963.73 (945.19 – 982.27)	379.60 (363.70 – 395.50)	92.72 (88.59 – 96.86)	165.85 (148.75 – 182.96)	239.60 (233.38 – 245.83)	47.28 (43.94 – 50.63)
85%	70%	821.00 (808.26 – 833.74)	406.59 (393.62 – 419.56)	**25.62 (23.91 – 27.34)[b]**	119.67 (108.75 – 130.60)	174.84 (170.63 – 179.04)	**27.44 (25.71 – 29.17)[b]**
	80%	1125.12 (1107.94 – 1142.30)	552.78 (535.48 – 570.07)	83.32 (79.76 – 86.88)	100.94 (90.84 – 111.05)	329.15 (322.65 – 335.65)	55.35 (52.12 – 58.57)
	85%	1293.51 (1274.11 – 1312.92)	633.89 (613.93 – 653.86)	144.77 (139.21 – 150.33)	112.33 (102.74 – 121.91)	421.80 (414.30 – 429.29)	74.35 (70.32 – 78.38)
70%	70%	1312.45 (1299.15 – 1325.74)	881.21 (865.54 – 896.89)	53.42 (51.17 – 55.67)	38.96 (35.86 – 42.06)	434.15 (428.21 – 440.09)	175.47 (170.43 – 180.52)
	80%	1692.34 (1674.98 – 1709.71)	1090.85 (1070.12 – 1111.59)	182.17 (176.77 – 187.57)	90.65 (86.56 – 94.73)	660.04 (652.03 – 668.06)	259.67 (252.48 – 266.85)
	85%	1891.49 (1871.88 – 1911.1)	1195.04 (1171.59 – 1218.49)	274.61 (267.57 – 281.65)	136.41 (130.89 – 141.93)	786.15 (776.89 – 795.41)	308.46 (299.98 – 316.94)

[a] Uncertainty intervals calculated as the 2.5th to 97.5th quantile of the mean squared error from 1,500 repeat (stochastic) simulations.

[b] Smallest mean squared error indicates best predictive performance.

Table S9. Aggregated (across all prefectures) predictive performance of EPIONCHO-IBM-projected versus observed anti-Ov16 IgG4 seroprevalence from 576 individuals living in four prefectures in Togo after 39 years of intervention, assuming different sensitivity and specificity of the horseradish peroxidase (HRP) Ov16 ELISA

Specificity	Sensitivity	Aggregated unnormalised Mean Squared Error (MSE)[a] (95% uncertainty interval)[b]	
		No seroreversion (H4i)	Finite seroreversion (H4iii)
95%	70%	246.81 (239.96 – 253.67)	**218.54 (204.34 – 232.73)[b]**
	80%	358.41 (350.3 – 366.52)	**224.26 (209.02 – 239.50)[b]**
	85%	438.83 (429.02 – 448.65)	**241.63 (225.85 – 257.40)[b]**
85%	70%	343.02 (336.9 – 349.15)	**225.76 (214.61 – 236.91)[b]**
	80%	501.08 (492.1 – 510.06)	273.87 (261.41 – 286.33)
	85%	605.18 (594.18 – 616.18)	312.72 (299.46 – 325.97)
70%	70%	562.94 (556.22 – 569.66)	373.87 (365.8 – 381.95)
	80%	793.21 (783.07 – 803.36)	488.27 (477.58 – 498.96)
	85%	928.02 (916.04 – 940.00)	556.51 (543.91 – 569.12)

[a] The aggregated mean squared error (and its associated uncertainty interval) was calculated by weighting the values for each sensitivity, specificity, and hypothesis combination according to the proportion of the population examined in each prefecture (Ôti/Kpendjal: 39.4%, Kéran: 55.2%, Bassar: 5.4%). The weighted values were then summed to obtain the final value.

[b] Uncertainty intervals calculated as the 2.5th to 97.5th quantile of the mean squared error from 1,500 repeat (stochastic) simulations.

Table S10. Policy-Relevant Items for Reporting Models in Epidemiology of Neglected Tropical Diseases (PRIME-NTD) summary table

For the analyses presented, we adhered to the Five Principles of the Neglected Tropical Diseases (NTD) Modelling Consortium for good practice in policy-relevant NTD modelling[12]. Table S10 briefly describes the five tenets, how they were fulfilled, and where in the Main Text and/or Supplementary Information file they can be found.

Principle	What has been done to satisfy the principle?	Where in the manuscript is this described?
Stakeholder engagement	Discussion with both modelling-focused collaborators and policy-focused collaborators on the underlying data and model results	Author list, acknolwedgements
Complete model documentation	Link to documented code and vignettes have been provided, in addition to a description of additions to the model, and a reference to the full description of the model	Methods, Supplementary Methods, References, Code Accessibility section
Complete description of data used	The data used consisted only of published data, and references have been provided to indicate where the data can be found and are fully described by the authors of the cited papers. Additionally, the data are described within the manuscript	Methods, Supplementary Meethods, References
Communicating uncertainty	Uncertainty was considered throughout the study, including varying sensitivity and specificity and sampling the annual biting rate (ABR). Additionally, ninety-five percent (Wlson score) confidence intervals and uncertainty and were calculated and presented for the data, the projections and the mean squared errors as pertinent	Methods, Results, Supplementary Figures and Tables
Testable model outcomes	Model outcomes were first tested and compared to pre-intervention age-stratified seroprevalence data from Gabon. Then they were validated against seroprevalence data from 11 villages in Togo, accounting for intervention history	Results and Discussion

Supplementary Methods

Supplementary Methods S1. Model Calibration

In hypoendemic settings, microfilarial prevalence is highly sensitive to changes in annual biting rate (ABR, no. bites/person/year). Conversely, in meso- and hyperendemic settings a much broader range of ABRs is compatible with similar microfilarial prevalence.[13] Due to the hypoendemic nature of the communities in Gabon, we aimed to find a single ABR—for values of the inter-individual exposure heterogeneity parameter, k_E = 0.2 or k_E = 0.3—that would minimise the discrepancy between the EPIONCHO-IBM predictions and the observed microfilarial prevalence. To achieve this, we undertook a two-stage calibration process, first identifying a sample of plausible ABR-k_E combinations and then fitting to the data to identify specific best-fit ABRs for each assumed value of k_E. For stage 1, we ran 100 simulations of EPIONCHO-IBM for a 100-year burn-in period and for a range of ABRs (for each k_E), comparing the mean microfilarial prevalence in those aged 5 years and older with that of the observed data[1]. When calculating the model-predicted mean prevalence, we sampled individuals in 5-year age groups to match the number of individuals in the respective age groups of the observed data (i.e., to weight correctly the prevalence by the sampled age demographic group). We selected and kept ABR-k_E combinations with a modelled mean microfilarial prevalence that was within the 95% (Wilson score) confidence interval (CI) of the observed microfilarial prevalence (7.13% - 8.75%) (Supplementary Fig. S1). For stage 2, we re-simulated EPIONCHO-IBM to endemic equilibrium 500 times for each of the selected ABR-k_E combinations and identified the ABR (for each k_E) that minimised the mean squared error (MSE) of the model predictions compared to the age-stratified (5-year groups) microfilarial prevalence data. The MSEs were calculated for each of the model runs by weighting each age group by the observed proportion of the population in that age-group (i.e., weighting more heavily more populated age groups). Supplementary Table S1 shows the range of ABRs considered and selected (in stage 1), and the final (fitted, stage 2) ABR-k_E combinations.

In Togo, the pre-intervention baseline microfilarial prevalence was not known for most of the villages, so model-derived inferred estimates from Amaral et al.[3] were used instead. Briefly, these values were inferred by identifying ABRs and parameters related to the effectiveness of interventions (vector control efficacy, treatment coverage and proportion of systematic non-

adherence) that best captured microfilarial prevalence data collected longitudinally (by repeated cross-sectional surveys) throughout the intervention period. Intervention effectiveness was classified by Amaral et al.[3] as 'minimal', 'reference' and 'enhanced' defined, respectively, as a vector control efficacy of 60%, 75% and 90% (the percentage reduction in the ABR for the vector control period), a coverage of total population increasing to 65%, 75% and 80% (from 2002), and a systematic non-adherence (the proportion of individuals never taking treatment) of 5%, 2.5% and 1%. Treatment coverage (of total population) and frequency were fixed among all villages but varied temporally over the history of intervention[3] (Supplementary Methods S2; Supplementary Table S5).

All four villages in Kéran, were identified as having 'enhanced' effectiveness (vector control efficacy 90%; total population coverage increasing from 65% in 1991-1995 to 80% from 2002, and systematic non-adherence 1%), with an inferred pre-intervention baseline microfilarial prevalence of 90%, excepting the village of Goulbi, which had an inferred prevalence of 70%. Hence, we used a prefecture-level aggregated baseline prevalence of 85% (the mean of three inferred prevalence values of 90% and one of 70%). In Bassar, all four villages were identified has having 'minimal' intervention effectiveness (vector control efficacy 60%; total population coverage increasing from 50% in 1991-1995 to 65% from 2002, and systematic non-adherence 5%) and an inferred baseline microfilarial prevalence of 70%. Hence, we used a prefecture-level aggregated prevalence of 70%. The three villages in Ôti/Kpendjal were identified has having different intervention effectiveness (one each of 'minimal', 'reference' and 'enhanced') but a consistent baseline microfilarial prevalence of 70%. Thus, we used a prefecture-level aggregate pre-intervention baseline prevalence of 70% and integrated variability in the intervention effectiveness when simulating interventions for the purposes of validation (Supplementary Methods S2).

Using the inferred prefecture-level aggregated pre-intervention microfilarial prevalence (Supplementary Table S2), we calibrated EPIONCHO-IBM by varying the ABR (using a $k_E = 0.3$[3]) informed by previous work on the relationship between ABR and pre-intervention microfilarial prevalence[3,13] and selected ABRs that yielded predictions within ± 1% of the inferred prefecture-level pre-intervention microfilarial prevalence. Because of the highly hyperendemic nature of the villages within each prefecture (minimum pre-intervention baseline microfilarial

prevalence of 70%), this approach yielded broad ranges of compatible ABRs (Supplementary Table S2).

Supplementary Methods S2. Modelling Interventions

The three prefectures in Togo have a long history of intervention—including vector control from 1976 to 2007 (excepting Ôti/Kpendjal, where vector control stopped in 1993) and MDA from 1991—before the seroprevalence data were collected in 2015. We followed Amaral et al.[3] in simulating the history of MDA and vector control. For MDA, the frequency and coverage were divided into temporal segments reflecting the evolution of the programme, which shifted from the initial goal of control to elimination. This consisted of early MDA delivered by mobile teams (1991-1995), increased coverage associated with the switch to community directed treatment with ivermectin (CDTI) (1996-2001) and the switch to higher coverage and biannual MDA (2002-2015 and 2003-2015, respectively). For each segment, we assumed a coverage (of the total population) as used by Amaral et al.[3], which was informed by national programme data.[2] For vector control, we also followed Amaral et al.[3] in defining the period of intervention, from 1976-2007 that applied to Special Intervention Zones (excepting Ôti/Kpendjal where vector control ceased in 1993[3]), and defined vector control efficacy as the reduction in ABR for the period of aerial larviciding of vector breeding sites. Variation in the effectiveness of intervention in each prefecture was simulated using parameters defining the efficacy of vector control, the total population ivermectin treatment coverage, and the proportion of systematic non-adherence (categorised as 'minimal', 'reference' and 'enhanced'; see Supplementary Methods S1 and Supplementary Table S5).

The microfilarial prevalence and anti-Ov16 IgG4 seroprevalence in 2015 were predicted by first using EPIONCHO-IBM to simulate to endemic equilibrium, sampling ABRs from the range that reflected a prefecture's pre-intervention baseline microfilarial prevalence (Supplementary Methods S1), and then simulating the history of intervention—assuming a 'minimal' 'reference' or 'enhanced' effectiveness—using 1,500 stochastic repeats. For Ôti/Kpendjal, we integrated variability in the identified effectiveness categorisation of each village (Supplementary Methods S1) by combining 500 stochastic repeats of each of the 'minimal', 'reference' and 'enhanced' categorisations. We assumed the best fitting seroconversion-seroreversion hypotheses (from the prior analysis of the Gabon data) and recorded microfilarial prevalence and anti-Ov16 IgG4

seroprevalence predictions at the start of 2015 to align with the year when the serological and parasitological data were collected by Komlan et al.[2] (microfilarial prevalence predictions are shown in Supplementary Table S6). Aggregated prevalence and seroprevalence were calculated using a sampled population from each prefecture-specific projection that matched the proportion of individuals in the study from each prefecture (i.e., weighted by the sample size from each prefecture; 324/1455 = 22% for microfilarial prevalence and 254/644 = 39% for anti-Ov16 IgG4 seroprevalence in Ôti/Kpendjal; 539/1455 = 37% and 355/644 = 55% in Kéran, and 592/1455 = 41% and 35/644 = 5% in Bassar).

Supplementary Methods S3. Sensitivity and Specificity Estimates

Ov16 Rapid Diagnostic Test. We conducted a literature search to identify studies reporting estimates of the sensitivity and specificity of the SD BIOLINE Ov16 rapid diagnostic test (Ov16 RDT) used in Gabon, and the horseradish peroxidase (HRP) Ov16 ELISA used in Togo. For the SD BIOLINE Ov16 RDT, we conducted a search on EMBASE using the following terms:

1. ("ov16" or "Ov16" or "IgG4").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
2. ("RDT" or "Rapid Diagnostic Test").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
3. ("SD" or "Bioline" or "SD Bioline").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
4. 1 and 2 and 3

We filtered the search results to identify studies using SD BIOLINE Ov16 RDTs on whole blood and reporting diagnostic characteristics (sensitivity and specificity). Additionally, studies discussing the diagnostic characteristics of Ov16 RDTs were also considered, along with the diagnostic performance of the RDT reported from Gabon dataset[1]. Of the 16 studies identified,

two estimated the sensitivity and specificity of the RDT using whole blood against skin snips, with sensitivities of 51% and 60% and specificities of 95% and 94%, respectively (Supplementary Table S3). Two studies used Ov16 ELISA as the reference test, estimating sensitivities of 29% and 40%, and specificities of 98.9% and 99.9% respectively (Supplementary Table S3). We did not consider the diagnostic sensitivity and specificity reported on the SD BIOLINE manufacturer instructions as reported by Dieye et al.[14], because these values were obtained in a laboratory setting. In the field, and especially in low prevalence areas, the performance of RDTs[9] (and whole-blood RDTs in particular[15]) is likely to be substantially lower. Indeed, in the Ov16 Technical Meeting (held in May 2026)[9], it was also noted that in Gabon, the sensitivity of RDTs was 78% in meso- to hyperendemic areas, but only 46% in hypoendemic areas (which matches the setting of our data). Consequently, the values we considered for our range of potential sensitivities were 40%, 50%, and 60%, and for our potential specificities, 95%, 97%, and 99%.

Ov16 Horse Radish Peroxidase (HRP) ELISA. For the Ov16 HRP ELISA, we conducted a search on EMBASE using the following terms:

1. ("onchocerciasis" or "oncho*").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
2. (("sensitivity" and "specificity") or ("sens" and "spec")).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
3. ("ELISA" or "Enzyme Linked Immunosorbent Assay").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
4. ("Ov16" or "IgG4").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]

5. 1 and 2 and 3 and 4

We filtered the search results to identify studies using HRP as the enzyme conjugate and reported the sensitivity and specificity or presented data permitting their calculation. We focused on studies using the HRP Ov16 ELISA as being the most similar to that used by Komlan et al.[2] for their study in Togo. The other main enzyme conjugate used in Ov16 ELISA assays is alkaline phosphatase (AP). There are varying reasons to use one or the other; however, with Thermo Scientific Kits, the ELISA substrates that can be used with HRP enzymes have lower detection limits (picogram range) than those with AP (nanogram range)[16,17]. This typically results in higher sensitivities[18] (at the compromise of lower specificity) for the HRP ELISA. Accordingly, the values considered for our range of potential sensitivities were 70%, 80%, and 85%, and of potential specificities, 70%, 85%, and 95% (Supplementary Table S7).

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