

博士論文

**Effects of sulfadoxine-pyrimethamine resistance on the effectiveness of policies
for preventive treatment of malaria in Africa: a systematic analysis of national
trends**

(スルファドキシシン-ピリメタミン耐性がマラリアの予防的治療に関する政策の有効性に
及ぼす影響：アフリカ諸国における系統的傾向分析)

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Statement of original authorship

This dissertation is submitted to the University of Tokyo in fulfilment of the requirements for the Degree of Doctor of Philosophy.

This dissertation represents my own work and contains no material which has been previously submitted for a degree or diploma at this university or any other institution, except where acknowledgment is made.

Abstract

Introduction

The rising burden of drug resistance is a major challenge to the global fight against malaria. I estimated national *Plasmodium falciparum* resistance to sulfadoxine-pyrimethamine (SP) across Africa, from 2000 to 2020.

Methods

I assembled molecular, clinical and endemicity data covering malaria-endemic African countries up to December 2018. Subsequently, I reconstructed georeferenced patient data, using pfdhps540E and pfdhps581G to measure mid-level and high-level SP resistance. Gaussian process regression was applied to model spatiotemporal standardised prevalence.

Results

In eastern Africa, mid-level SP resistance increased by 64.0% (95% uncertainty interval, 30.7%–69.8%) in Tanzania, 55.4% (31.3%–65.2%) in Sudan, 45.7% (16.8%–54.3%) in Mozambique, 29.7% (10.0%–45.2%) in Kenya and 8.7% (1.4%–36.8%) in Malawi from 2000 to 2010. This was followed by a steady decline of 76.0% (39.6%–92.6%) in Sudan, 65.7% (25.5%–85.6%) in Kenya and 17.4% (2.6%–37.5%) in Tanzania from 2010 to 2020. In central Africa, the levels increased by 28.9% (7.2%–62.5%) in Equatorial Guinea and 85.3% (54.0%–95.9%) in the Congo from 2000 to 2020, while in the other countries remained largely unchanged. In western Africa, the levels have

remained low from 2000 to 2020, except for Nigeria, with a reduction of 14.4% (0.7%–67.5%) and Mali, with an increase of 7.0% (0.8%–25.6%). High-level SP resistance increased by 5.5% (1.0%–20.0%) in Malawi, 4.7% (0.5%–25.4%) in Kenya and 2.0% (0.1%–39.2%) in Tanzania, from 2000 to 2020.

Conclusion

Under the World Health Organization protocols, SP is no longer effective for intermittent preventive treatment in pregnancy and infancy in most of eastern Africa and parts of central Africa. Strengthening health systems capacity to monitor drug resistance at subnational levels across the endemicity spectrum is critical to achieve the global target to end the epidemic.

Acknowledgment

This work was funded by Ministry of Education, Culture, Sports, Science and Technology of Japan.

Table of contents

Title	1
Statement of original authorship.....	2
Abstract.....	3
Acknowledgment.....	5
Table of contents.....	6
List of figures and tables	8
List of abbreviations	11
Key questions.....	12
What is already known?	12
What are the new findings?.....	12
What do the new findings imply?	13
Background	15
Methods	18
Study setting and data sources.....	18
Data processing and modelling framework	19
Sensitivity analysis and uncertainty quantification	21
Ethics approval	22
Results	23

Patient data coverage	23
Trends in sulfadoxine-pyrimethamine resistant malaria	27
Effectiveness of intermittent preventive treatment with sulfadoxine-pyrimethamine in pregnancy and infancy	41
Discussion	45
Supplements	54
References	56

List of figures and tables

Figure 1: Evidence gathering flowchart. The full description of the search algorithm and the eligibility criteria considered for each outcome cluster is provided in supplements 1.1–1.2.

Figure 2: Patient data coverage. The circle sizes are proportional to the number of surveys reporting patient data in each country. The shading depicts the number of clinical samples tested in each country. The intervals are left-opened and right-closed. (A) pfdhps540E patient data. (B) pfdhps581G patient data.

Figure 3: National scale temporal trends in, and projections of, *P. falciparum* resistance to sulfadoxine-pyrimethamine. The upper and lower lines denote upper and lower bounds of the 95% uncertainty interval, respectively, and the middle, the median of the posterior distribution. The estimates are population-level resistance levels per respective geography. The points and vertical bars indicate point estimates from each survey with respective uncertainty interval, whereas the colours denote the administrative level one of the sites where the patients were recruited, and clinical samples collected. National trends and projections are shown as graphs for selected countries. Countries with the smallest, largest and/or typical changes in resistance in each region (eastern, central, and western Africa) are shown, to illustrate the regional trends and cross-country heterogeneity across the continent. Figures for all countries analysed are provided in supplement 3.4. The full list of site-years is summarised

in supplement 1.3. Posterior probability distribution of prevalence per survey is given in supplement 3.5. (A) Mid-level *P. falciparum* resistance to sulfadoxine-pyrimethamine. (B) High-level *P. falciparum* resistance to sulfadoxine-pyrimethamine.

Table 1: Estimated change over time per geography in adjusted prevalence of *P. falciparum* resistance to sulfadoxine-pyrimethamine, with 95% uncertainty interval.

The results for 2001–2004, 2006–2009, 2011–2014 and 2016–2019 are available, and can be provided upon a reasonable request. The results for 2018–2020 are predictions beyond the available data. Unadjusted quantities per country are available and can be provided upon a reasonable request. For detailed year-specific prevalence levels, see supplement 3.1. Full posterior quantiles of prevalence per geography across time are provided in supplement 3.2. Evidence on mid-level and high-level SP resistance is based on pfdhps540E and pfdhps581G molecular markers, respectively.

Table 2: Effectiveness of Sulfadoxine-Pyrimethamine for intermittent preventive treatment in pregnancy (IPTp) and in infancy (IPTi).

The values in each country-year are posterior probability reflecting the amount of evidence that each intervention is effective under the current WHO frameworks. For IPTp, the WHO thresholds for withdrawal of policy are pfdhps540E >95% and pfdhps581G >10%. For IPTi, the WHO threshold for withdrawal of policy is pfdhps540E >50%. For each intervention, I consider the drug effective in those country-years whose posterior probability >95%. For detailed

year-specific policy effectiveness, see supplement 3.6. For South Africa, the data are not sufficient to generate evidence on drug effectiveness for IPTp. NA, not available.

List of abbreviations

ACT: artemisinin-based combination therapy

AMR: African Malaria Reports

AQ: amodiaquine

AS: artesunate

CQ: chloroquine

DHFR: dihydrofolate reductase

DHPS: dihydropteroate synthase

GPR: Gaussian process regression

IPTi: intermittent preventive treatment in infancy

IPTp: intermittent preventive treatment in pregnancy

LBW: low birthweight

NMCP: National Malaria Control Programmes

SDG: Sustainable Development Goals

SDI: Socio-demographic Index

SMC: seasonal malaria chemoprevention

SP: sulfadoxine-pyrimethamine

TMP-SMX: trimethoprim-sulfamethoxazole

WHO: World Health Organization

WMR: World Malaria Reports

WWARN: Worldwide Antimicrobial Resistance Network

Key questions

What is already known?

In the period from 2000 until 2015, malaria burden reduced substantially in Africa. The annual incidence, prevalence, deaths, and disability-adjusted life years were reduced by 40%, 50%, 57% and 24%, respectively.

However, the disease remains a major cause of morbidity and mortality throughout the continent, with more recent evidence indicating an increase in the number of cases.

The WHO recommends countries to withdraw intermittent preventive treatment in pregnancy when the prevalence of pfdhps540E >95% and pfdhps581G >10%, and intermittent preventive treatment in infancy when the prevalence of pfdhps540E >50%.

Comparable evidence on anti-malarial drug resistance, applicable to the general population at national level, that can reliably inform the translation of WHO recommendations into effective national policies, is currently limited.

What are the new findings?

This is the first systematic analysis of nationwide standardised levels of *P. falciparum* resistance to sulfadoxine-pyrimethamine (SP).

The evidence provided here allows comparability of trends across time and locations and helps policymakers understand the policy impact of the WHO frameworks at country level.

My metrics illustrate a gradual reduction of mid-level resistance to SP in eastern Africa since 2010, as well as increasing levels in central Africa and a largely stable drug efficacy in western and southern Africa in the period between 2000 and 2020.

However, there is a continued reduction of drug efficacy on the continent, driven by increasing levels of high-level resistance, mostly in eastern Africa.

Using my metrics in conjunction with the current WHO protocols, I identified countries where continued implementation of SP-based malaria control policies for maternal and child health outcomes is warranted, as well as regions where these policies are no longer effective.

What do the new findings imply?

I detected areas where a careful monitoring of resistance levels is critical. I also identified areas with limited coverage of patient data for resistance tracking in the regions where the largest share of *P. falciparum* infection is concentrated.

This includes Nigeria, the Democratic Republic of the Congo, Mozambique, and Uganda, which alone account for 45% of the global burden of malaria cases.

Therefore, to realise the global agenda to end the epidemic of malaria by 2030 in the context of the Sustainable Development Goals target 3.3, it is essential to strengthen health systems capacity to monitor resistance at subnational level across the endemicity spectrum on the continent.

Background

Malaria remains a major cause of morbidity and mortality in Africa. Annually, *Plasmodium falciparum* infection causes more than 200 million clinical cases and over 400 000 attributable deaths on the continent, which accounts for 92% of the global malaria burden.¹ In the period from 2000 to 2015, malaria burden reduced substantially in part due to a reinvigorated multilateral commitment to, and a 20-fold increase in international investment in, malaria control. The annual incidence, prevalence, deaths and disability-adjusted life years were reduced by 40%, 50%, 57% and 24%, respectively.²⁻⁴ Despite the declining trends through 2015, more recent estimates show that if the current increases in malaria cases and deaths continue, then the Sustainable Development Goals (SDG) target 3.3—ending the epidemic of malaria by 2030—might not be achieved.^{1,5}

The rising burden of *P. falciparum* resistance to essential anti-malarial drugs is a major challenge to the global fight against malaria.^{1,4} Despite the widely reported resistance to sulfadoxine-pyrimethamine (SP), it is still the drug of choice for intermittent preventive treatment in both pregnancy (IPTp) and infancy (IPTi). SP, combined with chloroquine (CQ) or artesunate (AS), was used as treatment in much of Africa, although most countries changed to artemisinin-based combination therapy (ACT) between 2003 and 2008.⁶ This change in usage reduced selection for antifolate resistance and may have allowed for changes in the prevalence of markers of resistance. Two countries, Somalia and Sudan, continued to use AS+SP until 2016 and 2017, respectively.⁷⁻⁹ This change

further reduced the selective pressure on antifolates. In Sudan, the adoption of AS+SP in 2004 as the first-line ACT was based on an open-label randomised controlled trial conducted in the country the same year that indicated superiority of AS+SP compared with SP for the treatment of uncomplicated malaria, which was confirmed by subsequent trials.^{7,10,11} Likewise, in Somalia, AS+SP was adopted in 2006 as the first-line ACT based on therapeutic efficacy studies conducted between 2003 and 2006 that indicated high therapeutic efficacy of this drug (as well as AS+amodiaquine (AQ)) compared with CQ, AQ and SP in the country.¹²

The World Health Organization (WHO) recommends member states to closely monitor the efficacy of essential anti-malarial drugs and use resistance levels to inform policymaking at the country-level.¹³⁻¹⁵ However, most malaria-endemic countries do not have the capacity to establish the needed networks of well-functioning resistance surveillance sites across their epidemiologically diverse territories to track resistance. To date, data on molecular markers measured in clinical samples have been used to infer country scale levels of drug-resistant *P. falciparum*. These molecular markers indicate mutations in the genes for two enzymes of the folate pathway, dihydropteroate synthase (DHPS) (mutations: 437G, 540E, 581G) and dihydrofolate reductase (DHFR) (mutations: 51I, 59R, 108N), which have been associated with resistance to S and P, respectively. The intensity of the resistance to SP increases with the number and types of mutant codons, with quintuple mutations (five mutations including 540E, excluding 581G) being associated with mid-level resistance, and sextuple mutations (six mutations including 581G) with high-level resistance. These can be measured using

pfdhps540E and pfdhps581G, respectively. A previous modelling study¹⁶ used data on pfdhps540E mutations from 1987 to 2008 to create predictive surfaces on the continent. The study provided maps visualising the variation of the prevalence of pfdhps540E across the continent, and probability distribution for locations without data. However, it covered only the period between 1990 and 2010. Therefore, the estimates provided do not reflect recent variations in SP resistance following the changes in anti-malarial policies.^{1,6} Additionally, the models used in the study¹⁶ did not account for real world data including clinical characteristics of patients, as well as population level anti-malarial immunity, which is a function of age and endemicity.¹⁷⁻²⁰ A more recent meta-analysis²¹ used pfdhps540E and pfdhps581G to measure the association between resistance and low birth weight (LBW). This did not provide country-specific adjusted estimates of prevalence levels, nor did it quantify the potential policy implications of mutation levels. Thus, no evidence is available to date on age-endemicity standardised prevalence of malaria resistance to SP, or its implication for anti-malarial policy. This complicates comparability of resistance trends across the continent and global efforts to tackle the burden of drug resistance.

I provide a comprehensive analysis that leverages data systematically derived from clinical records and community surveys conducted across the continent, over the last two decades. I employ recent advances in infectious disease modelling to generate comparable tempo-spatial trends and projections of *P. falciparum* resistance to SP and drug effectiveness for IPTp and IPTi policies at the national level from 2000 to 2020.

Methods

Study setting and data sources

I assembled molecular, clinical and endemicity data derived from multiple sources covering malaria-endemic African countries from January 1998 to December 2018. For data on pfdhps540E and pfdhps581G mutations associated with SP resistance, as well as national anti-malarial treatment policy implementations, I conducted an extensive search of medical databases detailed in supplements 1.1–1.2. I cross-validated my molecular data with Worldwide Antimicrobial Resistance Network (WWARN) databases. WWARN repository does not have clinical and endemicity data. I contacted the authors of the eligible trials and experts for clarification and/or additional molecular and/or clinical data (supplement 1.1). For data on anti-malarial treatment policy implementations, I additionally consulted National Malaria Control Programmes (NMCP), African Malaria Reports (AMR) and World Malaria Reports (WMR). From each eligible survey, the number of patients enrolled, clinical samples successfully genotyped and positive for each of the molecular markers under study, as well as demographic and clinical characteristics of patients tested, study design, geospatial coordinates, clinical context and year, as well as season of sample collection, were extracted. From NMCP, AMR, WMR and articles eligible for anti-malarial policy data, I extracted data on anti-malarial drug combination adopted and the year when policy implementation began (supplement 1.4).

Subsequently, I geolocated data on resistance markers from the eligible surveys and then linked with malaria endemicity data from the Malaria Atlas Project by matching sampling site and year that the clinical samples were collected.⁴ I further derived data on Socio-demographic Index (SDI) from the Global Burden of Disease Study 2017²² and HIV prevalence data from the Joint United Nations Programme on HIV/AIDS databases, matching them to each *P. falciparum* resistance survey datapoint using geolocation and year of sample collection. Finally, I used the resulting pool of evidence to reconstruct georeferenced patient data across space-time clusters. The current analysis was conducted within the context of a study exploring trends in comparative efficacy and safety of malaria control interventions for maternal and child health outcomes in Africa, which has been registered on PROSPERO under CRD42018095138.²³ The primary purpose of this current analysis is to provide country level data on the prevalence of *P. falciparum* resistance to SP. This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting statement²⁴ (supplements 1.1–3.6).

Data processing and modelling framework

I use pfdhps540E and pfdhps581G mutations validated to measure mid-level and high-level *P. falciparum* resistance to SP, respectively¹³⁻¹⁵ (see supplements 1.6–1.8 for marker groupings and diagnostic accuracy). I included a variable denoting the proportion of mixed genotype infections as a covariate in my model (supplement 1.5). I also incorporated SDI in my modelling framework to account for lag distributed income per capita, educational attainment for those aged ≥15 and total fertility rate among

women aged <25 years in my estimates.²² These are known to influence anti-malarial treatment-seeking behaviour in malaria-endemic countries.²⁵ The inclusion of HIV prevalence in the dataset aimed to account for any potential effect of trimethoprim-sulfamethoxazole (TMP-SMX), which is used to prevent opportunistic infections among HIV-infected patients. TMP-SMX targets the same folate pathway as SP (trimethoprim: DHFR; sulfamethoxazole: DHPS), although clinical evidence on cross-resistance is still limited.^{26,27} I used Bayesian principal component analysis to identify the principal subspace of the observed age data. This showed that four and three latent variables capture the most important variability in the age of the patients from whom the blood samples genotyped for pfdhps540E and pfdhps581G were collected, respectively (supplement 2.2). These latent variables for patient age along with the other covariates including malaria endemicity, were then incorporated in the modelling framework, for each marker. These covariates were evaluated by Bayesian additive regression trees to compute generalised propensity scores. This allowed me to effectively summarise and balance the covariate information, while accounting appropriately for non-linearities and interactions, thereby standardising my quantities. My approach allows effective redundancy reduction and stability optimisation by keeping only the best covariates. This helps achieve a parsimonious model and avoid overfitting (supplement 2.3).

Gaussian process regression (GPR) model was subsequently applied to compute country-level adjusted prevalence of, and temporal change in, malaria resistance to SP, spanning the period from 2000 through the end of 2020. I used inverse logit function to map my estimates from the real space into the probability space. The year of sample

collection is used as predictor and the administrative level one corresponding to the sampling site as a random effects variable. I employ predictive comparisons to derive temporal change in resistance quantities. Finally, I computed the posterior probability to quantify the amount of evidence in favour of IPTp and IPTi being effective in each country under the current WHO thresholds, ¹³⁻¹⁵ given the estimated levels of *P. falciparum* resistance to SP. For IPTp, the WHO thresholds for withdrawal of policy is when pfdhps540E >95% and pfdhps581G >10%. For IPTi, the WHO thresholds for withdrawal of policy is pfdhps540E >50%. For countries with limited data on pfdhps581G, I use regional trends of high-level resistance to compute the posterior probability of IPTp effectiveness. GPR is a high-level non-parametric probabilistic method with demonstrated prediction accuracy, reliable quantification of uncertainty, and ability to recover an underlying dynamic process from noisy observations in the face of data sparsity and non-linear problems, with minimal assumptions²⁸ (supplement 2.4). I developed my GPR model in Stan version 2.19.1 and implemented it in R version 3.5.1.

Sensitivity analysis and uncertainty quantification

I conducted out-of-sample cross-validation to check the performance of my model. This showed that the model was reasonably well calibrated, which was confirmed by Markov chain Monte Carlo diagnostics (supplements 2.4 and 3.3). I also assessed the robustness of my empirical estimates to sensible changes in model specification. The results were relatively stable, confirming that the predicted resistance quantities are not

artefacts of my modelling assumptions. Previous studies^{16,29,30} were used to draw my prior hypothesis in resistance patterns per region across the continent. This informed my hyperparameters' priors pool, from which I selected the best performing sets for each country. A detailed account of the method is provided in the appendix (supplements 1.1–2.5).

Ethics approval

Ethical approval is not necessary because this research did not collect identifiable human material and data.

Results

Patient data coverage

I identified a total of 703 unique records, of which 392 were found to be eligible for full-text eligibility assessment. Ultimately, 198 and 39 surveys reporting data on validated SP resistance markers and malaria control policy implementations, respectively, were included in the resistance quantities estimation (figure 1). Taking these eligible surveys into account, georeferenced data derived from 68 433 clinical samples successfully genotyped for pfdhps540E and collected between 1998 and 2017 in 38 countries from over 195 189 patients were included in the analysis. For pfdhps581G, georeferenced data derived from 39 916 successfully genotyped clinical samples collected between 1998 and 2016 in 30 countries from over 108 374 patients were included in the analysis (figure 2). The surveys included in the analysis enrolled patients with heterogeneous clinical presentations of *P. falciparum* infection, spanning all demographic groups and malaria endemicity classes (supplement 1.3).

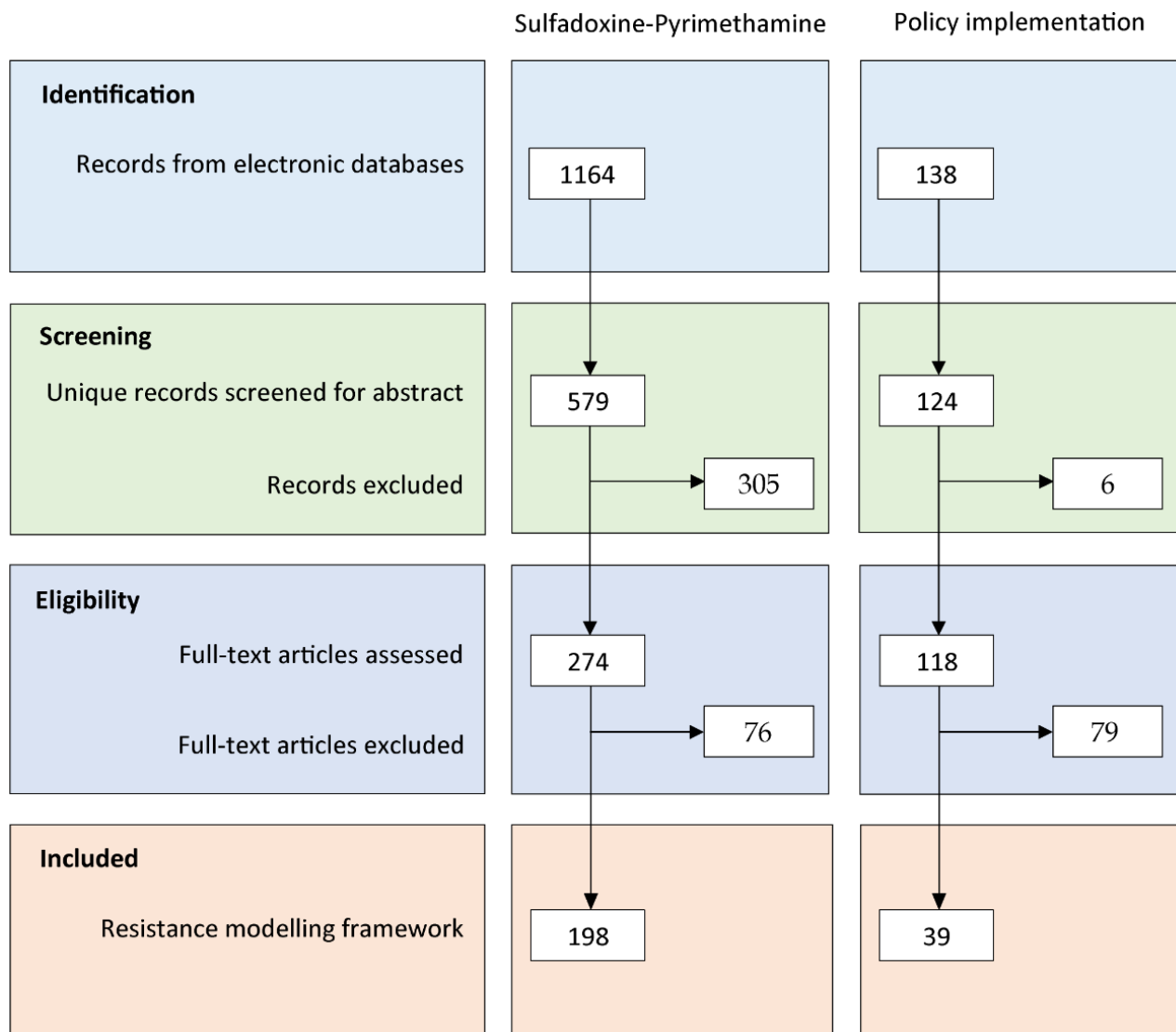


Figure 1: Evidence gathering flowchart. The full description of the search algorithm and the eligibility criteria considered for each outcome cluster is provided in supplements 1.1–1.2.

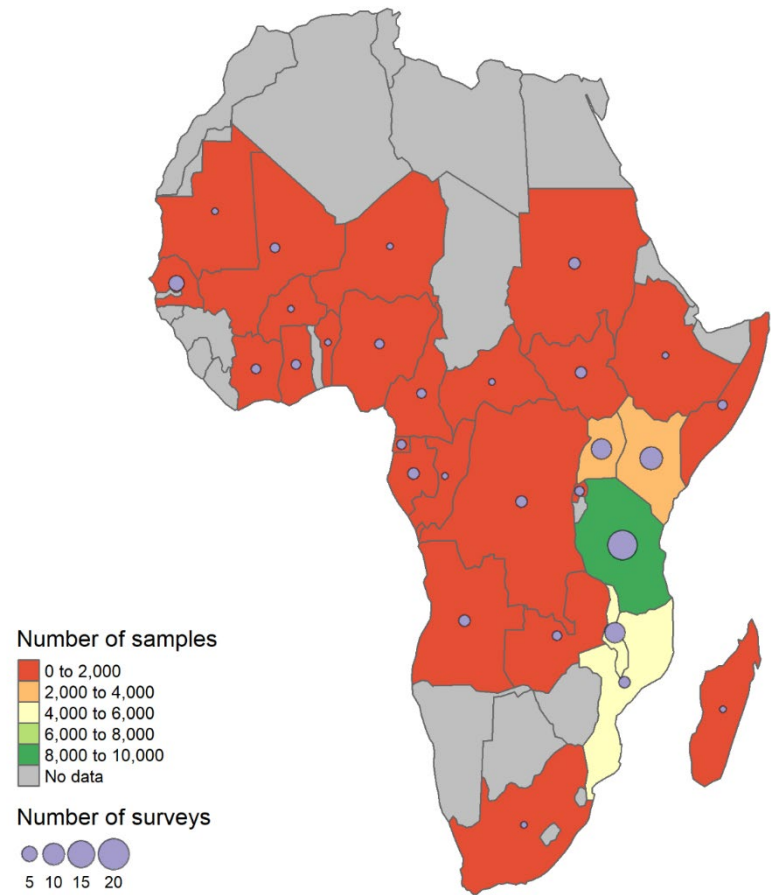
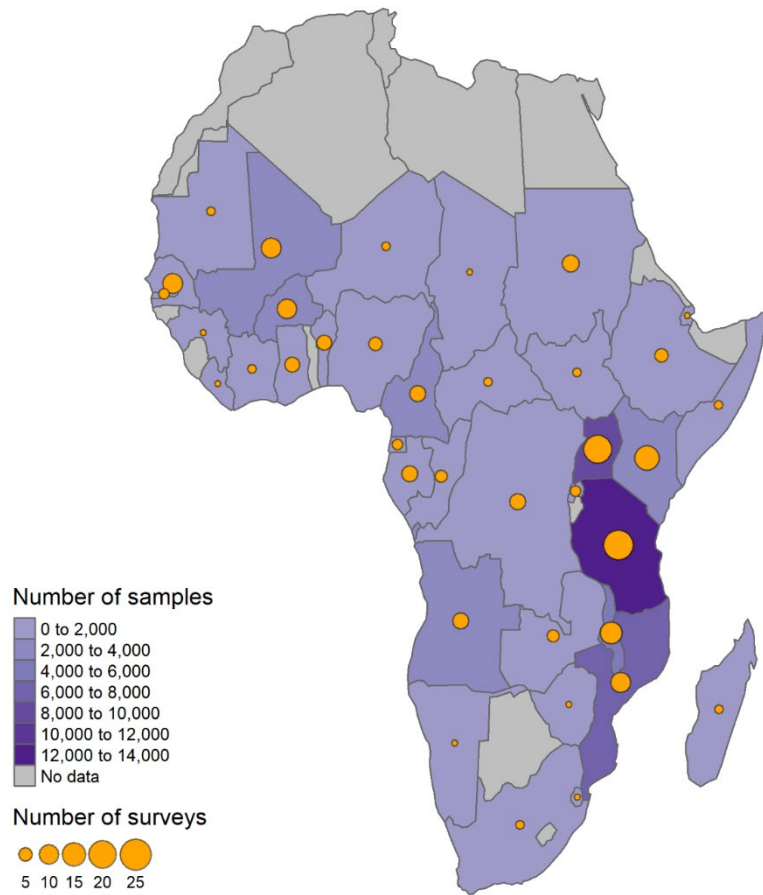


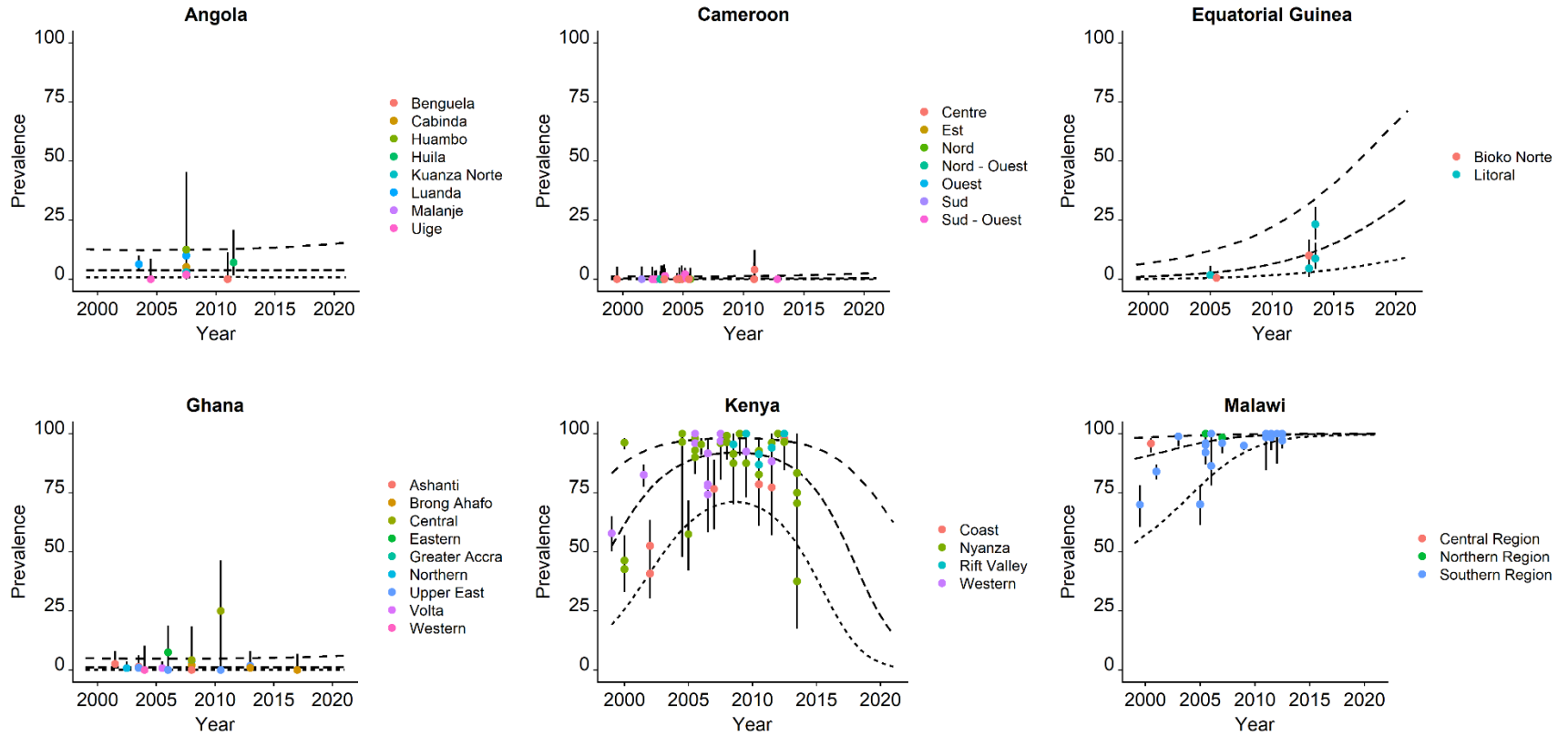
Figure 2: Patient data coverage. The circle sizes are proportional to the number of surveys reporting patient data in each country. The shading depicts the number of clinical samples tested in each country. The intervals are left-opened and right-closed. (A) pfdhps540E patient data. (B) pfdhps581G patient data.

Trends in sulfadoxine-pyrimethamine resistant malaria

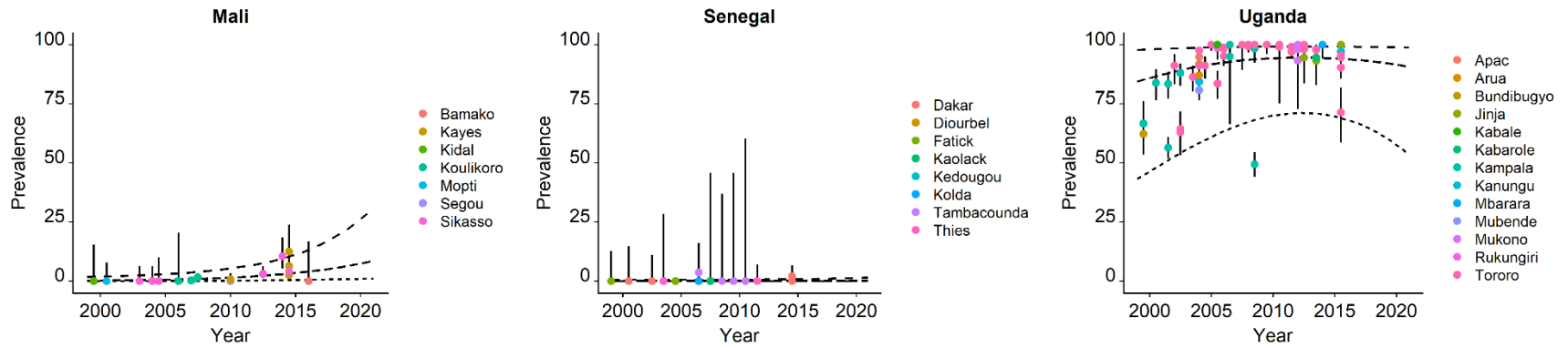
In the period from 2000 through 2020, the prevalence of *P. falciparum* resistance to SP rose in most malaria-endemic countries in Africa (figure 3). The largest variations in SP-resistant malaria were observed in eastern Africa, where despite important cross-country heterogeneity, mid-level resistance rose until 2010, dominated by Sudan with a net increase of 55.4% (95% uncertainty interval, 31.3%–65.2%), Kenya with 29.7% (10.0%–45.2%), Tanzania with 64.0% (30.7%–69.8%), Mozambique with 45.7% (16.8%–54.3%) and Malawi with 8.7% (1.4%–36.8%). Subsequent to 2010, mid-level resistance takes a downward trajectory as highlighted by a decline of 76.0% (–92.6% to –39.6%) in Sudan, 17.4% (–37.5% to –2.6%) in Tanzania and 65.7% (–85.6% to –25.5%) in Kenya. In Malawi, Ethiopia and Zambia, mid-level resistance to SP is estimated to remain largely unchanged until 2020. Malawi, however, is projected to have the highest levels of resistance among these countries at 100.0% (99.6%–100.0%). In central Africa, my evidence highlights two distinct patterns, with mid-level resistance showing a net increase of 28.9% (7.2%–62.5%) in Equatorial Guinea and 85.3% (54.0%–95.9%) in the Congo from 2000 to 2020, while remaining relatively unchanged in Angola, Cameroon and the Democratic Republic of the Congo. Apart from Nigeria, whose mid-level resistance levels decreased by 14.4% (–67.5% to –0.7%), and Mali, where the levels increased by 7.0% (0.8%–25.6%), in western Africa *P. falciparum* has remained highly sensitive to SP over the last two decades. High-level resistance to SP has remained largely unchanged in western Africa, most of central Africa and parts of eastern Africa. However, the levels increased by 5.5% (1.0%–20.0%)

in Malawi, 4.7% (0.5%–25.4%) in Kenya and 2.0% (0.1%–39.2%) in Tanzania in eastern Africa, and declined by 99.9% (–100.0% to –99.7%) in Equatorial Guinea in central Africa, from 2000 to 2020 (table 1).

A



A



B

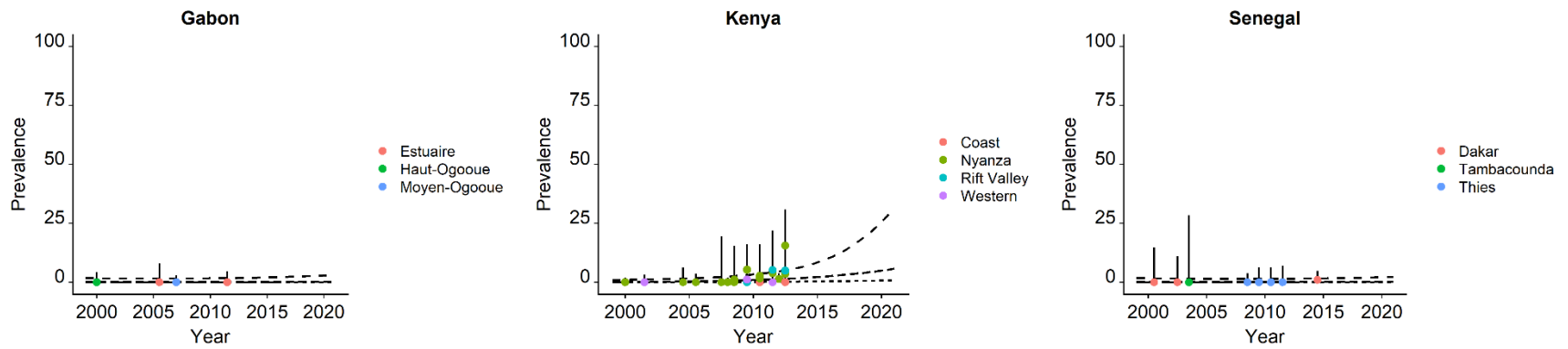


Figure 3: National scale temporal trends in, and projections of, *P. falciparum* resistance to sulfadoxine-pyrimethamine. The upper and lower lines denote upper and lower bounds of the 95% uncertainty interval, respectively, and the middle, the median of the posterior distribution. The estimates are population-level resistance levels per respective geography. The points and vertical bars indicate point estimates from each survey with respective uncertainty interval, whereas the colours denote the administrative level one of the sites where the patients were recruited, and clinical samples collected. National trends and projections are shown as graphs for selected countries. Countries with the smallest, largest and/or typical changes in resistance in each region (eastern, central, and western Africa) are shown, to illustrate the regional trends and cross-country heterogeneity across the continent. Figures for all countries analysed are provided in supplement 3.4. The full list of site-years is summarised in supplement 1.3. Posterior probability distribution of prevalence per survey is given in supplement 3.5. (A) Mid-level *P. falciparum* resistance to sulfadoxine-pyrimethamine. (B) High-level *P. falciparum* resistance to sulfadoxine-pyrimethamine.

Table 1: Estimated change over time per geography in adjusted prevalence of *P. falciparum* resistance to sulfadoxine-pyrimethamine, with 95% uncertainty interval

	Adjusted prevalence					Estimated change						
	2000	2005	2010	2015	2020	2000- 10	2010- 20	2000- 05	2005- 10	2010- 15	2015- 20	2000- 20
Mid-level resistance												
Angola	3.90 (0.95 to 12.63)	3.86 (0.99 to 12.46)	3.86 (1.01 to 12.75)	3.90 (1.00 to 13.49)	3.99 (0.96 to 15.09)	0.00 (-2.58 to 2.31)	0.06 (-1.44 to 4.15)	-0.01 (-1.49 to 0.98)	0.00 (-1.11 to 1.33)	0.02 (-0.82 to 1.80)	0.04 (-0.62 to 2.40)	0.05 (-4.00 to 6.44)
Benin	0.44 (0.06 to 2.53)	0.36 (0.05 to 1.67)	0.30 (0.05 to 1.35)	0.27 (0.04 to 1.25)	0.25 (0.03 to 1.36)	-0.10 (-1.50 to 0.13)	-0.03 (-0.41 to 0.33)	-0.06 (-1.00 to 0.05)	-0.04 (-0.51 to 0.08)	-0.02 (-0.27 to 0.13)	-0.01 (-0.15 to 0.20)	-0.13 (-1.92 to 0.44)

Burkina Faso	0.14	0.16	0.19	0.24	0.31	0.03	0.10	0.01	0.02	0.04	0.06	0.13
	(0.02	(0.02	(0.03	(0.03	(0.04	(-0.19	(-0.07	(-0.12	(-0.07	(-0.04	(-0.03	(-0.25
	to	to	to	to	to	to	to	to	to	to	to	to
	0.87)	0.83)	0.89)	1.09)	1.64)	0.26)	0.96)	0.09)	0.16)	0.31)	0.65)	1.20)
Cameroon	0.39	0.40	0.42	0.46	0.52	0.02	0.09	0.00	0.02	0.03	0.06	0.11
	(0.08	(0.08	(0.08	(0.08	(0.08	(-0.37	(-0.15	(-0.23	(-0.14	(-0.09	(-0.06	(-0.50
	to	to	to	to	to	to	to	to	to	to	to	to
	1.34)	1.29)	1.42)	1.80)	2.57)	0.48)	1.39)	0.18)	0.30)	0.51)	0.87)	1.84)
Congo	0.39	2.29	13.12	49.66	85.84	12.69	70.20	1.89	10.75	35.8	34.58	85.33
	(0.06	(0.49	(3.45	(18.36	(54.28	(3.36	(44.44	(0.42	(2.90	(14.40	(14.48	(54.01
	to	to	to	to	to	to	to	to	to	to	to	to
	1.94)	9.58)	39.88)	81.96)	97.04)	38.03)	81.58)	7.65)	30.51)	49.85)	45.81)	95.91)
Democratic Republic of the Congo	16.11	16.10	16.19	16.42	16.71	0.03	0.12	0.01	0.03	0.05	0.07	0.14
	(1.72	(1.73	(1.76	(1.77	(1.77	(-6.50	(-4.59	(-3.56	(-3.00	(-2.51	(-2.15	(-10.94
	to	to	to	to	to	to	to	to	to	to	to	to
	68.26)	68.09)	68.59)	69.33)	70.89)	6.88)	8.99)	3.18)	3.69)	4.21)	4.69)	15.51)

Equatorial Guinea	1.26	2.82	6.58	15.18	30.58	5.18	23.29	1.50	3.67	8.21	14.84	28.90
	(0.23	(0.67	(1.77	(4.15	(8.28	(1.35	(5.46	(0.38	(0.94	(1.96	(3.33	(7.24
	to	to	to	to	to	to	to	to	to	to	to	to
	6.92)	12.20)	22.33)	40.54)	66.34)	15.99)	49.58)	5.31)	10.79)	20.31)	31.24)	62.50)
Ethiopia	92.00	91.55	90.88	90.17	89.41	-0.33	-0.53	-0.14	-0.19	-0.24	-0.29	-0.87
	(47.28	(46.84	(44.89	(42.06	(37.59	(-10.81	(-17.18	(-4.72	(-6.15	(-7.94	(-9.22	(-28.19
	to	to	to	to	to	to	to	to	to	to	to	to
	99.33)	99.26)	99.22)	99.17)	99.14)	3.21)	2.33)	1.78)	1.48)	1.24)	1.10)	5.38)
Gabon	1.79	1.81	1.85	1.93	2.04	0.01	0.08	0.00	0.01	0.03	0.05	0.09
	(0.24	(0.25	(0.25	(0.24	(0.24	(-1.61	(-0.87	(-0.93	(-0.68	(-0.50	(-0.39	(-2.39
	to	to	to	to	to	to	to	to	to	to	to	to
	10.56)	10.36)	10.55)	11.39)	13.06)	1.83)	3.72)	0.76)	1.07)	1.54)	2.18)	5.50)
Ghana	1.15	1.14	1.15	1.19	1.25	0.00	0.05	-0.01	0.00	0.02	0.04	0.04
	(0.23	(0.24	(0.25	(0.25	(0.24	(-1.08	(-0.52	(-0.64	(-0.44	(-0.30	(-0.22	(-1.56
	to	to	to	to	to	to	to	to	to	to	to	to
	5.10)	4.82)	4.92)	5.29)	5.97)	0.85)	1.79)	0.36)	0.50)	0.73)	1.08)	2.55)

Kenya	61.81	88.49	91.64	75.81	23.06	29.69	-65.69	26.55	3.04	-15.37	-47.83	-34.07
	(25.84	(62.02	(69.92	(38.91	(3.20	(9.98	(-85.56	(9.16	(0.67	(-34.33	(-65.77	(-60.86
	to	to	to	to	to	to	to	to	to	to	to	to
	87.99)	97.24)	98.05)	93.87)	70.30)	45.21)	-25.46)	38.30)	8.56)	-3.77)	-19.88)	-4.90)
Malawi	90.48	96.13	99.15	99.85	99.96	8.66	0.80	5.58	3.01	0.69	0.10	9.48
	(57.19	(77.95	(94.22	(98.87	(99.58	(1.43	(0.12	(0.92	(0.46	(0.10	(0.01	(1.55
	to	to	to	to	to	to	to	to	to	to	to	to
	98.44)	99.41)	99.87)	99.98)	100.00)	36.82)	5.44)	20.72)	16.34)	4.71)	0.77)	42.36)
Mali	0.33	0.69	1.56	3.53	7.51	1.16	5.74	0.34	0.81	1.85	3.87	7.01
	(0.05	(0.12	(0.27	(0.55	(1.01	(0.17	(0.59	(0.05	(0.11	(0.22	(0.36	(0.81
	to	to	to	to	to	to	to	to	to	to	to	to
	1.98)	3.04)	5.45)	11.34)	26.37)	3.83)	22.36)	1.19)	2.63)	6.49)	15.86)	25.55)
Mozambique	19.12	34.69	68.94	87.57	89.42	45.68	17.60	14.62	30.62	17.83	1.46	64.49
	(2.68	(5.87	(20.76	(46.39	(45.54	(16.83	(-1.98	(3.05	(11.11	(3.58	(-15.47	(28.04
	to	to	to	to	to	to	to	to	to	to	to	to
	64.17)	79.82)	94.41)	98.25)	98.89)	54.28)	46.39)	23.22)	37.20)	33.29)	14.23)	81.14)

Nigeria	15.81	7.17	3.18	1.45	0.72	-11.79	-2.17	-8.04	-3.67	-1.53	-0.62	-14.35
	(0.96	(0.46	(0.20	(0.08	(0.03	(-53.07	(-16.79	(-32.51	(-22.41	(-11.52	(-5.52	(-67.45
	to	to	to	to	to	to	to	to	to	to	to	to
	73.03)	46.39)	26.05)	14.95)	10.06)	-0.58)	-0.10)	-0.38)	-0.19)	-0.08)	-0.02)	-0.71)
Senegal	0.15	0.16	0.17	0.20	0.24	0.01	0.06	0.00	0.01	0.02	0.04	0.07
	(0.02	(0.03	(0.03	(0.03	(0.04	(-0.22	(-0.08	(-0.14	(-0.08	(-0.05	(-0.03	(-0.30
	to	to	to	to	to	to	to	to	to	to	to	to
	0.72)	0.67)	0.70)	0.89)	1.42)	0.23)	0.85)	0.08)	0.15)	0.29)	0.56)	1.07)
South Africa	17.79	18.29	18.84	19.42	19.90	0.32	0.36	0.15	0.17	0.18	0.18	0.69
	(3.58	(3.75	(3.82	(3.85	(3.81	(-4.26	(-3.61	(-2.28	(-2.04	(-1.86	(-1.76	(-7.67
	to	to	to	to	to	to	to	to	to	to	to	to
	58.58)	59.83)	61.48)	64.46)	67.97)	12.35)	14.44)	5.72)	6.58)	7.09)	7.28)	26.47)
Sudan	18.89	82.06	77.99	16.96	0.68	55.37	-75.99	59.53	-3.45	-56.12	-15.94	-17.32
	(3.99	(45.43	(40.36	(3.20	(0.03	(31.30	(-92.57	(34.18	(-10.45	(-71.59	(-49.38	(-51.71
	to	to	to	to	to	to	to	to	to	to	to	to
	56.68)	96.32)	95.36)	58.22)	12.22)	65.21)	-39.60)	67.89)	1.09)	-29.23)	-3.12)	-3.19)

Tanzania	17.47	62.63	85.70	85.29	66.69	63.98	-17.36	42.17	22.66	-0.31	-17.25	44.05
	(2.63	(17.79	(43.77	(42.71	(18.86	(30.70	(-37.51	(14.65	(4.85	(-3.58	(-34.76	(14.96
	to	to	to	to	to	to	to	to	to	to	to	to
	63.18)	93.12)	98.01)	97.94)	94.70)	69.78)	-2.56)	49.00)	32.14)	2.07)	-2.81)	59.44)
The Gambia	0.18	0.18	0.19	0.21	0.24	0.00	0.03	0.00	0.00	0.01	0.02	0.03
	(0.01	(0.01	(0.01	(0.01	(0.01	(-0.41	(-0.18	(-0.25	(-0.16	(-0.11	(-0.07	(-0.57
	to	to	to	to	to	to	to	to	to	to	to	to
	4.05)	4.08)	4.39)	4.83)	5.80)	0.64)	1.67)	0.25)	0.39)	0.63)	1.03)	2.27)
Uganda	85.97	91.79	94.34	94.24	91.65	8.26	-2.10	5.66	2.51	-0.03	-2.23	4.81
	(46.42	(61.04	(70.08	(69.79	(57.67	(1.15	(-17.24	(0.80	(0.34	(-2.65	(-14.85	(-1.78
	to	to	to	to	to	to	to	to	to	to	to	to
	98.11)	98.92)	99.28)	99.28)	98.99)	24.04)	1.59)	15.82)	9.04)	2.13)	0.20)	18.96)
Zambia	51.37	51.47	51.28	51.40	51.45	0.01	0.01	0.01	0.01	0.01	0.01	0.03
	(13.93	(14.14	(14.07	(13.90	(13.64	(-7.21	(-7.36	(-3.67	(-3.64	(-3.67	(-3.73	(-14.15
	to	to	to	to	to	to	to	to	to	to	to	to
	88.08)	88.02)	88.07)	88.21)	88.46)	7.81)	7.69)	3.92)	3.90)	3.88)	3.84)	15.21)

High-level resistance

Equatorial Guinea	99.97	98.55	55.94	2.36	0.05	-44.03	-55.87	-1.42	-42.52	-53.46	-2.30	-99.91
	(99.84	(94.91	(27.75	(0.65	(0.01	(-72.12	(-80.13	(-4.93	(-67.40	(-73.71	(-6.92	(-99.97
	to	to	to	to	to	to	to	to	to	to	to	to
Gabon	100.00)	99.66)	80.24)	7.15)	0.21)	-19.75)	-27.73)	-0.33)	-19.34)	-27.02)	-0.64)	-99.69)
	0.22	0.21	0.22	0.24	0.28	0.00	0.03	0.00	0.00	0.01	0.02	0.03
	(0.01	(0.01	(0.01	(0.01	(0.01	(-0.48	(-0.18	(-0.30	(-0.18	(-0.11	(-0.07	(-0.64
Kenya	to	to	to	to	to	to	to	to	to	to	to	to
	1.76)	1.64)	1.77)	2.12)	2.94)	0.47)	1.40)	0.18)	0.30)	0.50)	0.88)	1.86)
	0.23	0.47	1.03	2.30	5.02	0.75	3.91	0.22	0.52	1.21	2.68	4.71
Malawi	(0.03	(0.09	(0.22	(0.45	(0.79	(0.12	(0.38	(0.04	(0.08	(0.15	(0.23	(0.53
	to	to	to	to	to	to	to	to	to	to	to	to
	1.11)	1.73)	3.41)	8.49)	25.76)	2.53)	23.13)	0.74)	1.83)	5.69)	17.35)	25.43)
Malawi	0.92	1.45	2.40	3.99	6.53	1.42	4.03	0.51	0.90	1.53	2.49	5.48
	(0.19	(0.30	(0.50	(0.80	(1.26	(0.26	(0.65	(0.10	(0.17	(0.26	(0.38	(0.95
	to	to	to	to	to	to	to	to	to	to	to	to

Mozambique	4.25)	6.19)	9.34)	14.76)	23.64)	5.41)	14.69)	2.02)	3.39)	5.62)	9.08)	19.98)
	0.02	0.02	0.02	0.02	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	(0.00	(0.00	(0.00	(0.00	(0.00	(-0.07	(-0.02	(-0.04	(-0.02	(-0.01	(-0.01	(-0.08
	to	to	to	to	to	to	to	to	to	to	to	to
Nigeria	0.20)	0.17)	0.18)	0.24)	0.37)	0.05)	0.20)	0.02)	0.03)	0.07)	0.13)	0.25)
	4.66	4.65	4.77	4.97	5.25	0.01	0.10	0.00	0.01	0.04	0.07	0.09
	(0.11	(0.12	(0.13	(0.14	(0.14	(-6.66	(-4.42	(-3.68	(-2.99	(-2.44	(-1.98	(-10.88
	to	to	to	to	to	to	to	to	to	to	to	to
Senegal	67.78)	67.22)	67.03)	67.33)	68.74)	6.03)	9.41)	2.60)	3.37)	4.23)	5.24)	15.33)
	0.24	0.23	0.24	0.26	0.31	0.00	0.04	0.00	0.00	0.01	0.03	0.04
	(0.02	(0.02	(0.02	(0.03	(0.03	(-0.56	(-0.20	(-0.35	(-0.21	(-0.13	(-0.08	(-0.75
	to	to	to	to	to	to	to	to	to	to	to	to
Tanzania	1.79)	1.55)	1.54)	1.74)	2.23)	0.33)	0.99)	0.12)	0.21)	0.36)	0.64)	1.30)
	0.15	0.41	0.92	1.6	2.12	0.78	1.08	0.26	0.51	0.65	0.39	1.96
	(0.00	(0.01	(0.03	(0.05	(0.06	(0.02	(0.01	(0.01	(0.01	(0.02	(-0.45	(0.05
	to	to	to	to	to	to	to	to	to	to	to	to

	5.14)	13.15)	25.09)	36.90)	44.54)	20.19)	19.68)	8.05)	12.07)	11.27)	9.03)	39.23)
Uganda	16.29	15.88	15.55	15.20	14.96	-0.25	-0.17	-0.13	-0.12	-0.10	-0.07	-0.43
	(2.43	(2.37	(2.31	(2.26	(2.18	(-6.92	(-5.74	(-3.63	(-3.34	(-3.06	(-2.74	(-12.54
	to	to	to	to	to	to	to	to	to	to	to	to
	61.95)	61.16)	60.44)	59.95)	59.88)	3.10)	3.64)	1.53)	1.60)	1.75)	1.93)	6.54)
Zambia	5.44	5.64	5.98	6.52	7.09	0.15	0.37	0.05	0.10	0.15	0.21	0.51
	(0.40	(0.45	(0.49	(0.53	(0.56	(-4.34	(-2.79	(-2.34	(-1.94	(-1.55	(-1.27	(-6.92
	to	to	to	to	to	to	to	to	to	to	to	to
	50.48)	50.03)	50.31)	51.47)	53.59)	6.43)	11.35)	2.71)	3.65)	4.89)	6.47)	17.51)

The results for 2001–2004, 2006–2009, 2011–2014 and 2016–2019 are available, and can be provided upon a reasonable request. The results for 2018–2020 are predictions beyond the available data. Unadjusted quantities per country are available and can be provided upon a reasonable request. For detailed year-specific prevalence levels, see supplement 3.1. Full posterior quantiles of prevalence per geography across time are provided in supplement 3.2. Evidence on mid-level and high-level SP resistance is based on pfdhps540E and pfdhps581G molecular markers, respectively.

Effectiveness of intermittent preventive treatment with sulfadoxine-pyrimethamine in pregnancy and infancy

In table 2 I provide the posterior probability that IPTp and IPTi with SP are effective in each country-year under the current WHO thresholds for eligibility of the drug for interventions for maternal and child health outcomes. The posterior probability value reflects the amount of evidence that each intervention is effective under the current WHO frameworks, given the observed levels of mid-level and high-level resistance. I consider the drug effective when the posterior probability >95%. This probability threshold means that the drug is considered effective when the strength of evidence in favour of it being effective is >95%, compared to the alternative hypothesis of it not being effective. For IPTp, the WHO thresholds for withdrawal of policy are pfdhps540E >95% and pfdhps581G >10%. For IPTi, the WHO threshold for withdrawal of policy is pfdhps540E >50%.

This measure shows that in 2000, 14 (63.6%) and 13 (59.1%) countries were fully eligible for IPTp and IPTi, respectively. For IPTp, these countries included Angola, Benin, Burkina Faso, Cameroon, Congo, Democratic Republic of the Congo, Gabon, Ghana, Kenya, Mali, Mozambique, Senegal, Tanzania, and The Gambia. For IPTi, the countries eligible in 2000 were Angola, Benin, Burkina Faso, Cameroon, Congo, Equatorial Guinea, Gabon, Ghana, Mali, Senegal, South Africa, Sudan, and The Gambia. In 2010, drug effectiveness for IPTp reduced notably in Angola, Benin, Cameroon, Congo, Democratic Republic of the Congo, Kenya, and Tanzania. In

Equatorial Guinea, SP was not effective for IPTp in the period from 2000 until 2010, due to high levels of high-level resistance. Subsequent to 2010, there is a continued reduction in drug effectiveness for IPTp in most of the continent; however, there is a recovery of drug effectiveness in Equatorial Guinea as a result of decline in high-level resistance in the country. As a result, in total only 7 (31.8%) countries are projected to exhibit full eligibility for IPTp in 2020. These include Burkina Faso, Equatorial Guinea, Gabon, Ghana, Mali, Senegal, and The Gambia. In relation to IPTi, 11 (50.0%) countries are projected to remain fully eligible on the continent in 2020. These include Angola, Benin, Burkina Faso, Cameroon, Gabon, Ghana, Mali, Nigeria, Senegal, Sudan, and The Gambia. For South Africa, no regional and national data on high-level resistance is available. Therefore, drug effectiveness for IPTp was not computed for this country.

Table 2: Effectiveness of Sulfadoxine-Pyrimethamine for intermittent preventive treatment in pregnancy (IPTp) and in infancy (IPTi)

	IPTp					IPTi				
	2000	2005	2010	2015	2020	2000	2005	2010	2015	2020
Angola	0.95	0.94	0.93	0.90	0.86	1.00	1.00	1.00	1.00	1.00
Benin	0.95	0.94	0.93	0.90	0.86	1.00	1.00	1.00	1.00	1.00
Burkina Faso	0.99	0.99	0.99	0.99	0.98	1.00	1.00	1.00	1.00	1.00
Cameroon	0.95	0.94	0.93	0.90	0.86	1.00	1.00	1.00	1.00	1.00
Congo	0.95	0.94	0.93	0.90	0.80	1.00	1.00	0.99	0.51	0.02
Democratic Republic of the Congo	0.95	0.94	0.93	0.90	0.86	0.92	0.92	0.91	0.91	0.91
Equatorial Guinea	0.00	0.00	0.00	0.99	1.00	1.00	1.00	1.00	0.99	0.89
Ethiopia	0.61	0.56	0.53	0.51	0.54	0.03	0.03	0.03	0.04	0.05
Gabon	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Ghana	0.99	0.99	0.99	0.99	0.98	1.00	1.00	1.00	1.00	1.00
Kenya	1.00	0.90	0.79	0.96	0.80	0.24	0.01	0.00	0.07	0.88
Malawi	0.78	0.38	0.03	0.00	0.00	0.02	0.00	0.00	0.00	0.00
Mali	0.99	0.99	0.99	0.99	0.98	1.00	1.00	1.00	1.00	1.00

Mozambique	1.00	1.00	0.98	0.84	0.76	0.92	0.74	0.21	0.03	0.03
Nigeria	0.67	0.67	0.67	0.66	0.65	0.90	0.98	1.00	1.00	1.00
Senegal	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
South Africa	NA	NA	NA	NA	NA	0.95	0.95	0.94	0.93	0.92
Sudan	0.92	0.79	0.73	0.71	0.73	0.96	0.04	0.06	0.95	1.00
Tanzania	0.99	0.95	0.79	0.75	0.80	0.93	0.31	0.04	0.05	0.26
The Gambia	0.99	0.99	0.99	0.99	0.98	1.00	1.00	1.00	1.00	1.00
Uganda	0.25	0.21	0.17	0.18	0.22	0.03	0.01	0.00	0.00	0.01
Zambia	0.70	0.69	0.68	0.66	0.62	0.48	0.47	0.47	0.47	0.47

The values in each country-year are posterior probability reflecting the amount of evidence that each intervention is effective under the current WHO frameworks. For IPTp, the WHO thresholds for withdrawal of policy are pfdhps540E >95% and pfdhps581G >10%. For IPTi, the WHO threshold for withdrawal of policy is pfdhps540E >50%. For each intervention, I consider the drug effective in those country-years whose posterior probability >95%. For detailed year-specific policy effectiveness, see supplement 3.6. For South Africa, the data are not sufficient to generate evidence on drug effectiveness for IPTp. NA, not available.

Discussion

This is the first study to employ mathematical models to rigorously quantify the policy impacts of the WHO protocols for preventive treatment of malaria in pregnancy (IPTp) and infancy (IPTi), using national trends of standardised levels of *P.*

falciparum resistance to SP. The WMR 2019 indicated that approximately 11 million pregnant women would have been exposed to malaria infection and 24 million children were infected with *P. falciparum* on the continent in 2018.¹ Controlled clinical trials have shown that a reduction of 38% (22%–50%) (data: 3 trials), 73% (56%–83%) (6 trials), 43% (28%–54%) (6 trials) and 27% (1%–47%) (3 trials) in the risk of severe antenatal anaemia, antenatal parasitaemia, LBW and perinatal death, respectively, is attainable with effective control of malaria in pregnancy.³¹ For IPTp, the WHO recommends at least three doses of SP to all pregnant women during antenatal care in the second trimester, each dose given at least a month apart.³² Based on the negative association between SP resistance and birth outcomes reported in meta-analyses and trials that explored the variation of the protective efficacy of SP across resistance levels and types, countries are recommended to withdraw IPTp with SP based on the levels of both mid-level and high-level resistance to SP.¹⁴ The WHO thresholds of >95% pfdhps540E and >10% pfdhps581G for IPTp used in the current analysis jointly reflect the fact that on the one hand SP retains a small protective efficacy when mid-level resistance levels are high (protection against LBW when pfdhps540E >90% but pfdhps581G <10%: relative risk reduction: 10% (7%–12%) (13 trials)), and on the other hand the drug is not efficacious to avert adverse birth outcomes even with relatively low

levels of high-level resistance (protection against LBW when pfdhps581G >10%: relative risk reduction: 0.5% (-16% to 14%) (13 trials); odds ratio: 1.0 (0.7–1.3) (9 trials)).^{21,33} For IPTi, the WHO recommends treatment with SP given three times during the first year of life at 10 weeks, 14 weeks and 9 months of age through immunisation services, in areas with <50% pfdhps540E.¹⁵ This treatment, which is contraindicated in HIV-infected infants receiving prophylactic TMP-SMX, has been associated with a protective effect against clinical malaria, anaemia, hospital admissions associated with parasitaemia and all-cause hospital admissions in infants of 30.3% (19.8%–39.4%) (6 trials), 21.3% (8.3%–32.5%) (6 trials), 38.1% (12.5%–56.2%) (6 trials) and 22.9% (10.0%–34.0%) (6 trials), respectively.¹³ However, SP resistance is not measured routinely across all subnational sites, so evidence to inform national level malaria control policy is usually unavailable in many countries. Therefore, my resistance quantities based on a rigorous analysis and two decades of data are paramount for timely and evidence-based translation of the WHO frameworks for decision-making at the country level. These estimates, for the first time, help identify countries where the current evidence on the dynamics of *P. falciparum* resistance to SP supports, as well as areas where there is no evidence to support the effectiveness of continued use of SP as IPTp and/or IPTi. These quantities may also be important in flagging areas that require additional surveillance.

My metrics illustrate a gradual decline of mid-level resistance to SP in eastern Africa since 2010, as well as increasing levels in central Africa and largely unchanged levels in western Africa in the period between 2000 and 2020. However, there is a continued

decline of drug efficacy in most of the continent, driven by increasing and/or relatively high prevalence of high-level resistance, mostly in eastern Africa. This finding is important because more recent WHO reports have neglected the implications of levels and temporal trends in sextuple mutations when making policy recommendations.^{32,34} Overall, under the WHO thresholds for drug eligibility for IPTp and IPTi,¹³⁻¹⁵ the national level metrics provided here indicate that SP is no longer effective for IPTp in eastern Africa and most of central Africa, and for IPTi in most of eastern Africa and parts of central Africa.

The reversal of trends in mid-level resistance observed since 2010 in eastern Africa might be because from 2003 through 2008 many countries in the region began adopting ACT as the first line for the treatment of uncomplicated malaria for the general population. Consequently, countries stopped using SP for curative treatment (as SP, CQ+SP or AQ+SP), but started or continued using SP for prophylactic treatment.¹ The period that countries initiated using SP varies across countries, from 1993 to 2007 (supplement 1.4). Those countries that started using SP sooner and/or that delayed withdrawing the drug as part of combinations for curative treatment tend to experience sustained increases in mid-level resistance levels. For instance, Malawi was the first African country to replace CQ with SP in 1993, and among the last to continue using SP as the first-line policy for malaria treatment, until 2007.⁶ Additionally, SP might continue to be used without prescription for malaria treatment (by populations other than pregnant women (IPTp) or infants (IPTi)) even after it stops being the official first-line treatment in the country. The prevalence of antimicrobial self-medication is high across

Africa, despite heterogeneity across countries and sociodemographic groups.³⁵ Illicit sale of drugs, including those that are no longer officially indicated for certain populations and/or conditions, has been documented as an important contributor.³⁶ Nevertheless, taken together, the trends in mid-level and high-level resistance in eastern Africa suggest that accumulation of pfdhps581G mutation in the population is a function of a relatively longer exposure to drug pressure, compared to pfdhps540E mutation (supplement 3.2).

My in-depth analysis on the effectiveness of SP for IPTp and IPTi for each country-year is valuable in the context of the current debate^{20,21,33,37-43} on whether the drug should continue to be used in areas of high resistance. A recent meta-analysis indicated that IPTp with SP is associated with improved birth outcomes even when pfdhps540E >90% but not when pfdhps581G >10%.²¹ However, this meta-analysis did not provide year-specific country-level data either on mid-level and high-level resistance or on the effectiveness of IPTp and IPTi policies. Nevertheless, SP resistance changes across space-time both subnationally and across countries as demonstrated here. Additionally, SP-based policies are implemented nationally in most countries, and SP resistance is not measured yearly in all subnational administrative level one sites or lower in each country (eg, in all provinces and/or districts). Therefore, the findings from this study²¹ cannot be translated into national policy across Africa. In my analysis of the effectiveness of SP for IPTp, I accounted for both mutations and standardised my quantities at national level. Overall, my evidence for eastern Africa converges with previous assessments that in this region the effectiveness of SP for IPTp and IPTi is

limited.^{20,38-40,42,43} Here I provide a detailed account of the spatial distribution and temporal dynamics at national level of the eligibility of SP for IPTp and IPTi across the continent. The variability across space-time in parasite resistance and its drivers might explain in part the current controversy in relation to the effectiveness of SP for interventions for maternal and child health outcomes in endemic countries. This is because the effect modification by year of sample collection and the geolocation of patients on *P. falciparum* resistance to SP has not been accounted for in previous assessments of SP effectiveness for IPTp and IPTi.^{13,21,37}

Even though the current analysis is focused on the use of SP for IPTp and IPTi, my evidence is relevant for seasonal malaria chemoprevention (SMC). This is because the drug combination recommended by the WHO for SMC is AQ+SP, which is administrated as intermittent courses of full treatment to children aged 3–59 months in geographies with highly seasonal malaria transmission in the Sahel subregion of Africa, typically during the rainy season (3–4 months), at 1-month intervals (SMC cycle) up to a maximum of four cycles in a year (SMC round).⁴⁴ SMC, recommended by the WHO in 2012 and previously referred to as intermittent preventive treatment in children, is indicated in areas where therapeutic efficacy of AQ+SP >90% and is contraindicated in locations where IPTi is being implemented and in HIV-infected children receiving prophylactic TMP-SMX.⁴⁵ Despite important heterogeneity across trials, it has been associated with a significant protection against all-cause mortality (protective efficacy: 57% (24%–76%) (12 trials); mortality rate ratio: 0.4 (0.2–0.9) (1 trial); risk ratio: 0.7 (0.3–1.4) (6 trials)), all clinical malaria episodes (rate ratio: 0.3 (0.2–0.4) (6 trials)), severe

malaria episodes (rate ratio: 0.3 (0.1–0.8) (2 trials)), all-cause hospital admission (incidence rate ratio: 0.6 (0.4–0.8) (1 trial)), moderate anaemia (odds ratio: 0.3 (0.1–0.7) (1 trial)), moderately severe anaemia (risk ratio: 0.7 (0.6–1.0) (5 trials)) and parasitaemia (odds ratio: 0.4 (0.2–0.6) (1 trial)).⁴⁶⁻⁴⁹ However, even though SP is one of the components of the drug combination recommended for SMC, no study has so far quantified how these protective effects of SMC are modified by pfdhps540E and pfdhps581G mutations. Therefore, no thresholds based on the levels and types of SP resistance markers have been established by the WHO for SMC to inform countries when to withdraw this policy. Nevertheless, given the relatively low levels of mid-level and high-level SP resistance across the Sahel subregion of Africa where SMC is deployed, my evidence indicates that this policy continues being largely effective in the subregion in those sites with low prevalence of parasite resistance to AQ. Trials providing data on the protective effect of SMC with AQ+SP stratified across levels and types of AQ and SP resistance markers are needed for a comprehensive assessment of the effectiveness of this policy.

The current analysis highlights the importance of standardised resistance quantities for effective policymaking. Several studies have linked age of patients with their anti-malarial immunity.^{19,20} Along with the endemicity, age is known to be an important confounder of the predictive performance and diagnostic accuracy of the molecular markers validated for measuring *P. falciparum* resistance to SP.^{17,18} However, surveys conducted across the continent usually provide sparse and inconsistent measures of patient age, thus making generation of reliable and comparable estimates of resistance

levels challenging. In an era of declining international funding,⁵ an inability to account for epidemiological and demographic dynamics, within and across populations and countries, inhibits the ability of the scientific community to provide evidence that can reliably inform the translation of the WHO recommendations into effective national policies. Therefore, national measures to strengthen health systems capacity to generate quality data through improved active surveillance of resistance, particularly high-level resistance, are critical to achieve the global target to end the epidemic.

In my analysis, data availability in southern Africa was limited. South Africa is the only country with data sufficient to generate national trends of mid-level resistance in the region; however, data from Namibia and Eswatini were also fed into the regional model. The eligible datasets used in my analysis indicated that the drug is stable in South Africa for IPTi, but the data are not sufficient to generate evidence on drug effectiveness for IPTp in the region due to unavailability of data on high-level resistance (supplements 1.3, 3.2, 3.5, and 3.6). I also detected areas of limited coverage of patient data in eastern Africa and central Africa. These are also the regions where the largest share of *P. falciparum* infection is concentrated on the continent.⁴ Importantly, nationally representative data on molecular markers of malaria resistance are limited in Africa. Therefore, while my modelling framework based on a random effects model and georeferenced covariates known to affect the variability in resistance patterns partially mitigates this issue, the national representativeness of my estimates might be limited in some countries. Most of the country data on resistance molecular markers are from prior to 2010, with some countries having no data on resistance molecular markers

beyond 2015. I address this limitation in data availability on resistance molecular markers analytically by leveraging regional temporal trends in parasite resistance in conjunction with subnational dynamics in malaria endemicity to project national trends in resistance quantities across time, provided that the available data points in each country are sufficient to model national trends (supplements 1.2–1.3, also see sensitivity analysis). To ensure quality in my geostatistical analysis, I did not conduct extrapolation to infer subnational resistance levels to attain a higher spatial–temporal resolution. Rather, I focus on providing adjusted national averages, whose relevance for nationwide policy regarding SP is my major theoretical justification. Furthermore, given the amount of variability in the prevalence of pfdhps540E and pfdhps581G within each country-year (supplements 3.2 and 3.5), the applicability of the WHO thresholds across the resistance spectrum at subnational level might be limited in some countries. For optimal drug effectiveness, a different set of malaria control policies might be required for each resistance cluster at subnational level. The feasibility of my proposed policy implementation has been demonstrated in Kenya, where IPTp is implemented in 14 of the 47 counties.⁵⁰ However, evidence-based implementation of this strategy requires predictions of resistance quantities with a higher spatial resolution, which should be the direction of future research. My survey of current evidence on preventive therapies for malaria indicates that most studies guiding the WHO protocols on IPTp,^{14,21,33,37,41} which informed my modelling framework, have generally focused on LBW, neglecting other maternal and child adverse outcomes that might be impacted differently by the effect of parasite resistance on SP protective efficacy.^{20,38-40,42} These outcomes, including fetal anaemia, stillbirth, preterm delivery, perinatal deaths, neonatal anaemia, neonatal

deaths, maternal anaemia, maternal deaths and others, should be a priority of future studies. Despite these limitations, my analysis, the first of its scope, provides results of unique practical value for effective policymaking in malaria-endemic countries.

Importantly, my metrics and recommendations are directly translatable into actions by informing the formulation and implementation of evidence-based responses at the national level in the face of the public health threat and uncertainty posed by drug-resistant malaria in resource-constrained settings, thus effectively helping African nations achieve the SDG for health.

Supplements

Supplement 1: Data assembly

- 1.1 Search algorithm
- 1.2 Eligibility criteria
- 1.3 Full list of the site-years of data among eligible surveys
- 1.4 Year of IPTp and ACT policy adoption and/or implementation
- 1.5 Full description of variables considered in the modelling framework
- 1.6 Molecular markers of *P. falciparum* resistance to sulfadoxine-pyrimethamine
- 1.7 Definition of the mutations validated to measure *P. falciparum* resistance to sulfadoxine-pyrimethamine
- 1.8 Diagnostic accuracy of pfdhps and pfdhfr mutations

Supplement 2: Modelling framework

- 2.1 Analytical strategy overview
- 2.2 Patient age subspace identification
- 2.3 Propensity score calibration
- 2.4 Hierarchical Gaussian Process Regression
- 2.5 Posterior probability interval of prevalence per survey

Supplement 3: Extended results

- 3.1 Year-specific standardized national and regional scale prevalence levels
- 3.2 Posterior quantiles of the GPR model prevalence estimates per geography
- 3.3 Trace plots showing post-warmup evolution of parameter over the iterations of the Markov chains
- 3.4 National scale temporal trends in, and projections of, *P. falciparum* resistance to sulfadoxine-pyrimethamine
- 3.5 Posterior probability distribution of prevalence per survey
- 3.6 Effectiveness of sulfadoxine-pyrimethamine for IPTp and IPTi policies per country-year

Supplement 4: Further references

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Supplementary appendix:

Supplement to: Effects of sulfadoxine-pyrimethamine resistance on the effectiveness of policies for preventive treatment of malaria in Africa: a systematic analysis of national trends

Table of contents:

Supplement 1: Data assembly	2
1.1 Search algorithm	2
1.2 Eligibility criteria	3
1.3 Full list of the site-years of data among eligible surveys	4
1.4 Year of IPTp and ACT policy adoption and/or implementation	13
1.5 Full description of variables considered in the modelling framework	15
1.6 Molecular markers of <i>P. falciparum</i> resistance to sulfadoxine-pyrimethamine.....	16
1.7 Definition of the mutations validated to measure <i>P. falciparum</i> resistance to sulfadoxine-pyrimethamine	17
1.8 Diagnostic accuracy of pfdhps and pfdhfr mutations	18
Supplement 2: Modelling framework	19
2.1 Analytical strategy overview.....	19
2.2 Patient age subspace identification	21
2.3 Propensity score calibration	26
2.4 Hierarchical Gaussian process regression	30
2.5 Posterior probability interval of prevalence per survey.....	32
Supplement 3: Extended results	33
3.1 Year-specific standardized national and regional scale prevalence levels	33
3.2 Posterior quantiles of the GPR model prevalence estimates per geography	40
3.3 Trace plots showing post-warmup evolution of parameter over the iterations of the Markov chains	47
3.4 National scale temporal trends in, and projections of, <i>P. falciparum</i> resistance to sulfadoxine-pyrimethamine	54
3.5 Posterior probability distribution of prevalence per survey	60
3.6 Effectiveness of sulfadoxine-pyrimethamine for IPTp and IPTi policies per country-year	176
Supplement 4: Further references	179

Supplement 1:

Data assembly

Supplement 1.1

Table S1: Search algorithm applied to Medline, Medline In-Process, Cochrane Central Register of Controlled Trials, Embase, CINAHL, African Index Medicus, and SciELO, as well as ClinicalTrials.gov and the Clinical Trial Register at the International Clinical Trials Registry Platform of the WHO. The search for evidence and data extraction were done from February 2018 to February 2019. Furthermore, I derived additional molecular and spatial data from the Worldwide Antimalarial Resistance Network (WWARN). I also contacted by e-mail and telephone the authors of the eligible trials and experts for clarification and/or additional data. I received positive responses and additional data and/or clarification from authors of the referenced studies.¹⁻¹⁰

Section	Set	Terms
I. pfdhps540E	1	"malaria" or "falciparum" or "plasmodium"
	2	"540E" or "K540" or "K540E"
	3	"resistance" or "sensitivity"
	4	"sulfadoxine" or "pyrimethamine"
	5	[Country]
	6	1 and (2 or 3) and 4 and 5
	7	Repeat 6 for each 5
II. pfdhps581G	1	"malaria" or "falciparum" or "plasmodium"
	2	"581G" or "A581" or "A581G"
	3	"resistance" or "sensitivity"
	4	"sulfadoxine" or "pyrimethamine"
	5	[Country]
	6	1 and (2 or 3) and 4 and 5
	7	Repeat 6 for each 5
III. Malaria control policy implementation	1	"malaria" or "falciparum" or "plasmodium"
	2	"protocol" or "norm" or "recommended" or "recommendation" or "guideline" or "policy" or "drug" or "program" or "intervention"
	3	"national" or "country" or "government" or "ministry"
	4	"artemisinin" or "sulfadoxine-pyrimethamine"
	5	"changing" or "changed" or "adopted" or "adoption" or "implementation" or "implemented" or "enforced"
	6	[Country]
	7	1 and 2 and 3 and 4 and 5 and 6
	8	Repeat 7 for each 6

Supplement 1.2

Table S2: Eligibility criteria used for the inclusion and exclusion of the clinical and community surveys on relevant pfdhps mutations identified through comprehensive search in medical databases

Inclusion Criteria	Exclusion Criteria
I included surveys: 1. involving human populations, 2. that were clinical or population-based studies 3. conducted in sub-Saharan Africa 4. reporting molecular data from clinical samples collected between January 1998 and December 2018 5. reporting data on the number of clinical samples tested and found positive for the respective molecular markers (i.e., pfdhpsK540E or pfdhpsA561G) 6. published in peer reviewed journals	I excluded from the analyses those studies that: 1. involved nonhuman populations 2. did not describe the demographic group of the patients from whom the genotyped clinical samples were collected 3. were conducted in a year and geography for which year-specific data on malaria endemicity is not available at the administrative level 1 or below within two-year period from the year of sample collection 4. did not report the year when the clinical samples were collected 5. were reviews or pooled-analyses or conducted in vitro 6. were conducted in a geography for which the eligible surveys following the criteria above do not span at least four different site-years of a lower administrative level

Supplement 1.3

Table S3. Full list of the site-years of data among eligible surveys from the systematic review used in the analysis for each resistance marker, consolidated per geography, where the country names and assignment to specific groupings are based on the United Nations Terminology Database. Data are sufficient to compute national trends for the countries whose names are colored in red in the table. These are the countries where the number of eligible surveys meet the criteria indicated in supplement 1.2. However, data from all countries listed in the table are used per respective region to compute regional trends, except for high-level resistance in central Africa where due to marked differences in temporal trends between Equatorial Guinea and the rest of the region as noted in my sensitivity analysis I do not include data from this country when computing regional trends in high-level resistance. Additionally, I assign Sudan to eastern Africa elsewhere throughout the manuscript as well as in the analysis due to similarity of its national trends in resistance with temporal trends observed in most of eastern Africa. For pfdhps540E, almost 200,000 patients provided <70,000 samples. Likewise, for pfdhps581G, almost 110,000 patients provided <40,000 samples. This is because clinical samples collected from some patients are not successfully genotyped for these pfdhps mutations, and therefore are not used for resistance measuring. Technical difficulties to conduct genotyping is one of the contributing factors, among others.

Region	Country	Sites	Years	Marker	Tested Samples	Positive Samples	Surveys
Northern Africa	Sudan	Gadaref, Kassala, Khartoum, Northern Kordofan, Sennar, White Nile	1998, 1999, 2000, 2001, 2003, 2011, 2012	pfdhps540E	1411	748	Abdel-Muhsin et al, 2003; Abdel-Muhsin et al, 2004; Adeel et al, 2016; A-Elbasit et al, 2008; A-Elbasit et al, 2007; Al-Saai et al, 2009; Gadalla et al, 2013; Osman et al, 2007; Pearce et al, 2009
Western Africa	Benin	Atlantique Borgou, Littoral, Mono, Oueme	2005, 2007, 2008, 2010, 2011, 2012	pfdhps540E	1126	3	Bertin et al, 2011; Dahlstrom et al, 2013; Moussiliou et al, 2013; Nahum et al, 2009; Oguyemi-Hounto et al, 2013a; Oguyemi-Hounto et al, 2013b
Western Africa	Burkina Faso	Centre-Ouest, Hauts-bassins, Plateau-Central, Sud-ouest	2002, 2003, 2004, 2009, 2010, 2011, 2012, 2015	pfdhps540E	2880	6	Cisse et al, 2017; Coulibaly et al, 2014; Dokomajilar et al, 2006; Pearce et al, 2009; Ruizendaal et al, 2017; Some et al, 2014a; Ruizendaal et al, 2017; Some et al, 2014b; Some et al, 2016; Tahita et al, 2015; Tinto et al, 2007
Western Africa	Gambia	North Bank	1998, 2000, 2001, 2004, 2007, 2008	pfdhps540E	581	0	Dunyo et al, 2006; Nwakanma et al, 2014; Pearce et al, 2009

Western Africa	Ghana	Ashanti, Brong Ahafo, Central, Eastern, Greater Accra, Northern, Upper East, Volta, Western	2001, 2002, 2003, 2004, 2005, 2006, 2008, 2010, 2013, 2017	pfdhps540E	1909	21	Abugri et al, 2018 Alam et al, 2011; Duah et al, 2012; Marks et al, 2005; Mockenhaupt et al, 2005; Pearce et al, 2009
Western Africa	Guinea	N'Zerekore	2004	pfdhps540E	135	14	Bonnet et al, 2007
Western Africa	Guinea-Bissau	Bissau Autonomous Sector, Tombali	2001, 2016	pfdhps540E	383	1	Kofoed et al, 2004; Nag et al, 2017
Western Africa	Ivory Coast	Abidjan, Comoe, Lagunes	2001, 2005	pfdhps540E	189	0	Ako et al, 2012; Djaman et al, 2007
Western Africa	Liberia	Maryland	2000	pfdhps540E	14	0	Checchi et al, 2002
Western Africa	Mali	Kayes, Kidal, Koulikoro, Mopti, Segou, Sikasso, Bamako	1999, 2000, 2003, 2004, 2006, 2007, 2010, 2012, 2014, 2016	pfdhps540E	2046	45	Coulibaly et al, 2014; Desai et al, 2016; Diallo et al, 2019; Diawara et al, 2017; Dicko et al, 2010; Djimde et al, 2004; Djimde et al, 2008; Dumbo et al, 2013; Maiga et al, 2016; Tekete et al, 2009; Thera et al, 2005
Western Africa	Mauritania	Hodh el Gharbi	1998, 2010	pfdhps540E	423	4	Eberl et al, 2001; Salem et al, 2017
Western Africa	Niger	Maradi, Niamey, Zinder	2003, 2006, 2012	pfdhps540E	261	0	Grais et al, 2018; Ibrahim et al, 2009
Western Africa	Nigeria	Borno, Cross River, Edo, Enugu, FCT – Abuja, Lagos, Oyo	2003, 2004, 2005, 2008, 2010, 2011, 2012, 2014, 2015	pfdhps540E	633	53	Esu et al, 2018; Happi et al, 2005; Iwalokun et al, 2015; Oguike et al, 2016; Pearce et al, 2009
Western Africa	Senegal	Dakar, Diourbel, Fatick,	1999, 2000, 2002,	pfdhps540E	1996	3	Boussaroque et al, 2016; Cisse et al, 2009; Faye et al, 2011;

		Kaolack, Kedougou, Kolda, Tambacounda, Thies	2003, 2004, 2006, 2007, 2008, 2009, 2010, 2011, 2014				Lo et al, 2013; Mbaye et al, 2017; Ndiaye et al, 2005; Ndiaye et al, 2013a; Ndiaye et al, 2013b; Ndiaye et al, 2017; Noranat et al, 2007; Pearce et al, 2009
Central Africa	Angola	Benguela, Cabinda, Huambo, Huila, Kuanza Norte, Luanda, Malanje, Uige	2003, 2004, 2007, 2011,	pdfhps540E	2712	31	Figueiredo et al, 2008; Fortes et al, 2011; Gama et al, 2011; Kaingona-Daniel et al, 2016; Menegon et al, 2009; Ngane et al, 2015; Pearce et al, 2009
Central Africa	Cameroon	Centre, Est, Nord, Nord – Ouest, Ouest, Sud, Sud - Ouest	1999, 2001, 2002, 2003, 2004, 2005, 2011, 2013	pdfhps540E	2529	11	Chauvin et al, 2015; Mbacham et al, 2010; McCollum et al, 2008; Menemedengue et al, 2011; Moyeh et al, 2018; Pearce et al, 2009; Tahar et al, 2007
Central Africa	Central African Republic	Ombella-mpoko	2004, 2010	pdfhps540E	268	5	Menard et al, 2006; Nambei et al, 2013
Central Africa	Chad	Mayo-Dala	2015	pdfhps540E	30	0	Souleymane et al, 2018
Central Africa	Congo	Kouilou, Pool	1999, 2002, 2004, 2013	pdfhps540E	516	31	Koukouikila-Koussounda et al, 2015; Ndounga et al, 2007; Nsimba et al, 2005; Pearce et al, 2009
Central Africa	Democratic Republic of the Congo	Bandundu, Bas-Congo, Equateur, Kasai-Occidental, Kasai-Oriental, Katanga, Kinshasa, Maniema, Nord Kivu, Province Orientale, Sud Kivu	2002, 2004, 2007, 2008, 2014	pdfhps540E	1173	304	Alker et al, 2008; Baraka et al, 2017; Cohuet et al, 2006; Mobula et al, 2009; Ruh et al, 2018; Swarthout et al, 2006; Taylor et al, 2013
Central Africa	Equatorial Guinea	Bioko Norte, Litoral	2005, 2013	pdfhps540E	699	58	Berzosa et al, 2017; Guerra et al, 2017; Mendes et al, 2013

Central Africa	Gabon	Estuaire, Haut-Ogooue, Moyen-Ogooue, Woleu-Ntem	1998, 2000, 2005, 2007, 2008, 2011	pdfhps540E	543	10	Aubouy et al, 2003; Bouyou-Akotet et al, 2015; Mawili-Mboumba et al, 2001; Mombo-Ngoma et al, 2011; Ngomo et al, 2016; Nsimba et al, 2008; Pearce et al, 2009
Eastern Africa	Djibouti	Djibouti	1998, 1999, 2002	pdfhps540E	139	15	Rogier et al, 2005
Eastern Africa	Ethiopia	Amhara, Benishangul, Gumuz, Oromia, SNNP, Tigray,	2004, 2005, 2008, 2009	pdfhps540E	501	438	Hailemeskel et al, 2013; Mula et al, 2011; Pearce et al, 2009; Schunk et al, 2006; Tessema et al, 2015
Eastern Africa	Kenya	Coast, Nyanza, Rift Valley, Western	1998, 1999, 2000, 2001, 2002, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013	pdfhps540E	3553	2957	Bonizzoni et al, 2009; Iriemenam et al, 2012; Juma et al, 2014; Juma et al, 2019; Lucchi et al, 2015; McCollum et al, 2012; Nzila et al, 2000; Oesterholt et al, 2009; Ogutu et al, 2005; Omar et al, 2001; Pearce et al, 2009; Shah et al, 2011; Shah et al, 2015; Spalding et al, 2010; Wendler et al, 2013; Zhong et al, 2008
Eastern Africa	Madagascar	Atsimo Andrefana, Atsimo Atsinanana, Atsinanana, Menabe, Sava, Sofia	2006, 2007	pdfhps540E	653	0	Andriantsoanirina et al, 2009; Checchi et al, 2002
Eastern Africa	Malawi	Central Region, Northern Region, Southern Region	1999, 2000, 2001, 2003, 2005, 2006, 2007, 2009, 2011, 2012	pdfhps540E	5600	5334	Alker et al, 2005; Artimovich et al, 2015a; Artimovich et al, 2015b; Bell et al, 2008; Bridges et al, 2009; Bwijo et al, 2003; Gutmann et al, 2015; Kublin et al, 2002; Lin et al, 2013; Nkhoma et al, 2007; Ocholla et al, 2014; Ravenshall et al, 2016 Taylor et al, 2014

Eastern Africa	Mozambique	Cabo Delgado, Gaza, Maputo, Maputo (city), Sofala, Tete	1999, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2015	pdfhps540E	7899	3668	Alifrangis et al, 2003; Enosse et al, 2008; Fernandes et al, 2007a; Fernandes et al, 2007b; Gupta et al, 2018; Mayor et al, 2008; Menendez et al, 2011; Pearce et al, 2009; Raman et al, 2008; Raman et al, 2010; Raman et al, 2011
Eastern Africa	Rwanda	East/Iburasirazuba, South/Amajepfo, West/Iburengerazuba	2006, 2010, 2015,	pdfhps540E	1243	1149	Karema et al, 2010; Kateera et al, 2016; Zeile et al, 2012
Eastern Africa	Somalia	Bari Jubbada Hoose Shabeellaha Dhexe Shabeellaha Hoose	2011, 2015	pdfhps540E	357	179	Warsame et al, 2015; Warsame et al, 2017
Eastern Africa	South Sudan	Jonglei, Northern Bahr El Ghazal	2001, 2002	pdfhps540E	119	7	Anderson et al, 2003; van den Broek et al, 2003
Eastern Africa	Tanzania	Dodoma, Kagera, Kilimanjaro, Lindi, Mara, Mbeya, Morogoro, Mtwara, Mwanza, Pwani, Ruvuma, Tanga	1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2011, 2013, 2014, 2015	pdfhps540E	13311	7205	Alifrangis et al, 2003; Alifrangis et al, 2009; Baraka et al, 2015; Baraka et al, 2017; Curtis et al, 2002; Enevold et al, 2007; Gesase et al, 2009; Harrington et al, 2009; Kamugisha et al, 2012; Kavishe et al, 2016; Kidima et al, 2006; Malisa et al, 2010; Malisa et al, 2011; Matondo et al, 2014; Mbugi et al, 2006; Mugittu et al, 2004; Ndiaye et al, 2017; Ngondi et al, 2017; Pearce et al, 2013; Pearce et al, 2003; Pearce et al, 2009; Pearce et al, 2013; Schonfeld et al, 2007
Eastern Africa	Uganda	Apac, Arua, Bundibugyo, Jinja, Kabale,	1999, 2000, 2001, 2002, 2003,	pdfhps540E	8697	7639	Barak et al, 2017; Braun et al, 2015; Conrad et al, 2017; Dorsey et al, 2003; Francis et al, 2006;

		Kabarole, Kampala, Kanungu, Mbarara, Mubende, Mukono, Rukungiri, Tororo	2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015				Gasasira et al, 2010; Jelinek et al, 1999; Kanya et al, 2007; Kyabayinze et al, 2003; Lynch et al, 2008; Malamba et al, 2006; Malamba et al, 2010; Mbogo et al, 2014; Mbonye et al, 2015; Sandison et al, 2011; Sendagire et al, 2005a; Sendagire et al, 2005b; Staedke et al, 2004; Talisuna et al, 2004; Tumwebaze et al, 2015; Tumwebaze et al, 2017
Eastern Africa	Zambia	Central, Copperbelt, Eastern, Luapula, Lusaka, 2011, Muchinga, Southern	2000, 2003, 2004, 2006, 2011, 2013	pdfhps540E	510	220	Mkulama et al, 2008; Pearce et al, 2009; Siame et al, 2015; Tan et al, 2014
Eastern Africa	Zimbabwe	Mashonaland Central, Mashonaland West, Masvingo	2003	pdfhps540E	112	16	Mlambo et al, 2007
Southern Africa	Namibia	Kavango	2005	pdfhps540E	76	7	Pearce et al, 2009
Southern Africa	South Africa	Kwazulu-Natal, Mpumalanga	1998, 1999, 2000, 2002	pdfhps540E	523	83	Barnes et al, 2008; Roper et al, 2003
Southern Africa	Eswatini	Lubombo	1999, 2007	pdfhps540E	29	2	Dlamini et al, 2010
Northern Africa	Sudan	Sennar, Gadaref, White Nile, Kassala	2003, 2011, 2012	pdfhps581G	488	109	Adeel et al, 2016; Gadalla et al, 2013; Osman et al, 2007
Western Africa	Benin	Mono	2010	pdfhps581G	212	0	Moussiliou et al, 2013
Western Africa	Burkina Faso	Plateau-Central	2011	pdfhps581G	312	0	Coulibaly et al, 2014
Western Africa	Ghana	Northern, Upper East, Brong Ahafo, Ashanti, Central	2002, 2008	pdfhps581G	297	1	Mockenhaupt et al, 2005; Alam et al, 2011

Western Africa	Guinea-Bissau	Bissau Autonomous Sector	2016	pdfhps581G	306	0	Nag et al, 2017
Western Africa	Ivory Coast	Abidjan, Comoe, Lagunes,	2001, 2005	pdfhps581G	189	0	Djaman et al, 2007; Ako et al, 2012
Western Africa	Mauritania	Hodh el Gharbi	1998, 2010	pdfhps581G	430	0	Salem et al, 2017
Western Africa	Mali	Segou, Kayes	2010	pdfhps581G	402	0	Desai et al, 2016; Coulibaly et al, 2014
Western Africa	Niger	Niamey	2003	pdfhps581G	40	0	Ibrahim et al, 2009
Western Africa	Nigeria	Oyo, Edo, Enugu, Cross River	2003, 2008, 2010, 2014, 2015	pdfhps581G	382	20	Oguike et al, 2016; Esu et al, 2018
Western Africa	Senegal	Thies, Dakar, Fatick, Tambacounda	1999, 2000, 2002, 2003, 2008, 2009, 2010, 2011, 2014	pdfhps581G	790	1	Ndiaye et al, 2013; Ndiaye et al, 2017; Boussaroque et al, 2016; Noranat et al, 2007; Ndiaye et al, 2005
Central Africa	Gabon	Haut-Ogooue, Estuaire, Moyen-Ogooue	1998, 2000, 2005, 2007, 2011	pdfhps581G	363	0	Mawili-Mboumba et al, 2001; Aubouy et al, 2003; Bouyou-Akotet et al, 2015
Central Africa	Angola	Benguela, Luanda, Uige	2004, 2007, 2011	pdfhps581G	713	2	Ngane et al, 2015; Gama et al, 2011; Menegon et al, 2009
Central Africa	Cameroon	Centre, Sud - Ouest	2003, 2005, 2011	pdfhps581G	648	7	Chauvin et al, 2015; Mbacham et al, 2010
Central Africa	Central African Republic	Ombella-mpoko	2004	pdfhps581G	84	0	Menard et al, 2006
Central Africa	Congo	Pool	2004	pdfhps581G	80	0	Ndounga et al, 2007
Central Africa	Democratic Republic of the Congo	Nord Kivu, Kinshasa, Bandundu, Bas-Congo, Equateur,	2002, 2007, 2014	pdfhps581G	385	67	Alker et al, 2008; Baraka et al, 2017; Taylor et al, 2013

		Kasai-Occidental, Kasai-Oriental, Katanga, Maniema, Province Orientale, Sud Kivu					
Central Africa	Equatorial Guinea	Litoral, Bioko Norte	2005 2013	pdfhps581G	699	331	Guerra et al, 2017; Berzosa et al, 2017
Eastern Africa	Ethiopia	Benishangul Gumuz, SNNP	2004, 2005, 2008	pdfhps581G	531	0	Tessema et al, 2015
Eastern Africa	Kenya	Nyanza, Western, Coast, Rift Valley	1998, 2000, 2001, 2004, 2005, 2007, 2008, 2009, 2010, 2011, 2012	pdfhps581G	2442	224	Shah et al, 2015; Shah et al, 2011; Juma et al, 2014; Lucchi et al, 2015; Omar et al, 2001; Zhong et al, 2008; Iriemenam et al, 2012; Wendler et al, 2013; Oesterholt et al, 2009; Spalding et al, 2010; Nzila et al, 2000
Eastern Africa	Madagascar	Atsinanana, Menabe, Sofia, Atsimo Andrefana, Sava, Atsimo Atsinanana	2006, 2007	pdfhps581G	653	0	Andriantsoanirina et al, 2009
Eastern Africa	Malawi	Southern Region, Central Region	2000, 2001, 2003, 2005, 2009, 2011, 2012	pdfhps581G	4588	119	Gutman et al, 2015; Artimovich et al, 2015; Ravenhall et al, 2016; Gutmann et al, 2015; Bwijo et al, 2003; Alker et al, 2005; Taylor et al, 2014; Bell et al, 2008; Ocholla et al, 2014
Eastern Africa	Mozambique	Maputo, Gaza	1999, 2001, 2002, 2003, 2004, 2006, 2007, 2008, 2009, 2010	pdfhps581G	4616	0	Raman et al, 2008; Enosse et al, 2008; Raman et al, 2011

Eastern Africa	Rwanda	East/Iburasirazuba, West/Iburengerazuba, South/Amajepfo	2010, 2015	pdfhps581G	506	405	Kateera et al, 2016; Zeile et al, 2012
Eastern Africa	Somalia	Jubbada Hoose, Shabeellaha Hoose, Shabeellaha Dhexe, Bari	2011, 2015	pdfhps581G	357	58	Warsame et al, 2015; Warsame et al, 2017
Eastern Africa	South Sudan	Northern Bahr El Ghazal, Jonglei	2001, 2002	pdfhps581G	119	0	Anderson et al, 2003; van den Broek et al, 2003
Southern Africa	South Africa	Kwazulu-Natal	1999	pdfhps581G	198	0	Roper et al, 2003
Eastern Africa	Tanzania	Tanga, Kagera, Lindi, Mbeya, Mtwara, Mwanza, Pwani, Mara, Ruvuma, Morogoro, Kilimanjaro, Dodoma	1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2011, 2013, 2014, 2015	pdfhps581G	9097	446	Mutabingwa et al, 2001; Baraka et al, 2015; Kavishe et al, 2016; Ngondi et al, 2017; Baraka et al, 2017; Ndiaye et al, 2017; Mugittu et al, 2004; Curtis et al, 2002; Malisa et al, 2010; Pearce et al, 2003; Alifrangis et al, 2009; Gesase et al, 2009; Malisa et al, 2011; Enevold et al, 2007; Kidima et al, 2006; Mbugi et al, 2006; Harrington et al, 2009; Schonfeld et al, 2007
Eastern Africa	Uganda	Jinja, Kanungu, Tororo, Mukono, Mbarara, Rukungiri, Kabale, Kabarole, Bundibugyo	1999, 2004, 2005, 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015	pdfhps581G	2463	210	Tumwebaze et al, 2017; Conrad et al, 2017; Mbogo et al, 2014; Mbonye et al, 2015; Barak et al, 2017; Francis et al, 2006; Tumwebaze et al, 2015; Lynch et al, 2008; Jelinek et al, 1999
Eastern Africa	Zambia	Luapula, Southern	2000, 2003, 2006, 2013	pdfhps581G	241	10	Siame et al, 2015; Mkulama et al, 2008

Supplement 1.4

Table S4: Year of IPTp and ACT policy adoption and/or implementation. IPT2 denotes two doses of SP during pregnancy. IPT3 denotes three doses of SP during pregnancy. IPT2+ denotes two or more doses of SP during pregnancy. For ACT, many countries changed their policy over time, therefore only the current policy and its year of adoption are shown below. When applicable, for ACT the first-row drugs and year of adoption refer to drugs for first-line treatment of unconfirmed malaria, and the second-row drugs and year of adoption refer to the first-line treatment of confirmed *P. falciparum* infection, with the exception of Tanzania where the first-row refers to Mainland and the second row Zanzibar. ACT artemisinin-based combination therapy, AL Artemether-Lumefantrine, AS Artesunate, AQ Amodiaquine, DHA Dihydroartemisinin, IPTp intermittent preventive treatment in pregnancy, PPQ Piperaquine, QN Quinine, CL Clindamycin, D Doxycycline, PQ Primaquine, SP Sulphadoxine-pyrimethamine. CAR and DRC denote Central African Republic and the Democratic Republic of the Congo, respectively. NA denotes data not available.

Country	IPTp policy	Year of IPTp policy adoption	ACT policy	Year of ACT policy adoption
Angola	IPT2	2005	AL	2006
Benin	IPT2	2005	AL	2004
Burkina Faso	IPT2	2005	AL; AS+AQ	2005
Cameroon	IPT2	2004	AS+AQ	2004
CAR	IPT2	2007	AL	2005
Chad	IPT2	2004	AL; AS+AQ	NA
Congo	IPT2	2006	AS+AQ	NA
Djibouti	IPT2	NA	AL AL+PQ	2014 2014
DRC	IPT2	2004	AS+AQ	2005
Equatorial Guinea	IPT2	2005	AS+AQ	2004
Ethiopia	NA	NA	AL	2004
Gabon	IPT2	2003	AS+AQ	2003
Gambia	IPT2	2003	AL	2005
Ghana	IPT3	2003	AS+AQ AL; AS+AQ	2004 2004
Guinea	IPT2	2005	AS+AQ	NA
Guinea-Bissau	IPT2	2004	AL	NA
Ivory Coast	IPT2	2005	AS+AQ	2003
Kenya	IPT2+	1999	AL	2004
Liberia	IPT2	2004	AS+AQ	2004
Madagascar	IPT2	2004	AS+AQ	2006
Malawi	IPT2	1993	AL	2007
Mali	IPT2	2003	AS+AQ	2007
Mauritania	IPT2	2006	AS+AQ AL; AS+AQ	NA NA
Mozambique	IPT2	2006	AL AL	2004 2004
Namibia	IPT2	2005	AL AL	2006 2006
Niger	IPT2	2005	AL AL	2005 2005
Nigeria	IPT2	2004	AL; AS+AQ	2004
Rwanda	IPT2	2005	AL	2005

Senegal	IPT2	2004	AL; AS+AQ; DHA-PPQ	2005
Somalia	IPT2	2002	AL AL+PQ	2016 2016
South Africa	IPT2	NA	AL; QN+CL; QN+D	2001
South Sudan	IPT2	2005	AS+AQ	2006
Sudan	IPT2	2005	AL AL	2017 2017
Eswatini	NA	NA	AL	2009
Tanzania	IPT2	2001	AL (Mainland) AS+AQ (Zanzibar)	2004 2004
Uganda	IPT2	2000	AL	2004
Zambia	IPT3	2001	AL	2002
Zimbabwe	IPT2+	2004	AL	2004

Supplement 1.5

Table S5: Full description of variables considered in the modelling framework

Variable	Description	Levels
X1	Malaria endemicity	Low, Intermediate, High
X2	Research group	Provided in Table S3
X3	Publication year	Provided in Table S3
X4	Sample collection setting	Hospital, Community
X5	Study design	Observational, Interventional
X6	Sample collection country	Provided in Table S3
X7	Sample collection site administrative level 1	Provided in Table S3
X8	Proportion of mixed mutations	Numeric
X9	PMID	Numeric
X10	Sample collection site longitude	Numeric
X11	Sample collection site latitude	Numeric
X12	HIV prevalence	Numeric
X13	SDI	Numeric
X14	Region	Provided in Table S3
X15	PC1	Numeric
X16	PC2	Numeric
X17	PC3	Numeric
X18	PC4	Numeric
X19	Drug used for anti-malarial prophylaxis	Not used, CTX, SP
X20	Patients screened enrolled meeting inclusion criteria	Numeric
X21	Samples infected successfully genotyped	Numeric
X22	Anti-malarial drug combination policy adopted	IPT0, IPT2, IPT2+, IPT3;
X23	Clinical samples collection time period in relation to policy implementation	Before, After
X24	Year policy implementation initiated	Numeric
X25	Mutation name	See Tables S6-S7
X26	Marker group	See Tables S6-S7
X27	Year of sample collection	Numeric
X28	Clinical malaria	Symptomatic, Asymptomatic
X29	HIV infection status	Infected, Not infected
X30	Number of samples tested for each marker	Numeric
X31	Number of samples positive for each marker (mutant = pure + mixed)	Numeric
X32	Sample collection timing in relation to anti-malaria drug administration	Pre-treatment, Post-treatment

Supplement 1.6

Table S6: Molecular markers of *P. falciparum* resistance to sulfadoxine-pyrimethamine and groupings used, following the current WHO designations. In my analysis I did not use pfdhps437G because this marker (when not associated with either pfdhps540E or pfdhps581G) has been associated with low-level resistance.⁹ Therefore, it is not recommended by the WHO as a marker to track SP resistance to inform policy regarding SP use.¹¹⁻¹⁴

Drug	Marker	Location	Group	Outcome
Sulfadoxine-pyrimethamine	540E	pfdhps	Associated	Mid-level Resistance
Sulfadoxine-pyrimethamine	437G-540E	pfdhps	Associated	Mid-level Resistance
Sulfadoxine-pyrimethamine	511-108N-437G-540E	pfdhfr+pfdhps	Associated	Mid-level Resistance
Sulfadoxine-pyrimethamine	511-437G-540E	pfdhfr+pfdhps	Associated	Mid-level Resistance
Sulfadoxine-pyrimethamine	511-540E	pfdhfr+pfdhps	Associated	Mid-level Resistance
Sulfadoxine-pyrimethamine	511-59R-108N-437G-540E	pfdhfr+pfdhps	Validated	Mid-level Resistance
Sulfadoxine-pyrimethamine	581G	pfdhps	Associated	High-level Resistance
Sulfadoxine-pyrimethamine	511-108N-540E-581G	pfdhps	Associated	High-level Resistance
Sulfadoxine-pyrimethamine	511-59R-108N-437G-581G	pfdhfr+pfdhps	Associated	High-level Resistance
Sulfadoxine-pyrimethamine	511-59R-108N-581G	pfdhfr+pfdhps	Associated	High-level Resistance
Sulfadoxine-pyrimethamine	437G-540E-581G	pfdhfr+pfdhps	Associated	High-level Resistance
Sulfadoxine-pyrimethamine	511-59R-108N-437G-540E-581G	pfdhfr+pfdhps	validated	High-level Resistance

Supplement 1.7

Table S7: Definition of the mutations validated to measure *P. falciparum* resistance to sulfadoxine-pyrimethamine

Genes	Location	Wild-type codon	Wild-type aminoacid	Mutant codon	Mutant aminoacid
pfdhfr	51	AAT AAC	Asn (N)	ATT	Ile (I)
pfdhfr	59	TGT	Cys (C)	CGT	Arg (R)
pfdhfr	108	AGC	Ser (S)	AAC	Asn (N)
pfdhps	437	GCT	Ala (A)	GGT	Gly (G)
pfdhps	540	AAA	Lys (K)	GAA	Glu (E)
pfdhps	581	GCG	Ala (A)	GGG	Gly (G)

Supplement 1.8

Table S8: Diagnostic accuracy of pfdhps and pfdhfr mutations for sulfadoxine-pyrimethamine treatment failure.¹⁵ PPV denotes positive predictive value. NPV denotes negative predictive value.

Transmission	Marker	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)
Stable	dhfr mutation	100	39	76	100
	dhfr Asn- 108	100	39	76	100
	≥2 dhfr mutations	92	100	100	87
	≥2 dhfr mutations + mutated dhps	64	100	100	59
	dhps mutation	68	46	71	43
	dhps Gly-437	36	69	69	36
	dhfr Asn-108 + dhps Gly-437	36	77	75	39
	Mutated dhfr and dhps	68	62	77	50
Seasonal and unstable	dhfr mutation	90	73	75	89
	dhfr Asn- 108	90	73	75	89
	≥2 dhfr mutations	30	100	100	61
	dhps mutation	70	91	88	77
	dhps Gly-437	40	100	100	65
	dhfr Asn-108 + dhps Gly-437	40	100	100	65
	Mutated dhfr and dhps	70	91	88	77

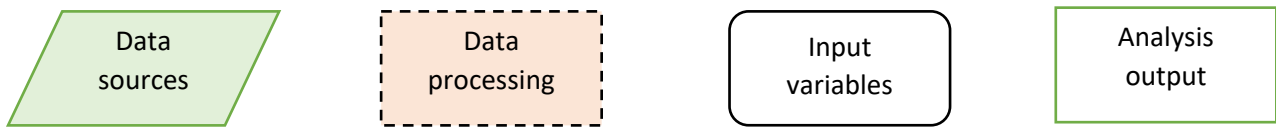
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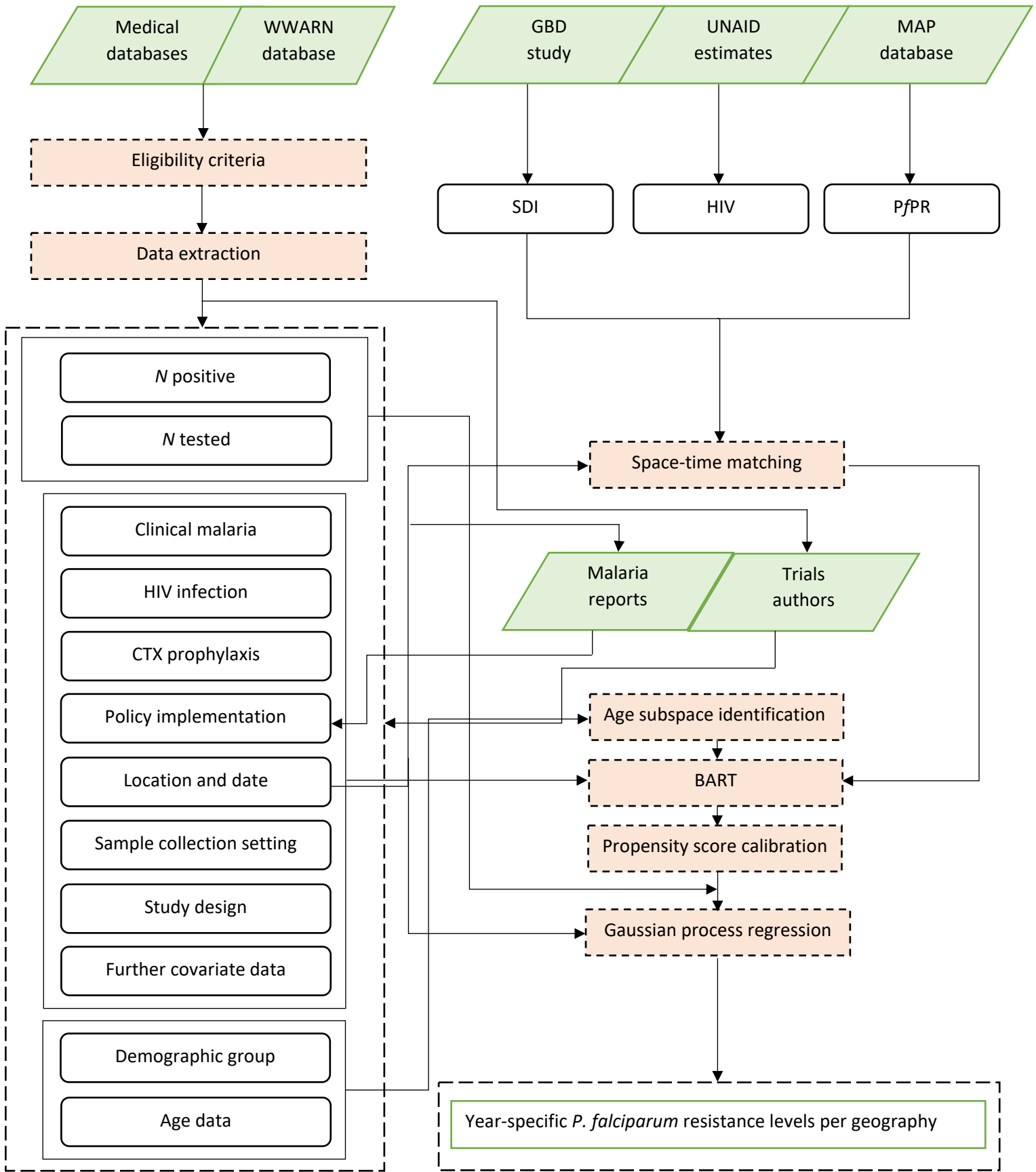
Modelling framework

Supplement 2.1

Figure S1: Analytical strategy overview

Key





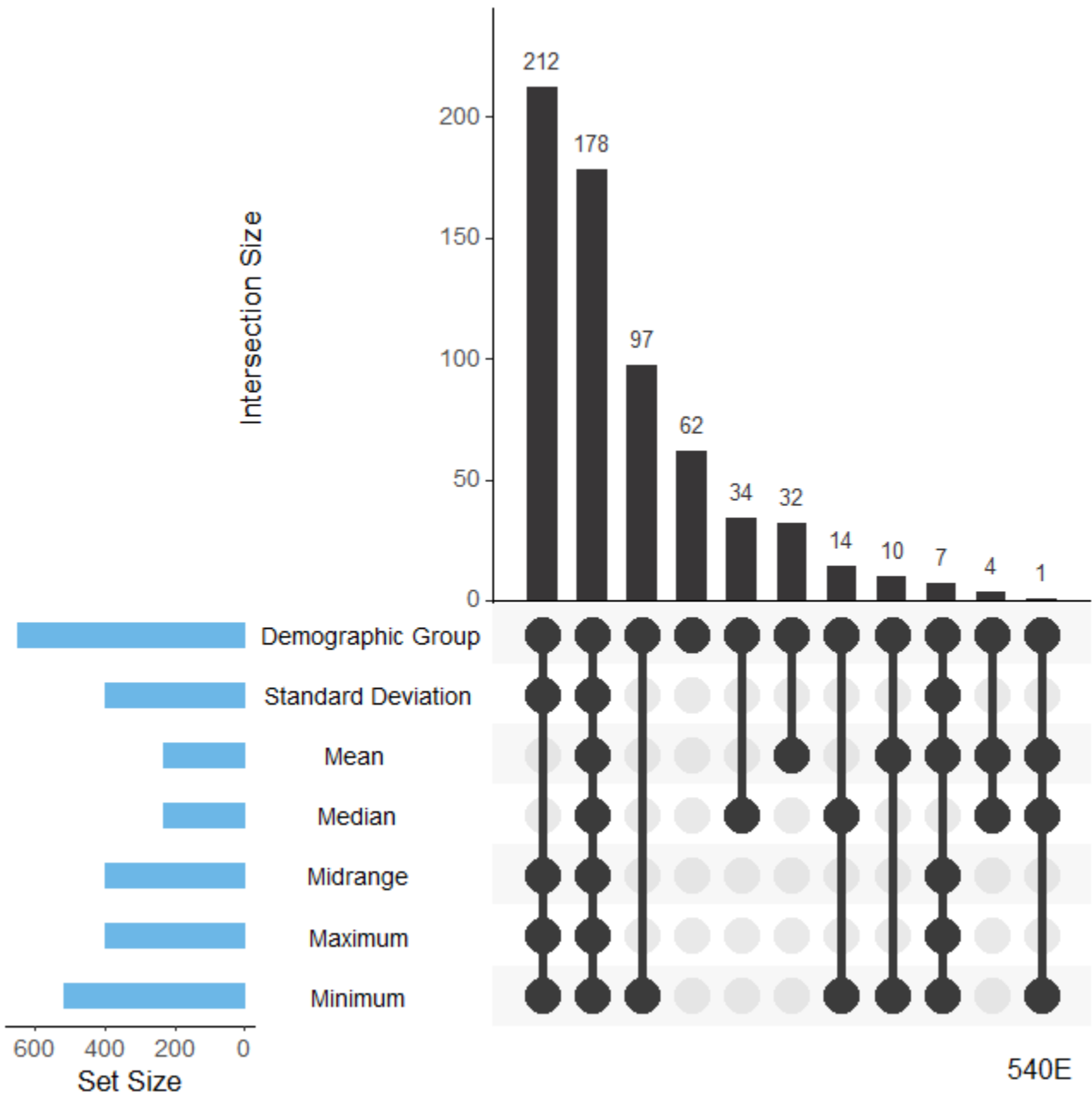
Supplement 2.2

Patient age principal subspace identification

Here I employ a Bayesian principal component analysis. A variational Bayes framework is used to compute the posterior distribution of the latent variable model parameters and the missing values concurrently through optimization.^{16,17} Following Hay et al 2009, I use as input measures the minimum, maximum, midrange, median, and mean age.¹⁸ I apply the formulas provided by Wan et al 2014 whenever applicable.¹⁹ The lower and upper bounds defined by the observed demographic groups as reported in each eligible survey were used to initialize the algorithm.¹⁶ After convergence, 10-fold cross-validation with 2,000 iterations was performed to determine the optimal number of dimensions of the computed patients' age latent space.²⁰ This procedure identified four and three dominant patterns in pfdhps540E and pfdhps581G data, respectively. Following previous work,²¹ these dimensions were then incorporated in the subsequent modelling stages, thus allowing effective age standardization of the predicted quantities for each resistance outcome. I use Q^2 distance,²² a cross-validated version of R^2 defined as follows for a given mean centered data matrix x , to quantify the ratio of variance that can be predicted independently by the BPCA model:

$$Q^2 = 1 - \frac{\sum(x_{ij} - \hat{x}_{ij})^2}{\sum(x_{ij})^2}$$

Figure S2: Joint distribution of the measures used as input for the age subspace identification algorithm



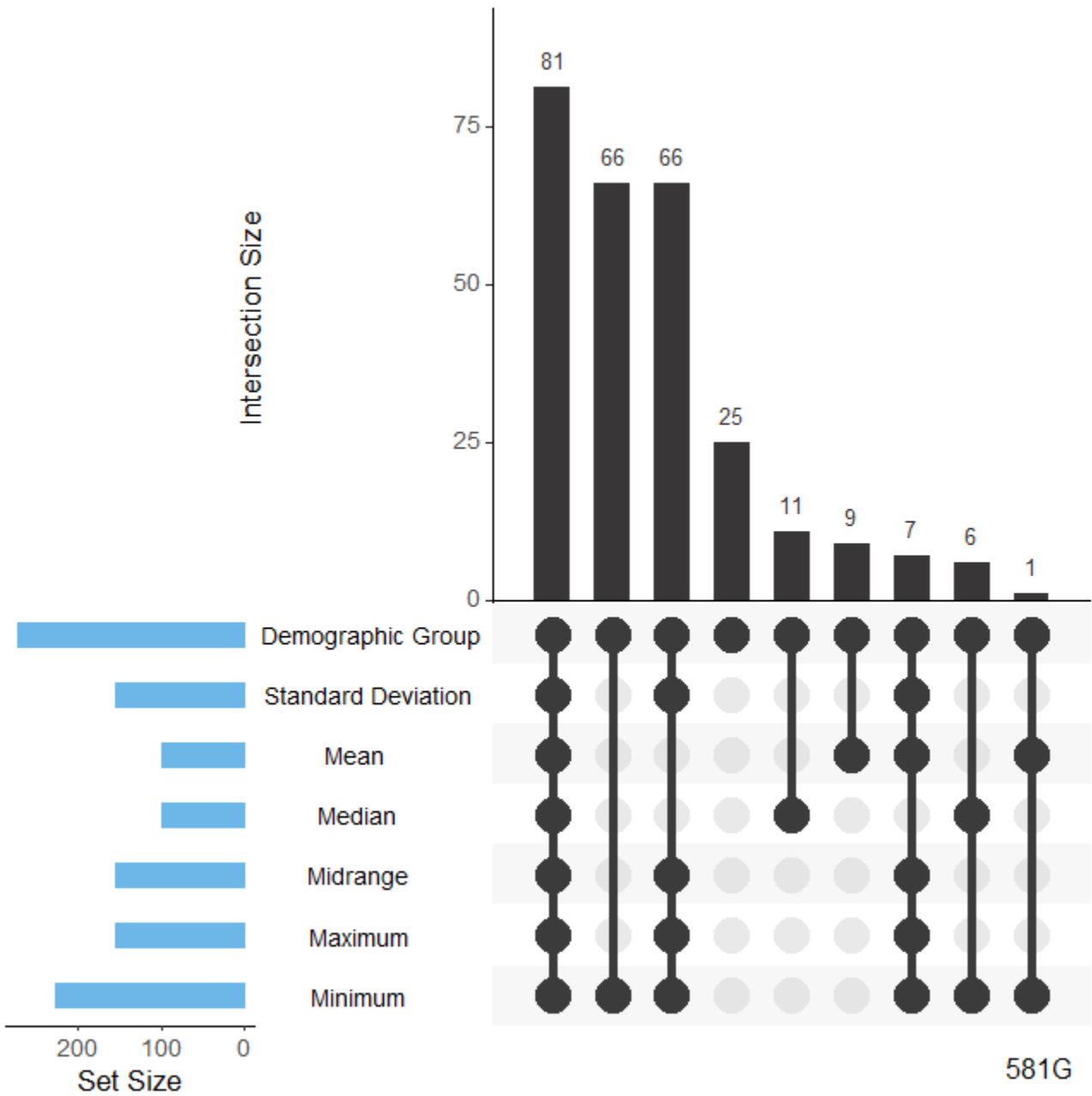
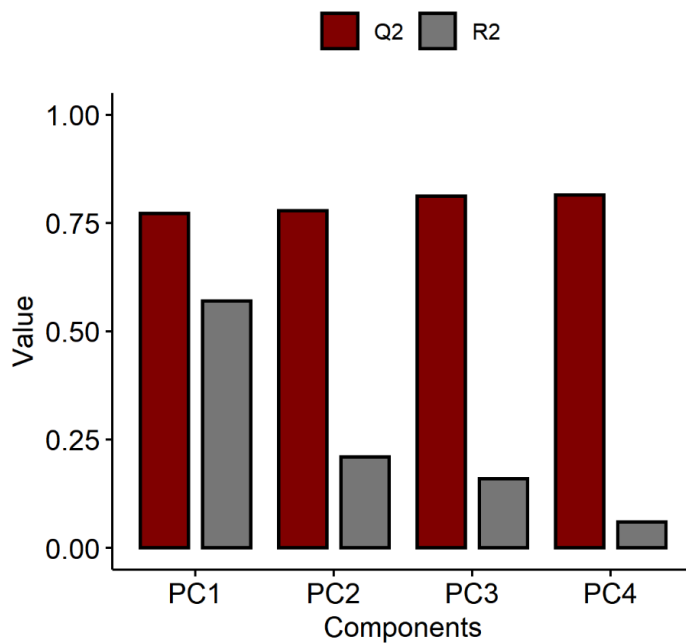


Figure S3: Q^2 distances and R^2 values across components. (A) Values for pfdhps540E data. (B) Values for pfdhps581G data.

A.



B.

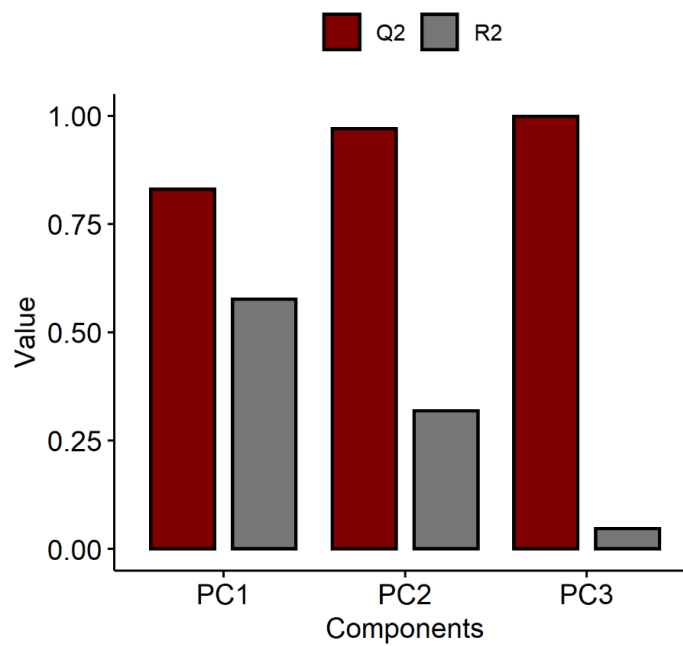
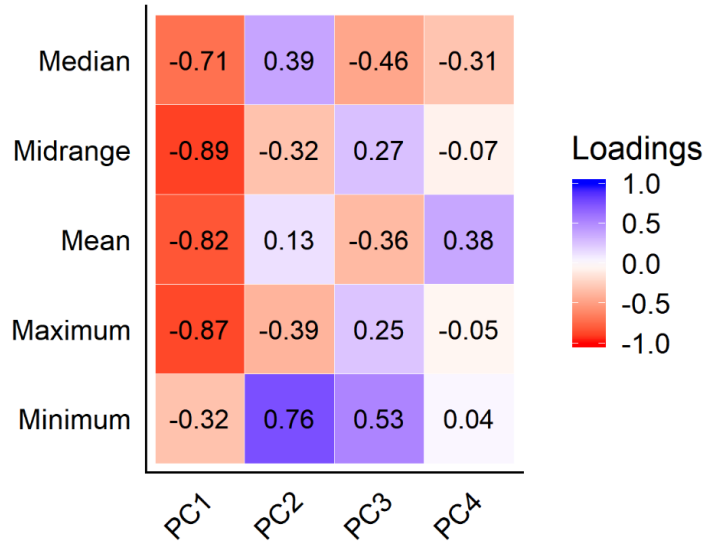
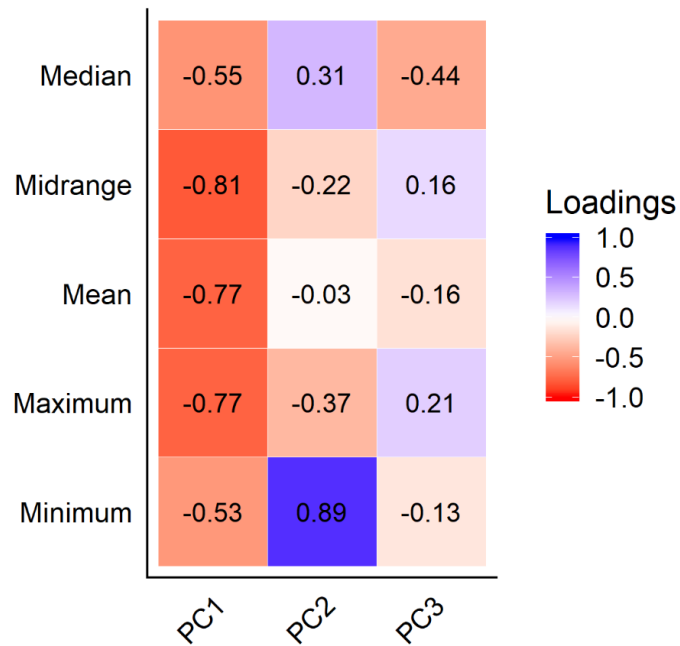


Figure S4: Component loadings. (A) Values for pfdhps540E data. (B) Values for pfdhps581G data.

A.



B.



Supplement 2.3

Propensity score calibration

Following Rubin 1985, I use randomization probabilities and their generalizations to adjust my quantities to potential confounders.²³ My motivation to use generalized propensity scores is because I have many potential confounders which have been reported in previous studies as being related to SP resistance. Including all covariates in the model might create model instability. Additionally, despite being referenced in previous studies as potential confounders, imbalance in covariate distribution in the observed data might be more pronounced for some variables as opposed to others. This means that including all covariates might not be efficient. Therefore, to achieve a parsimonious model and avoid overfitting I apply Bayesian additive regression trees (BART) to evaluate variable importance and then use the most relevant variables to compute my generalized propensity scores. This summarizes the relevant covariate information into a single dimension. The method uses sum of trees to model an unknown function and exhibits high-level predictive performance under both linear and non-linear settings,²⁴ making it appropriate for modelling complex epidemiological and clinical data.²⁵ I use the formulas recommended by Austin 2018²⁶ to compute my generalized propensity scores η as follows:

$$\eta_i = f_{Z|X}(z_i|x_i) = \frac{1}{\sqrt{2\pi\hat{\sigma}^2}} e^{-\frac{(z_i - \hat{\beta}^Z X)^2}{2\hat{\sigma}^2}}$$

where i denotes the observations whose η I seek to compute, z_i the observed value of the exposure variable for a given observation, $\hat{\beta}^Z X$ the mean value of the exposure variable estimated using BART, and $\hat{\sigma}$ the estimated standard deviation of the residual computed using BART.

By employing Bayesian techniques to construct decision tree ensembles, my approach allows effective redundancy reduction and stability optimization by keeping only the best covariates, while accounting for all relevant interactions and nonlinearities among the covariates in the propensity score computation. Regression trees recursively partition the covariate space into homogeneous segments with respect to the outcome. More details regarding performance of ensemble-of-trees methods in propensity score modelling compared to alternative strategies are provided elsewhere.²⁷⁻²⁹ In my implementation, Bayesian back fitting Markov chain Monte Carlo (MCMC) was employed to derive a posterior sample by iteratively fitting the sum-of-trees model, while using a prior to regularize each decision tree. Scalar propensity scores were obtained by evaluating these sum-of-trees model draws using 10,000 samples after discarding 2,000 burn-in iterations. Optimal tuning of hyperparameters and the selection of thresholds were determined using cross-validation. My sum-of-trees model can be expressed as:

$$Y = \sum_{j=1}^m g(x; T_j, M_j) + \varepsilon, \quad \varepsilon \sim N(0, \sigma^2)$$

where Y denotes the treatment or predictor, x the covariate space, m the number of trees, T_j each regression tree, M_j the terminal node parameters, and $g(\cdot)$ a function that assigns the parameter value associated with each terminal node $\mu_{ij} \in M_j$ to each value of x . The average frequency v_i of a given covariate $x_i \in x$ across all splitting rules Z_{ik} of the sum-of-trees model, where K denotes the number of MCMC samples, is used to derive its relative importance in explaining the variation in the treatment or predictor. This quantity is known as inclusion proportion, and computed as follows:

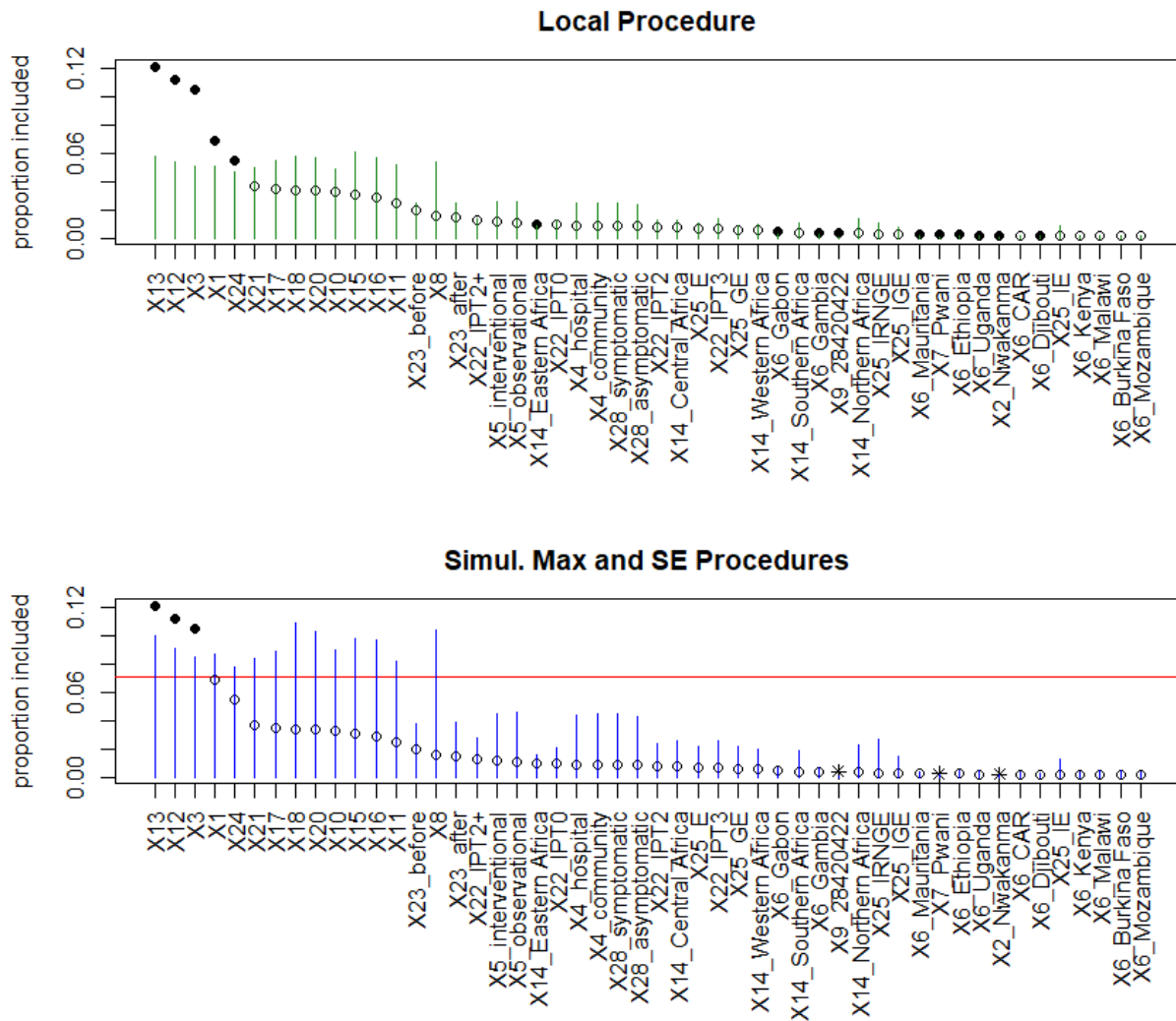
$$v_i = \frac{1}{K} \sum_{k=1}^K Z_{ik}$$

Interactions among the confounders are identified by evaluating the co-occurrence of a given pair of covariates in at least one Z_{ik} in each T_j .³⁰ Figure S5 provides these quantities, which reflect the dominant features in each propensity score model, where, Y is the exposure variable, that is, the variable over which trends in each resistance outcome I seek to compute, and x the design matrix of potential confounders, that is, covariates with respect to which I seek to

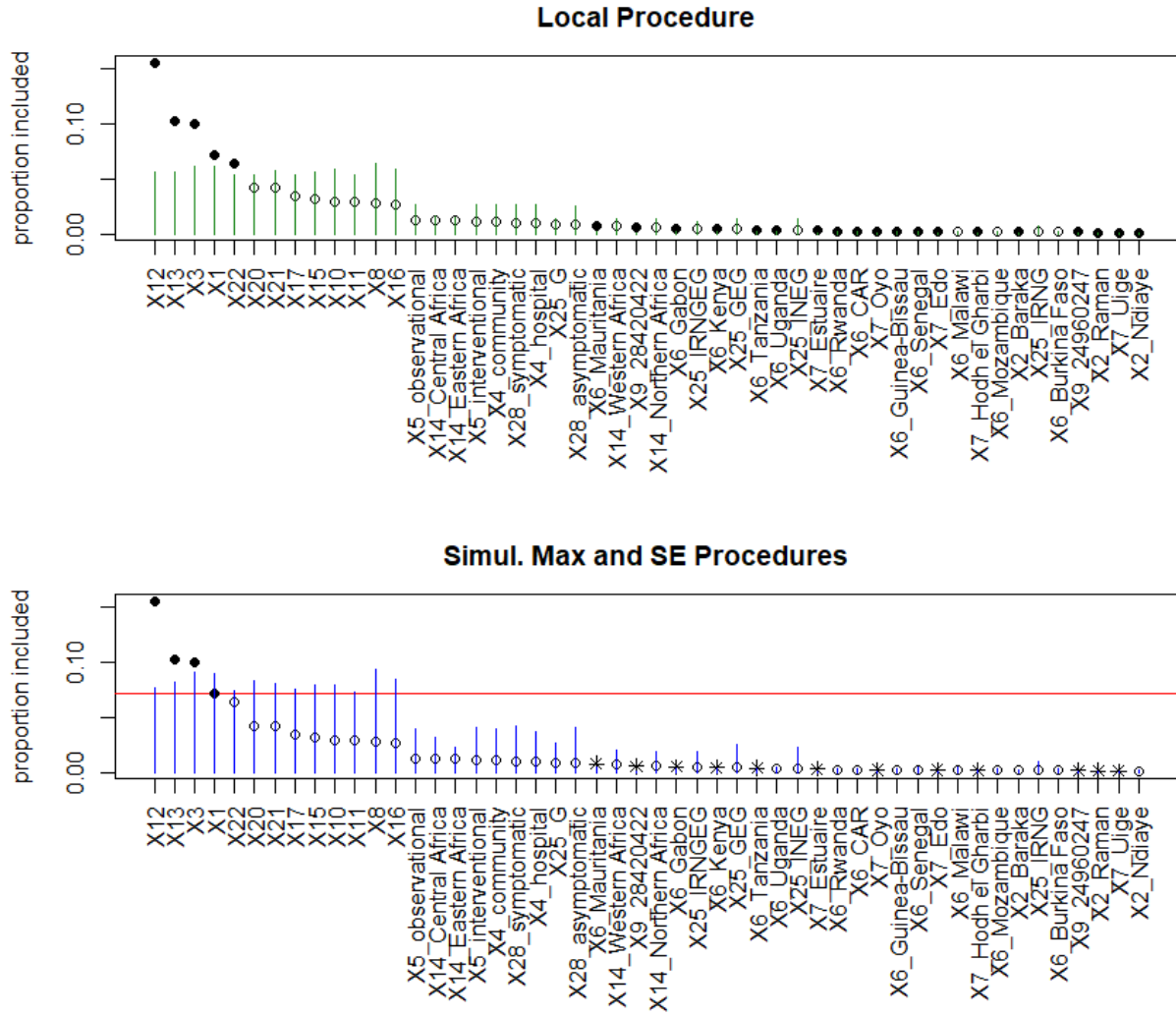
standardize our quantities of interest. A full description of the variables considered in the overall modelling framework is provided in Table S5.

Figure S5: Variable importance. Three variable selection rules are considered, namely local, global max, and global SE thresholds. For the graphs illustrating results based on local threshold, relevant confounders are those with inclusion proportion greater than the green bar. For the global max procedure, relevant confounders are those with inclusion proportion greater than the threshold indicated by the red line and those indicated with star, while for the global SE procedure, relevant confounders are those with inclusion proportion passing the blue bar. By selecting only the most important covariates, my approach ensures that the most important confounding factors are accounted for, while avoiding overfitting. (A) Values for pfdhps540E data. (B) Values for pfdhps581G data.

A.



B.



Supplement 2.4

Hierarchical Gaussian process regression

I use a Bayesian hierarchical framework based on binomial likelihood and random effects model via Gaussian process regression (GPR) to compute my quantities of interest. For an exhaustive treatment of GPR, see Rasmussen & Williams 2006.³¹ I summarize my modelling strategy and its rationale as follows.

To derive my quantities in relation to national and regional-scale *P. falciparum* resistance temporal trends, I first compute the expectation, at a certain values of the predictor space, of a function $f(x)$ that accurately models the outcome y given the predictor x :

$$y = f(x) + \varepsilon, \quad \varepsilon \sim N(0, \sigma^2)$$

Subsequently, I perform predictive comparisons to derive temporal change in resistance quantities per geography by applying the following formula:^{32,33}

$$\delta_u(u^{(1)} \rightarrow u^{(2)}, v, \phi) = \frac{E(y | u^{(2)}, v, \phi) - E(y | u^{(1)}, v, \phi)}{u^{(2)} - u^{(1)}}$$

where ϕ denotes the model parameters, u the predictor of interest, and v the other $\kappa - 1$ components of the predictor space, such that $x_\kappa = (u, v)$.

Nevertheless, the functional form for $f(x)$ is unknown and potentially nonlinear.³⁴ Therefore, I place a GP prior over $f(x)$, which assumes a mean function $m(x)$ and a covariance function $K(x, x')$. GP provides accurate predictions and reliable quantification of uncertainty of complex processes with minimal assumptions, making it the natural modelling strategy for my data. Given a set of covariates, GP marginalizes to a Multivariate Gaussian distribution with mean and covariance components:

$$\begin{aligned} \mu &= m(x) \\ \Sigma &= K(x, x') \end{aligned}$$

In my implementation, following Rasmussen & Williams 2006,³¹ I use $m(x) = 0$ and apply the squared exponential covariance function defined as follows:

$$K(x, x') = \sigma_{GP}^2 \exp\left(-\frac{1}{2l^2} (x - x')^2\right)$$

where σ_{GP}^2 and l^2 denote marginal variance and length scale, respectively. The marginal variance defines the variation in the dependent variable, whereas the length scale defines how quickly the dependent variable changes between x and x' . I infer these hyperparameters from the observed data using an empirical approach based on Bayesian framework with a weakly informative prior.

Under this setup, I compute the expectation $f(x^*)$ at a new value of the predictor x^* by means of the model:

$$f(x^*) | x, y \sim \text{MultiNormal}(\mu^*, \sigma_{GP}^2 - \Sigma^*)$$

where μ^* and Σ^* denote the posterior mean and covariance components, respectively. I apply this model to my binomial outcome defined as follows:

$$\text{Binomial}(n|N, \theta) = \binom{N}{n} \theta^n (1 - \theta)^{N-n}$$

where N denotes the number of patients tested, n the number of patients positive, and θ the estimated resistance prevalence. The year of sample collection is used as predictor and the administrative level 1 (i.e., province or state) corresponding to the sampling site as a random effects variable.

I employ the inverse logit function to map my estimates from the real space $]-\infty, +\infty[$ into the probability space $[0, 1]$.³⁵ Therefore, the predicted prevalence P for each space-time cluster was finally derived using the formula:

$$P = 100 \times \frac{\exp(y)}{1 + \exp(y)}$$

I compute the posterior probability to quantify the amount of evidence in favor of IPT_p and IPT_i being effective in each country-year under the current WHO thresholds,¹¹⁻¹³ given the estimated levels of *P. falciparum* resistance to SP. This measure is defined as follows:³⁶

$$\Pr(H_1|P) = BF \times PO \times \Pr(H_0|P)$$

where BF denotes the bayes factor, PO the prior odds, H_1 the hypothesis being tested, and H_0 , the alternative hypothesis, for each intervention per country-year. For IPT_p, the WHO thresholds for withdrawal of policy is when pfdhps540E >95% and pfdhps581G >10%. For IPT_i, the WHO thresholds for withdrawal of policy is pfdhps540E >50%.

I developed my GPR model in Stan and implemented it in R.^{37,38} I used a total of 20,000 post-warmup samples. I applied effective sample size per transition and split \hat{R} statistic to validate my model and leave-one-out cross-validation along with the widely applicable information criterion to assess its overall performance. These measures showed that my GPR model was well calibrated.^{39,40} See Figures S8 and S9 for posterior quantiles and visual MCMC diagnostics of the GPR model for each geography, respectively.

I conducted extensive sensitivity analysis to validate my model. For instance, I computed the resistance quantities using GPR without adjusting for confounders and/or using different hyperparameters and/or parameters priors. The results were relatively stable, confirming that the predicted resistance quantities are not artifacts of my modeling assumptions. These can be provided upon a reasonable request.

My modelling framework allows effective translation of clinical, epidemiological, and demographic heterogeneity across patients, surveys, and geographies on the continent into uncertainty quantified by means of uncertainty intervals around the point estimates, while ensuring applicability of the generated quantities to the general population.

Supplement 2.5

Posterior probability interval of prevalence per survey

Following Brown 2001, I use the modified Jeffreys interval to quantify uncertainty from each site-year of data. This interval is known to have desirable properties.⁴¹⁻⁴³ I apply non-informative beta prior $Beta(1/2, 1/2)$ for inference on the prevalence distribution for each binomial data point:

$$\text{positive} \sim \text{Binomial}(\text{tested}, \text{prevalence})$$

My posterior uncertainty boundaries for each data point are therefore computed as follows, where P denotes the prevalence at the lower and upper limits of the interval, respectively:

$$[P_{\text{lower}}, P_{\text{upper}}] = [B_{\alpha/2, \text{positive}+1/2, \text{tested}-\text{positive}+1/2}, B_{1-\alpha/2, \text{positive}+1/2, \text{tested}-\text{positive}+1/2}]$$

This formula is used to compute the uncertainty interval represented by the vertical bars in Figure 3. Full posterior probability distribution of prevalence per data point is provided in Figure S11.

Supplement 3:

Extended results

Supplement 3.1

Table S9: Year-specific standardized national and regional scale prevalence levels (top row) and uncertainty limits (middle and lower rows) of *P. falciparum* resistance sulfadoxine-pyrimethamine. Evidence on mid- and high-level SP resistance is based on pfdhps540E and pfdhps581G molecular markers, respectively. I do not report low-level resistance based on other pfdhps and pfdhfr markers given their poor diagnostic accuracy.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
--	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------	------

Mid-level resistance																					
Angola	3.90	3.89	3.88	3.87	3.86	3.86	3.86	3.85	3.86	3.86	3.86	3.86	3.87	3.87	3.89	3.90	3.91	3.93	3.96	3.97	3.99
	0.95	0.96	0.98	0.98	0.98	0.99	1.00	1.01	1.01	1.01	1.01	1.01	1.01	1.01	1.00	1.00	0.99	0.98	0.97	0.97	0.96
	12.63	12.54	12.46	12.46	12.39	12.46	12.50	12.55	12.56	12.64	12.75	12.82	12.90	13.12	13.33	13.49	13.72	14.07	14.35	14.69	15.09
Benin	0.44	0.42	0.40	0.39	0.37	0.36	0.35	0.34	0.32	0.31	0.30	0.29	0.29	0.28	0.27	0.27	0.26	0.26	0.25	0.25	0.25
	0.06	0.06	0.06	0.06	0.06	0.05	0.05	0.05	0.05	0.05	0.05	0.04	0.04	0.04	0.04	0.04	0.03	0.03	0.03	0.03	0.03
	2.53	2.27	2.08	1.92	1.78	1.67	1.58	1.50	1.43	1.38	1.35	1.32	1.29	1.26	1.26	1.25	1.26	1.28	1.30	1.33	1.36
Burkina Faso	0.14	0.14	0.14	0.15	0.15	0.16	0.16	0.17	0.17	0.18	0.19	0.20	0.21	0.22	0.23	0.24	0.25	0.27	0.28	0.29	0.31
	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.04	0.04	0.04	0.04

	0.87	0.86	0.85	0.84	0.83	0.83	0.84	0.84	0.86	0.87	0.89	0.92	0.95	0.98	1.03	1.09	1.16	1.25	1.35	1.47	1.64
Cameroon	0.39	0.39	0.39	0.39	0.39	0.40	0.40	0.41	0.41	0.42	0.42	0.43	0.44	0.44	0.45	0.46	0.47	0.48	0.50	0.51	0.52
	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08
	1.34	1.31	1.31	1.29	1.28	1.29	1.31	1.33	1.35	1.38	1.42	1.48	1.54	1.61	1.70	1.80	1.91	2.05	2.21	2.38	2.57
	0.39	0.55	0.78	1.12	1.60	2.29	3.27	4.68	6.67	9.42	13.12	18.04	24.27	31.84	40.48	49.66	58.79	67.31	74.79	80.94	85.84
Congo	0.06	0.10	0.14	0.22	0.33	0.49	0.73	1.09	1.60	2.36	3.45	5.00	7.11	9.82	13.56	18.36	24.28	31.07	38.66	46.63	54.28
	1.94	2.63	3.64	5.04	6.94	9.58	13.11	17.81	23.85	31.27	39.88	49.15	58.60	67.37	75.32	81.96	87.04	90.87	93.67	95.66	97.04
	16.11	16.09	16.08	16.10	16.07	16.10	16.14	16.14	16.16	16.17	16.19	16.24	16.27	16.30	16.38	16.42	16.51	16.54	16.57	16.65	16.71
Democratic Republic of the Congo	1.72	1.74	1.74	1.74	1.74	1.73	1.74	1.74	1.75	1.76	1.76	1.77	1.77	1.77	1.77	1.77	1.77	1.75	1.76	1.77	1.77
	68.26	68.07	68.08	67.97	68.01	68.09	68.13	68.25	68.27	68.46	68.59	68.68	68.82	68.98	69.26	69.33	69.69	69.88	70.28	70.58	70.89
	1.26	1.48	1.73	2.03	2.39	2.82	3.32	3.94	4.67	5.54	6.58	7.82	9.29	10.99	12.96	15.18	17.66	20.46	23.58	26.97	30.58
Equatorial Guinea	0.23	0.28	0.35	0.44	0.55	0.67	0.82	1.00	1.22	1.48	1.77	2.13	2.54	3.01	3.54	4.15	4.82	5.58	6.41	7.31	8.28
	6.92	7.69	8.55	9.57	10.82	12.20	13.71	15.27	17.16	19.51	22.33	25.23	28.57	32.16	36.37	40.54	45.13	50.48	55.53	61.20	66.34
	92.00	91.92	91.84	91.73	91.64	91.55	91.42	91.29	91.14	91.01	90.88	90.75	90.61	90.47	90.33	90.17	90.03	89.87	89.72	89.56	89.41
Ethiopia	47.28	47.38	47.41	47.23	47.04	46.84	46.52	46.30	45.85	45.61	44.89	44.53	43.88	43.48	42.75	42.06	41.42	40.60	39.64	38.70	37.59
	99.33	99.31	99.29	99.28	99.27	99.26	99.25	99.24	99.23	99.22	99.22	99.20	99.20	99.20	99.18	99.17	99.16	99.15	99.16	99.15	99.14
	1.79	1.79	1.79	1.79	1.80	1.81	1.81	1.82	1.83	1.84	1.85	1.87	1.88	1.90	1.91	1.93	1.95	1.97	2.00	2.02	2.04
Gabon	0.24	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.24	0.24	0.24	0.24	0.24	0.24	0.24
	10.56	10.53	10.45	10.42	10.40	10.36	10.40	10.44	10.47	10.46	10.55	10.63	10.70	10.86	11.14	11.39	11.62	11.88	12.29	12.71	13.06
	1.15	1.15	1.14	1.14	1.14	1.14	1.14	1.14	1.14	1.14	1.15	1.15	1.16	1.17	1.18	1.19	1.20	1.21	1.22	1.24	1.25
Ghana																					

	0.23	0.24	0.24	0.24	0.24	0.24	0.24	0.24	0.24	0.24	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.24	0.24	0.24	0.24
	5.10	4.98	4.93	4.87	4.85	4.82	4.84	4.85	4.85	4.87	4.92	4.98	5.07	5.11	5.20	5.29	5.36	5.49	5.61	5.80	5.97
Kenya	61.81	69.98	76.76	81.95	85.81	88.49	90.30	91.43	91.99	92.06	91.64	90.63	88.88	86.10	81.92	75.81	67.55	56.99	45.12	33.30	23.06
	25.84	33.41	41.48	49.31	56.36	62.02	66.49	69.38	70.91	71.13	69.92	67.43	63.22	56.87	48.72	38.91	28.62	19.00	11.31	6.18	3.20
	87.99	91.34	93.74	95.39	96.50	97.24	97.72	98.01	98.15	98.16	98.05	97.80	97.35	96.63	95.52	93.87	91.44	87.94	83.13	77.33	70.30
Malawi	90.48	91.61	92.80	93.99	95.11	96.13	97.02	97.75	98.34	98.81	99.15	99.40	99.58	99.70	99.79	99.85	99.89	99.92	99.94	99.95	99.96
	57.19	60.70	64.69	68.95	73.52	77.95	82.21	86.03	89.36	92.07	94.22	95.86	97.03	97.87	98.46	98.87	99.13	99.31	99.45	99.52	99.58
	98.44	98.64	98.85	99.05	99.24	99.41	99.55	99.66	99.75	99.82	99.87	99.91	99.94	99.96	99.97	99.98	99.99	99.99	99.99	100.00	100.00
Mali	0.33	0.38	0.44	0.51	0.59	0.69	0.81	0.95	1.12	1.32	1.56	1.84	2.17	2.56	3.02	3.53	4.13	4.80	5.57	6.49	7.51
	0.05	0.06	0.07	0.09	0.10	0.12	0.14	0.17	0.20	0.23	0.27	0.31	0.36	0.42	0.47	0.55	0.62	0.71	0.81	0.91	1.01
	1.98	2.13	2.31	2.51	2.76	3.04	3.34	3.74	4.20	4.74	5.45	6.29	7.15	8.28	9.59	11.34	13.29	15.76	18.79	22.19	26.37
Mozambique	19.12	20.42	22.56	25.56	29.57	34.69	40.84	47.76	55.11	62.34	68.94	74.63	79.31	82.91	85.64	87.57	88.89	89.67	89.98	89.88	89.42
	2.68	2.92	3.29	3.87	4.70	5.87	7.47	9.67	12.58	16.32	20.76	25.98	31.35	37.00	42.24	46.39	49.94	51.47	51.56	49.09	45.54
	64.17	65.72	68.35	71.70	75.71	79.82	83.77	87.27	90.26	92.60	94.41	95.71	96.67	97.40	97.89	98.25	98.50	98.67	98.77	98.85	98.89
Nigeria	15.81	13.55	11.61	9.90	8.43	7.17	6.12	5.18	4.41	3.74	3.18	2.70	2.29	1.96	1.68	1.45	1.25	1.08	0.94	0.82	0.72
	0.96	0.83	0.72	0.63	0.54	0.46	0.40	0.33	0.28	0.24	0.20	0.17	0.14	0.12	0.10	0.08	0.07	0.06	0.05	0.04	0.03
	73.03	67.85	62.73	57.13	51.86	46.39	41.73	36.88	32.58	29.13	26.05	22.96	20.56	18.25	16.50	14.95	13.74	12.60	11.67	10.68	10.06
Senegal	0.15	0.15	0.15	0.15	0.15	0.16	0.16	0.16	0.17	0.17	0.17	0.18	0.18	0.19	0.19	0.20	0.21	0.22	0.22	0.23	0.24
	0.02	0.02	0.02	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.04	0.04	0.04
	0.72	0.70	0.68	0.67	0.67	0.67	0.67	0.68	0.68	0.69	0.70	0.72	0.75	0.79	0.83	0.89	0.96	1.05	1.15	1.27	1.42

South Africa	17.79	17.84	17.97	18.05	18.18	18.29	18.40	18.49	18.62	18.74	18.84	18.94	19.10	19.21	19.32	19.42	19.53	19.65	19.75	19.81	19.90
	3.58	3.64	3.68	3.72	3.73	3.75	3.78	3.81	3.82	3.81	3.82	3.84	3.85	3.86	3.85	3.85	3.82	3.82	3.81	3.80	3.81
	58.58	58.73	59.04	59.14	59.53	59.83	59.98	60.35	60.61	60.96	61.48	62.15	62.81	63.48	63.98	64.46	65.30	66.02	66.65	67.33	67.97
Sudan	18.89	34.42	51.84	66.47	76.29	82.06	85.06	86.01	85.27	82.78	77.99	70.05	58.36	43.75	28.93	16.96	9.13	4.74	2.42	1.26	0.68
	3.99	8.67	16.32	26.19	36.77	45.43	50.92	53.15	51.99	47.64	40.36	30.89	21.17	12.71	6.73	3.20	1.37	0.54	0.21	0.08	0.03
	56.68	74.76	85.86	91.84	94.81	96.32	97.05	97.27	97.11	96.55	95.36	93.18	89.11	82.52	71.77	58.22	44.18	31.84	22.34	16.11	12.22
Tanzania	17.47	24.54	33.35	43.32	53.38	62.63	70.31	76.26	80.63	83.68	85.70	86.89	87.40	87.31	86.62	85.29	83.27	80.42	76.81	72.11	66.69
	2.63	4.00	6.04	8.94	12.85	17.79	23.44	29.43	35.15	40.13	43.77	46.21	47.30	46.99	45.62	42.71	39.00	34.21	29.22	23.92	18.86
	63.18	72.47	80.26	86.10	90.24	93.12	95.04	96.31	97.14	97.68	98.01	98.20	98.27	98.25	98.14	97.94	97.63	97.16	96.52	95.73	94.70
The Gambia	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.19	0.19	0.19	0.19	0.20	0.20	0.20	0.21	0.22	0.22	0.23	0.23	0.24
	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
	4.05	4.05	4.01	4.02	4.04	4.08	4.11	4.14	4.20	4.31	4.39	4.46	4.53	4.59	4.71	4.83	5.02	5.15	5.32	5.53	5.80
Uganda	85.97	87.37	88.67	89.85	90.88	91.79	92.56	93.17	93.69	94.07	94.34	94.51	94.59	94.57	94.45	94.24	93.96	93.54	93.02	92.39	91.65
	46.42	49.57	52.78	55.73	58.55	61.04	63.44	65.57	67.42	68.91	70.08	70.75	71.16	71.07	70.68	69.79	68.19	66.54	64.09	61.14	57.67
	98.11	98.32	98.49	98.66	98.81	98.92	99.03	99.12	99.19	99.24	99.28	99.31	99.32	99.32	99.31	99.28	99.24	99.20	99.14	99.07	98.99
Zambia	51.37	51.39	51.38	51.41	51.42	51.47	51.42	51.39	51.37	51.33	51.28	51.34	51.34	51.33	51.37	51.40	51.43	51.44	51.47	51.43	51.45
	13.93	14.00	14.07	14.07	14.12	14.14	14.16	14.12	14.01	14.08	14.07	14.03	14.03	13.91	13.91	13.90	13.88	13.80	13.73	13.66	13.64
	88.08	88.09	88.07	88.05	88.02	88.02	88.04	88.08	88.04	88.04	88.07	88.12	88.19	88.19	88.22	88.21	88.33	88.35	88.38	88.39	88.46
Central Africa	0.75	0.91	1.11	1.36	1.66	2.03	2.50	3.07	3.77	4.65	5.73	7.01	8.60	10.51	12.78	15.43	18.51	22.02	26.06	30.45	35.18
	0.03	0.03	0.04	0.05	0.06	0.07	0.09	0.11	0.14	0.17	0.21	0.27	0.33	0.41	0.51	0.63	0.79	0.97	1.20	1.47	1.81

	17.60	20.42	23.75	27.44	31.56	35.92	41.01	46.42	51.86	57.50	62.91	67.82	72.54	76.90	80.79	84.04	87.12	89.43	91.39	93.09	94.39
Southern Africa	13.38	13.39	13.41	13.43	13.46	13.52	13.58	13.60	13.65	13.69	13.73	13.78	13.83	13.88	13.93	13.97	14.04	14.09	14.15	14.21	14.25
	3.05	3.08	3.09	3.13	3.14	3.14	3.13	3.12	3.11	3.11	3.12	3.11	3.10	3.10	3.09	3.08	3.07	3.05	3.05	3.03	3.01
	42.82	42.98	43.08	43.21	43.39	43.60	43.90	44.25	44.63	44.96	45.28	45.59	46.12	46.48	46.87	47.30	47.70	48.35	48.77	49.29	49.74
Western Africa	0.44	0.42	0.40	0.38	0.37	0.36	0.35	0.33	0.33	0.32	0.31	0.31	0.30	0.30	0.30	0.29	0.29	0.30	0.30	0.30	0.30
	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
	11.76	11.15	10.64	10.20	9.79	9.43	9.09	8.82	8.57	8.43	8.21	8.03	8.00	7.96	7.98	8.00	8.09	8.12	8.19	8.40	8.63
High-level resistance																					
Equatorial Guinea	99.97	99.93	99.86	99.69	99.33	98.55	96.86	93.29	86.24	73.84	55.94	36.40	20.54	10.46	5.04	2.36	1.10	0.51	0.24	0.11	0.05
	99.84	99.69	99.39	98.77	97.51	94.91	89.77	80.37	65.24	45.87	27.75	14.64	7.13	3.29	1.47	0.65	0.29	0.12	0.05	0.02	0.01
	100.00	99.99	99.97	99.94	99.86	99.66	99.20	98.13	95.69	90.47	80.24	64.08	44.27	26.54	14.12	7.15	3.49	1.71	0.83	0.42	0.21
Gabon	0.22	0.22	0.22	0.22	0.21	0.21	0.21	0.21	0.22	0.22	0.22	0.22	0.23	0.23	0.24	0.24	0.25	0.25	0.26	0.27	0.28
	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
	1.76	1.72	1.69	1.67	1.66	1.64	1.64	1.67	1.68	1.73	1.77	1.82	1.88	1.95	2.01	2.12	2.25	2.41	2.56	2.75	2.94
Kenya	0.23	0.26	0.30	0.35	0.40	0.47	0.55	0.64	0.75	0.88	1.03	1.21	1.42	1.67	1.96	2.30	2.69	3.16	3.68	4.30	5.02
	0.03	0.04	0.05	0.06	0.08	0.09	0.11	0.14	0.16	0.19	0.22	0.26	0.30	0.34	0.39	0.45	0.51	0.57	0.64	0.72	0.79
	1.11	1.21	1.31	1.42	1.56	1.73	1.94	2.20	2.52	2.91	3.41	3.99	4.69	5.65	6.89	8.49	10.59	13.20	16.71	20.71	25.76
Malawi	0.92	1.00	1.10	1.20	1.32	1.45	1.60	1.77	1.96	2.17	2.40	2.66	2.95	3.26	3.61	3.99	4.40	4.87	5.38	5.93	6.53
	0.19	0.20	0.22	0.25	0.28	0.30	0.33	0.37	0.41	0.45	0.50	0.55	0.61	0.66	0.73	0.80	0.88	0.97	1.06	1.16	1.26
	4.25	4.56	4.89	5.29	5.71	6.19	6.69	7.24	7.94	8.63	9.34	10.33	11.32	12.36	13.53	14.76	16.14	17.72	19.60	21.53	23.64

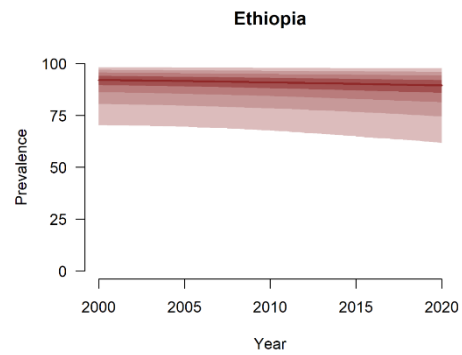
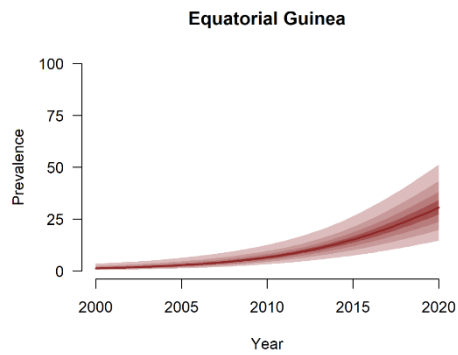
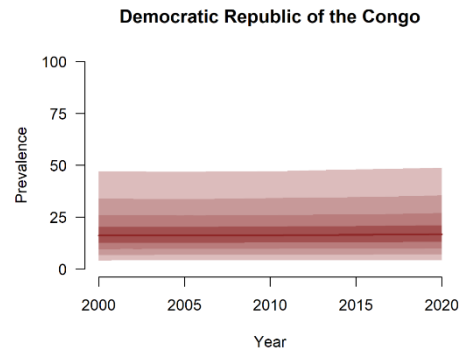
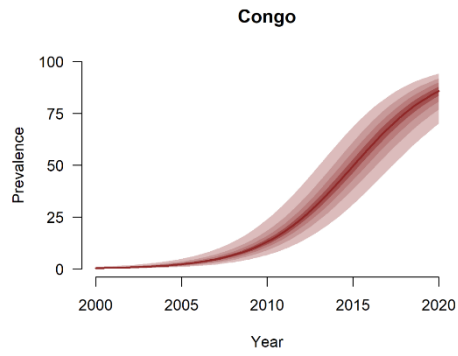
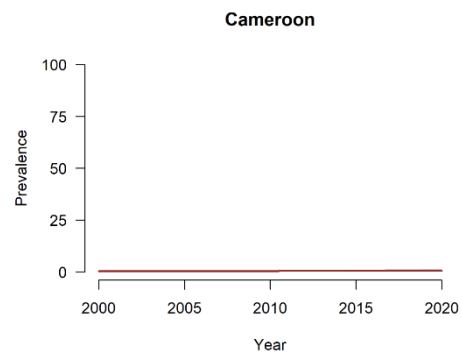
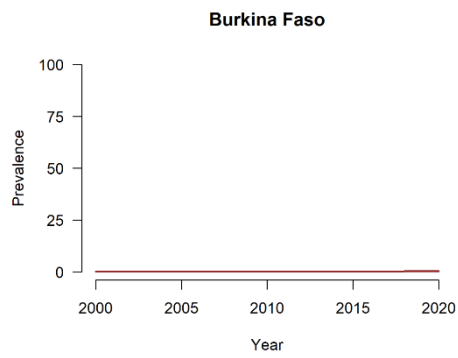
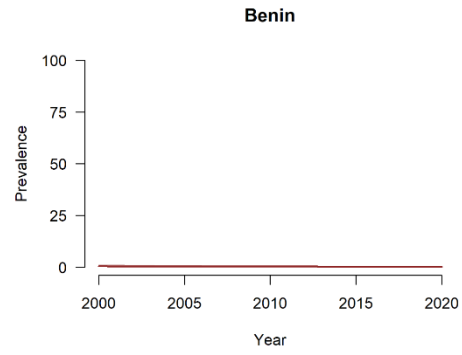
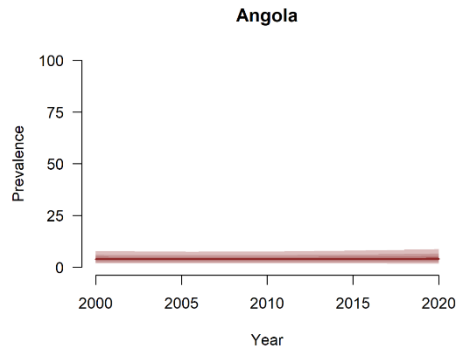
Mozambique	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	0.20	0.19	0.18	0.18	0.17	0.17	0.17	0.17	0.18	0.18	0.18	0.19	0.20	0.21	0.22	0.24	0.26	0.28	0.31	0.34	0.37
Nigeria	4.66	4.65	4.64	4.64	4.64	4.65	4.67	4.68	4.70	4.74	4.77	4.81	4.84	4.89	4.93	4.97	5.01	5.06	5.13	5.19	5.25
	0.11	0.11	0.11	0.12	0.12	0.12	0.12	0.12	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.14	0.14	0.14	0.14	0.14	0.14
	67.78	67.76	67.49	67.14	67.14	67.22	67.25	67.17	67.00	66.83	67.03	67.21	67.06	67.13	67.02	67.33	67.38	67.98	68.09	68.30	68.74
Senegal	0.24	0.24	0.24	0.23	0.23	0.23	0.23	0.23	0.24	0.24	0.24	0.24	0.25	0.25	0.26	0.26	0.27	0.28	0.29	0.30	0.31
	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
	1.79	1.71	1.65	1.61	1.58	1.55	1.53	1.52	1.52	1.53	1.54	1.56	1.59	1.63	1.68	1.74	1.81	1.89	2.00	2.10	2.23
Tanzania	0.15	0.18	0.23	0.28	0.34	0.41	0.49	0.59	0.69	0.80	0.92	1.05	1.19	1.33	1.46	1.60	1.73	1.85	1.95	2.05	2.12
	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.02	0.02	0.03	0.03	0.03	0.04	0.04	0.05	0.05	0.05	0.05	0.06	0.06
	5.14	6.36	7.75	9.34	11.19	13.15	15.34	17.71	20.07	22.59	25.09	27.60	30.15	32.61	34.87	36.90	38.87	40.71	42.30	43.24	44.54
Uganda	16.29	16.21	16.10	16.00	15.95	15.88	15.80	15.71	15.64	15.61	15.55	15.48	15.40	15.33	15.25	15.20	15.15	15.09	15.04	14.98	14.96
	2.43	2.42	2.42	2.41	2.38	2.37	2.35	2.34	2.34	2.33	2.31	2.30	2.29	2.28	2.27	2.26	2.25	2.25	2.23	2.21	2.18
	61.95	61.79	61.60	61.55	61.40	61.16	60.97	60.85	60.77	60.68	60.44	60.38	60.21	60.09	60.11	59.95	60.08	59.98	59.91	59.95	59.88
Zambia	5.44	5.45	5.49	5.52	5.58	5.64	5.67	5.73	5.80	5.89	5.98	6.08	6.17	6.25	6.38	6.52	6.64	6.73	6.84	6.97	7.09
	0.40	0.41	0.42	0.43	0.44	0.45	0.46	0.47	0.47	0.48	0.49	0.50	0.51	0.52	0.53	0.53	0.54	0.55	0.55	0.56	0.56
	50.48	50.44	50.43	50.37	50.22	50.03	50.04	50.06	50.20	50.25	50.31	50.47	50.64	50.84	51.16	51.47	51.80	52.05	52.34	52.96	53.59
Central Africa	0.97	0.99	1.02	1.05	1.08	1.12	1.16	1.20	1.24	1.29	1.34	1.40	1.46	1.52	1.59	1.66	1.75	1.83	1.92	2.01	2.11
	0.04	0.04	0.04	0.05	0.05	0.05	0.05	0.06	0.06	0.06	0.06	0.07	0.07	0.07	0.07	0.07	0.08	0.08	0.08	0.09	0.09

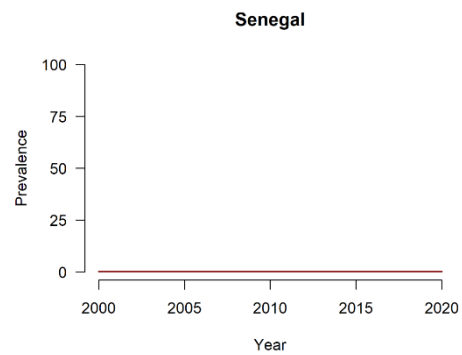
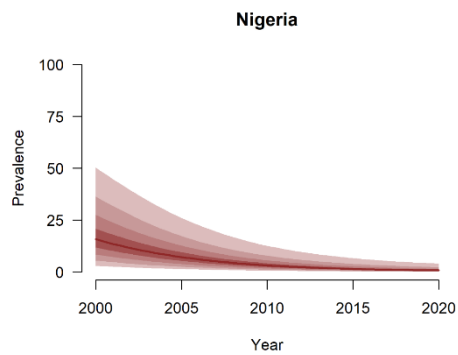
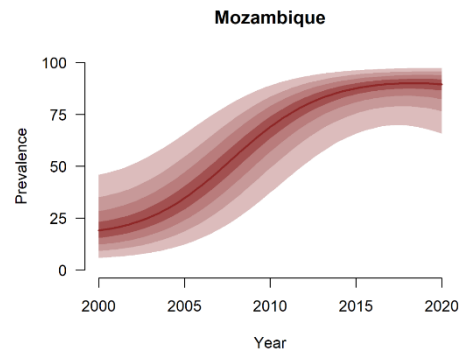
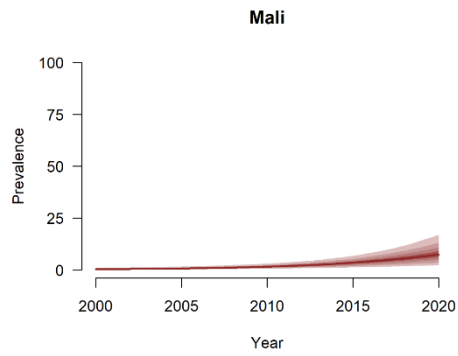
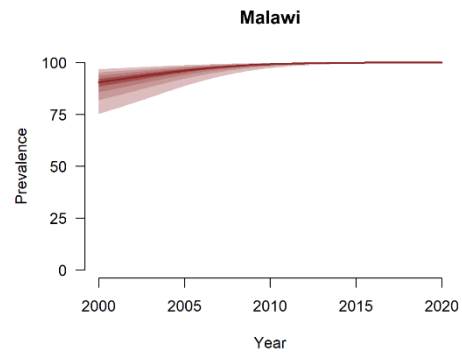
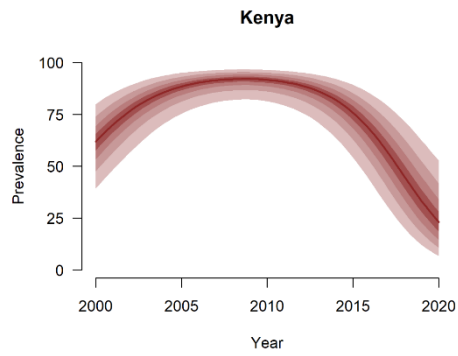
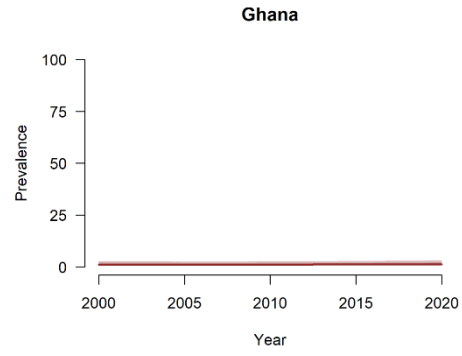
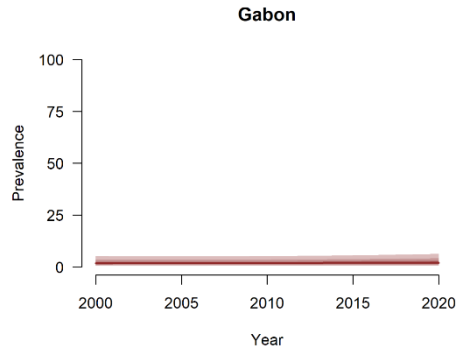
	15.38	15.50	15.67	15.89	16.25	16.56	17.03	17.35	17.77	18.38	19.16	20.02	20.86	21.94	23.12	24.40	25.72	27.50	29.10	30.79	32.61
Eastern Africa	0.32	0.41	0.52	0.65	0.81	0.98	1.16	1.36	1.57	1.78	1.98	2.17	2.35	2.49	2.59	2.66	2.67	2.64	2.57	2.46	2.33
	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
	31.94	37.84	43.41	49.01	54.02	58.77	63.01	66.75	70.12	72.63	74.72	76.45	77.75	78.57	79.29	79.50	79.81	79.88	79.37	78.73	77.98
Western Africa	0.10	0.10	0.10	0.10	0.10	0.11	0.11	0.11	0.12	0.12	0.13	0.13	0.14	0.14	0.15	0.16	0.17	0.18	0.19	0.20	0.21
	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	4.40	4.30	4.30	4.30	4.27	4.30	4.35	4.43	4.51	4.71	4.88	5.13	5.36	5.62	5.93	6.28	6.68	7.19	7.69	8.36	8.97

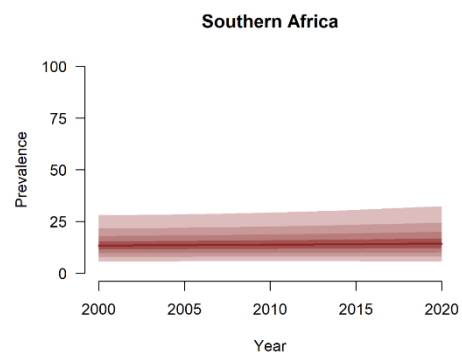
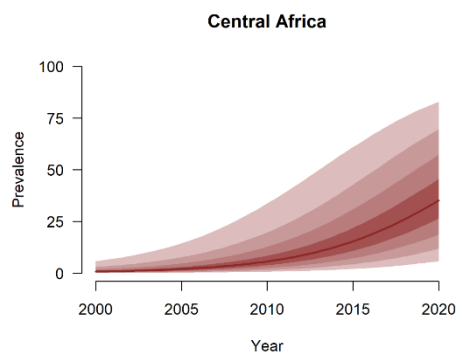
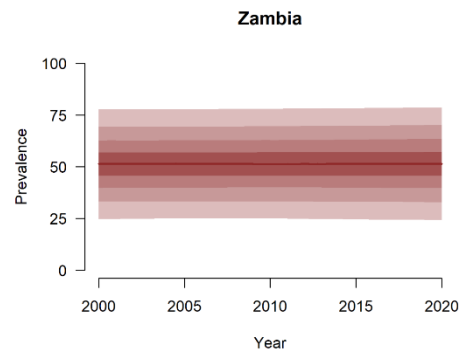
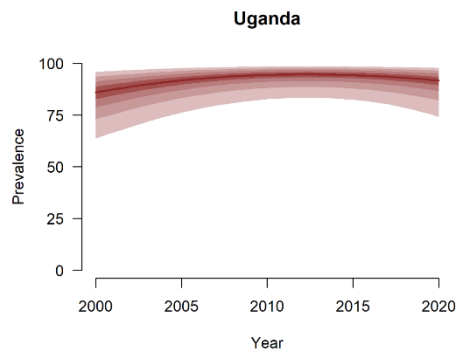
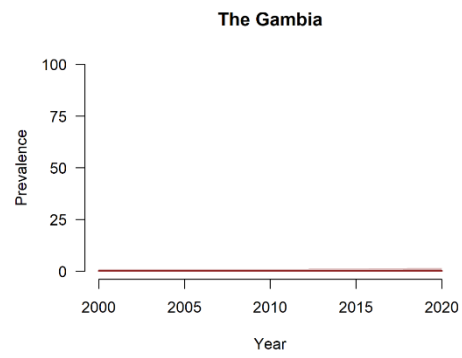
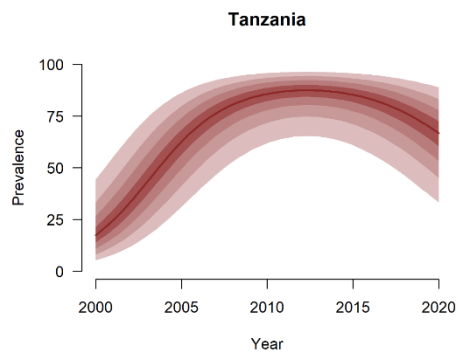
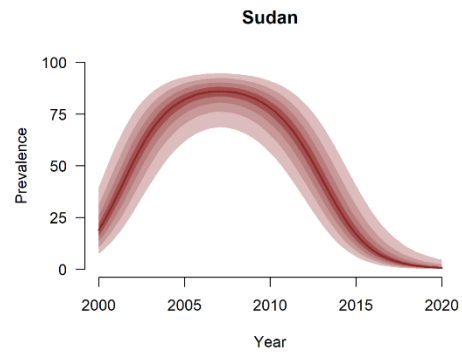
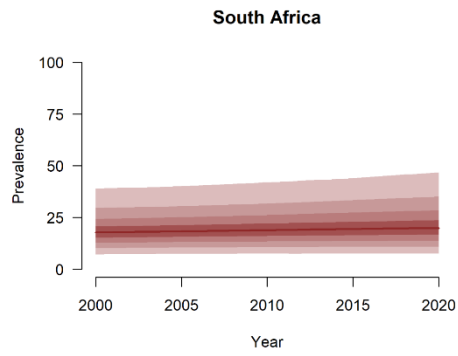
Supplement 3.2

Figure S8: Posterior quantiles of the GPR model prevalence estimates per geography. (A) Mid-level resistance. (B) High-level resistance.

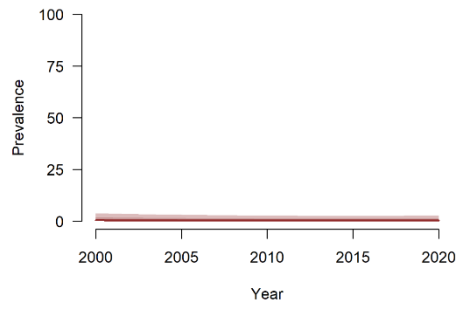
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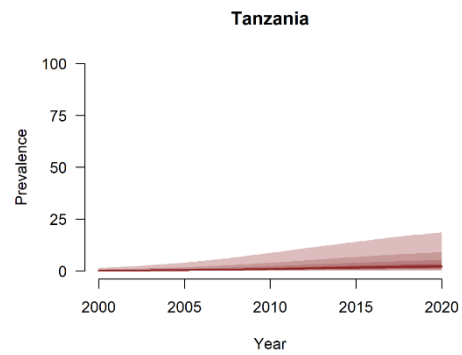
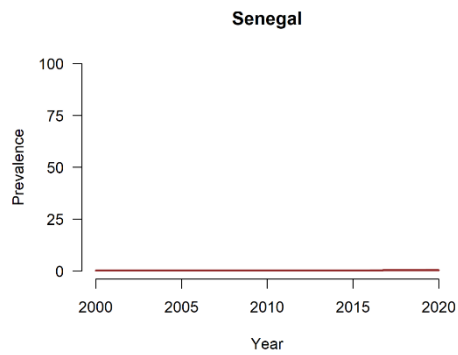
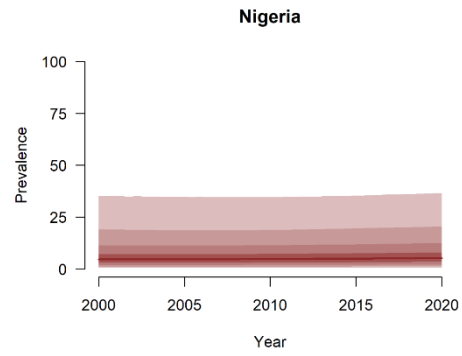
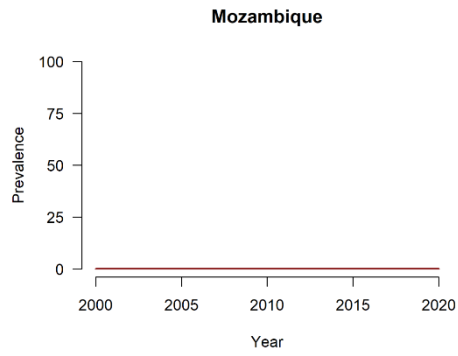
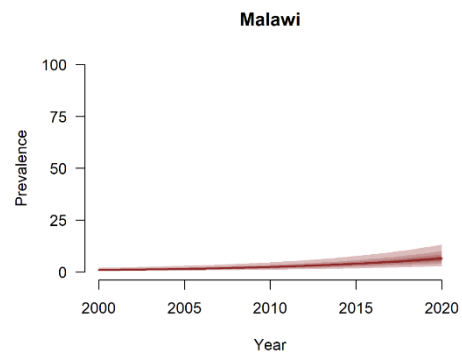
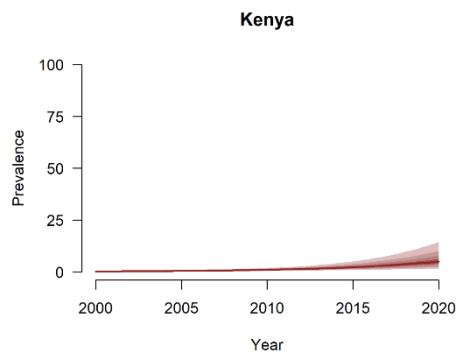
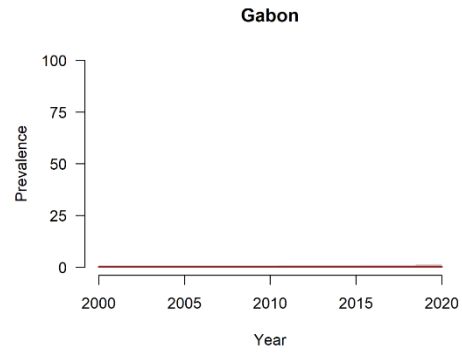
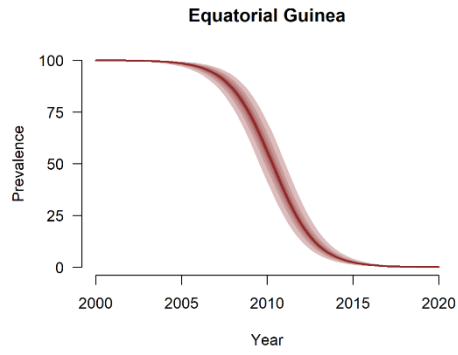


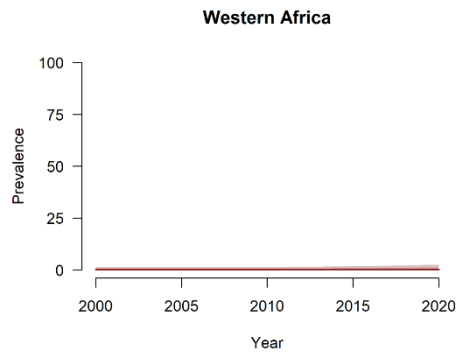
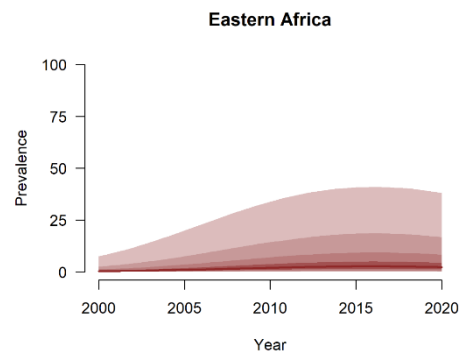
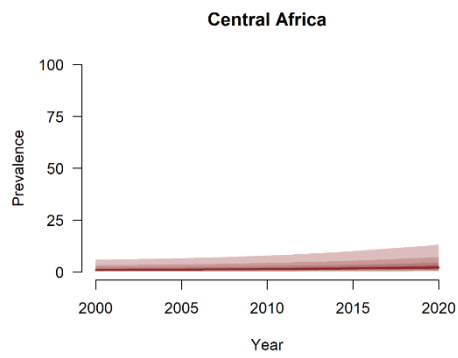
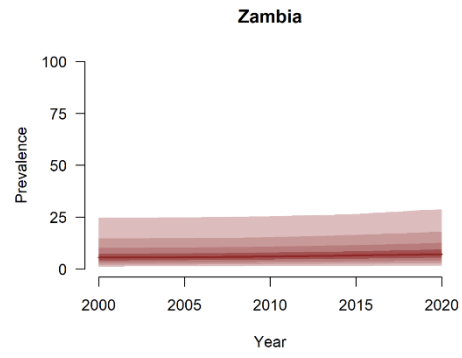
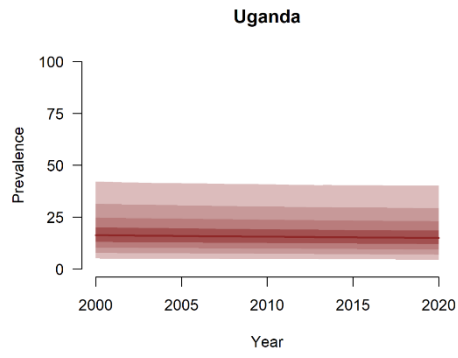


Western Africa



B.



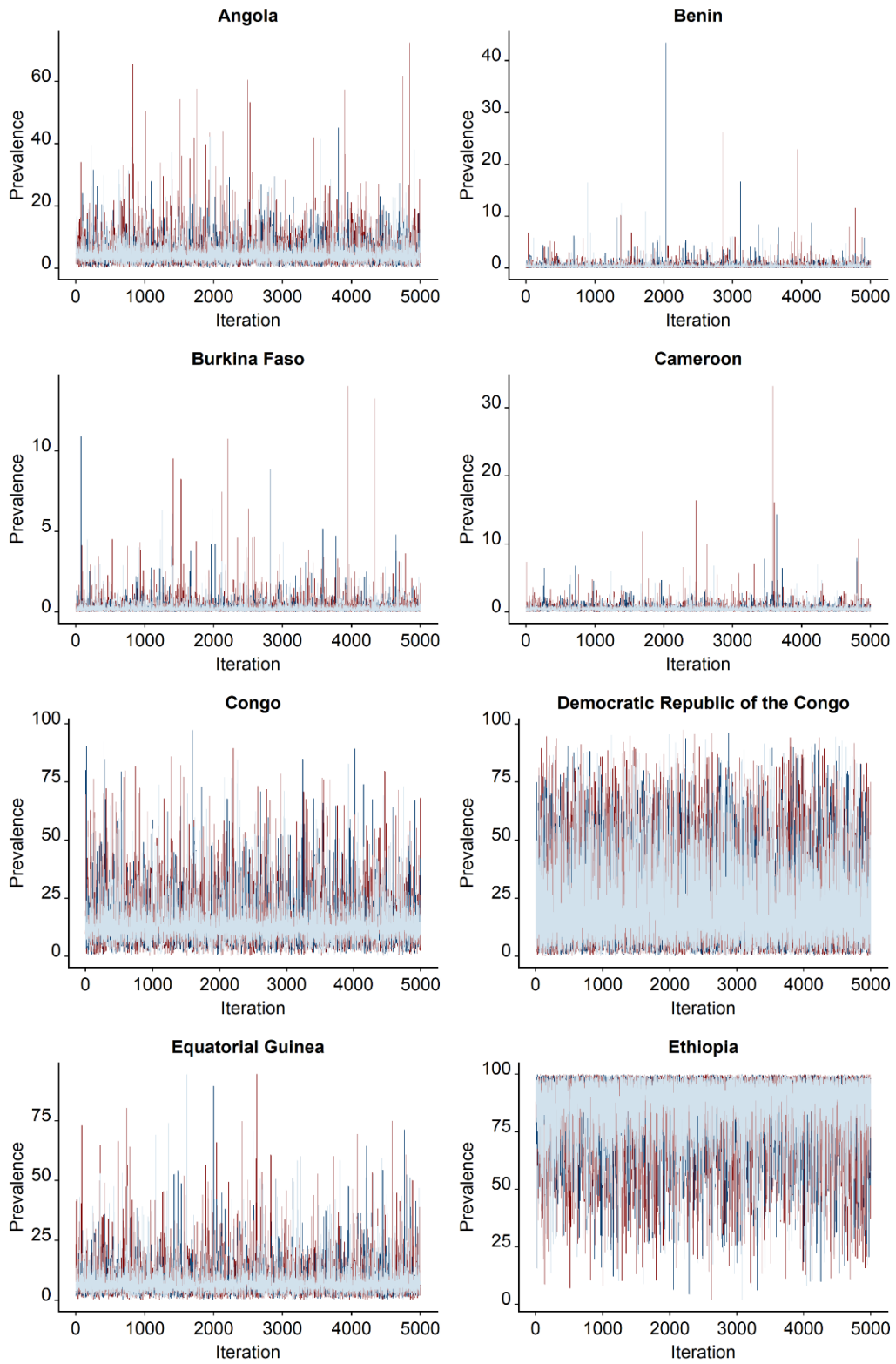


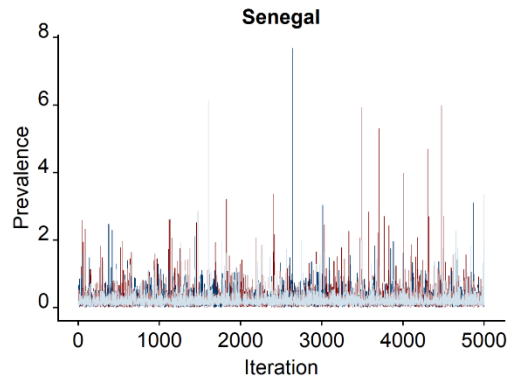
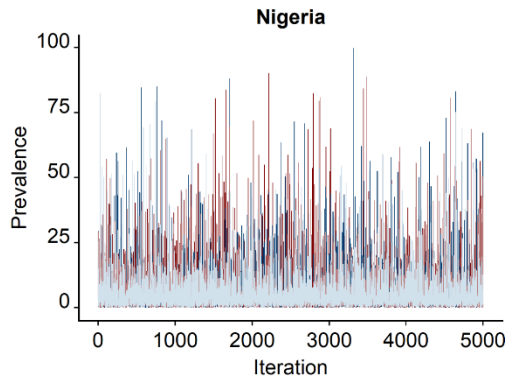
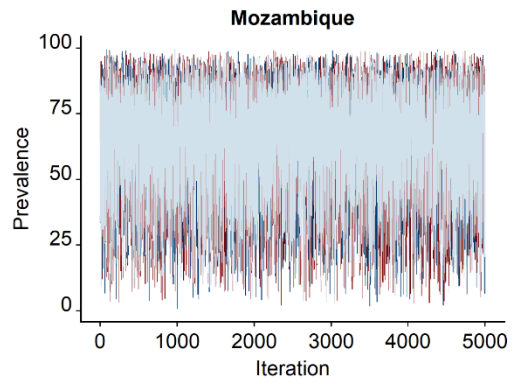
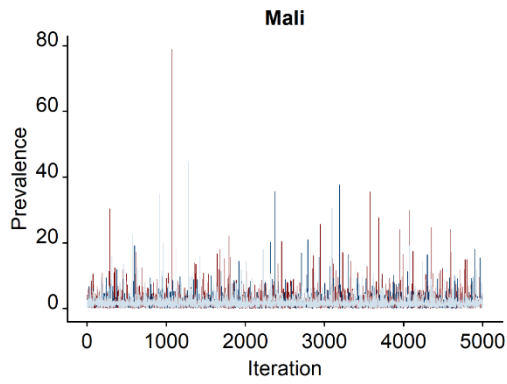
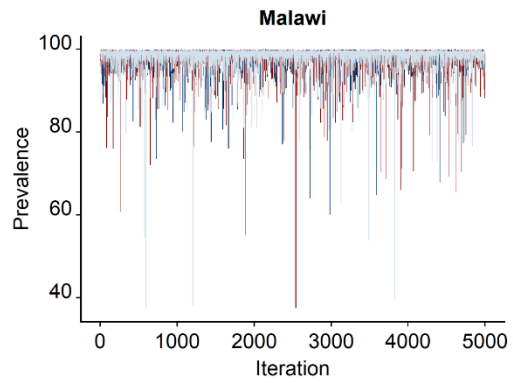
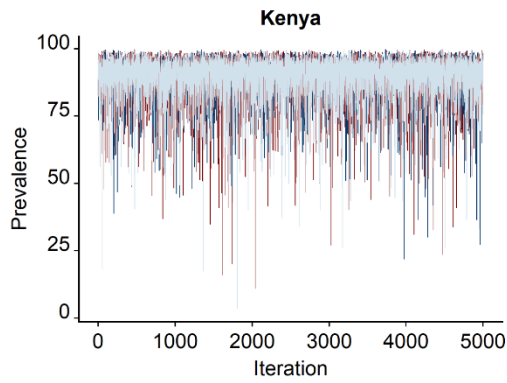
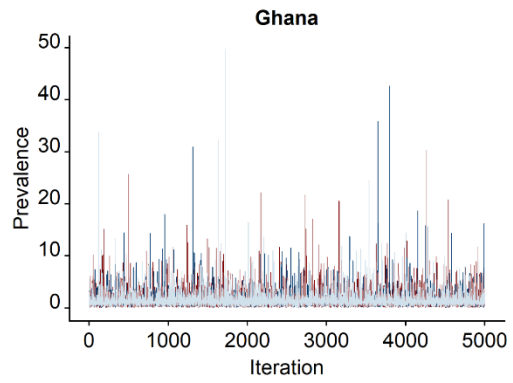
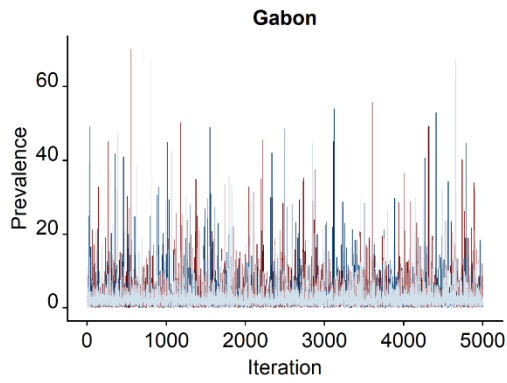
Supplement 3.3

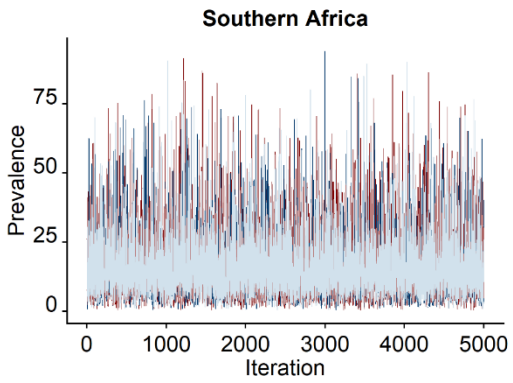
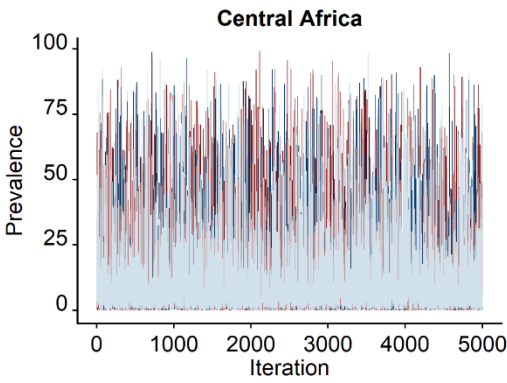
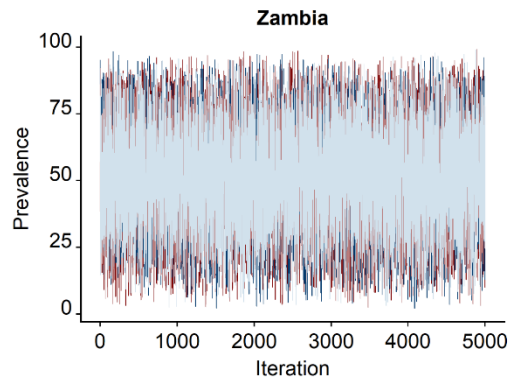
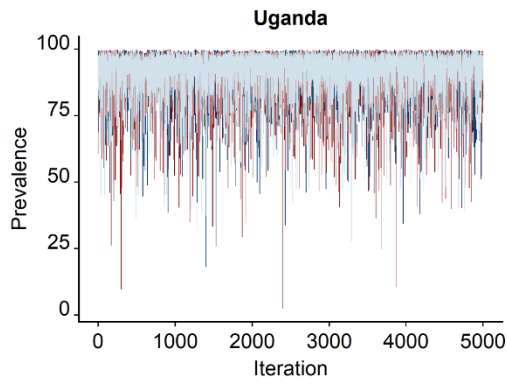
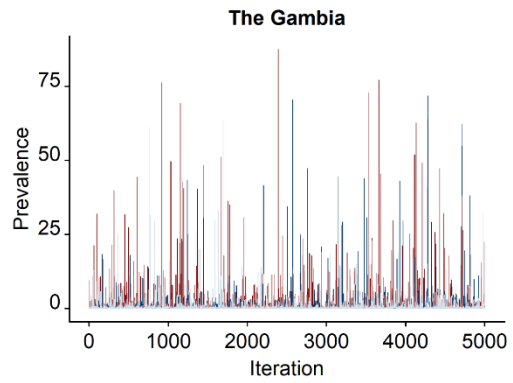
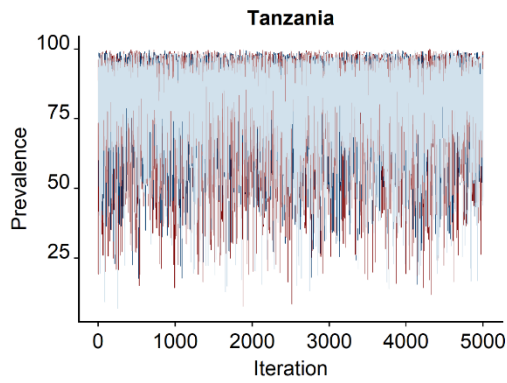
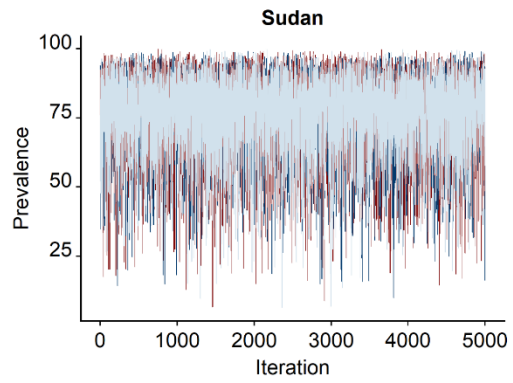
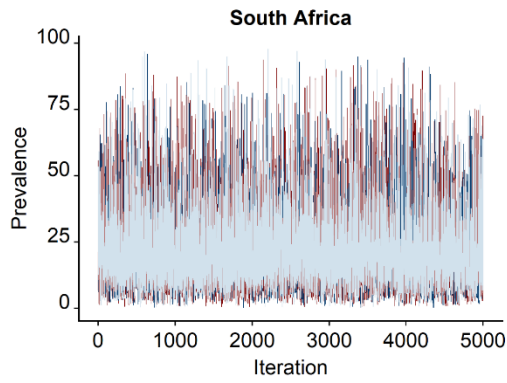
Figure S9: Trace plots showing post-warmup evolution of parameter vector over the iterations of the Markov chains. For GPR model, one parameter vector out of the 89 units computed per geography and outcome is shown. The remaining can be provided at request. (A) Mid-level resistance. (B) High-level resistance.

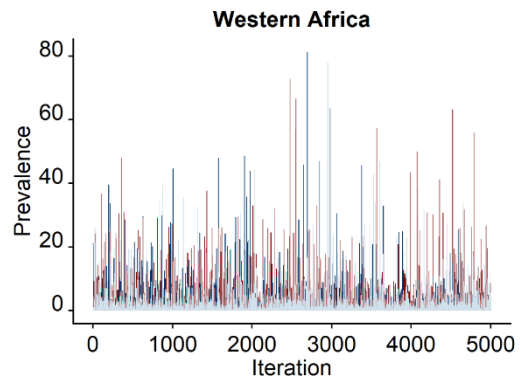
Chain
— 1
— 2
— 3
— 4

A.

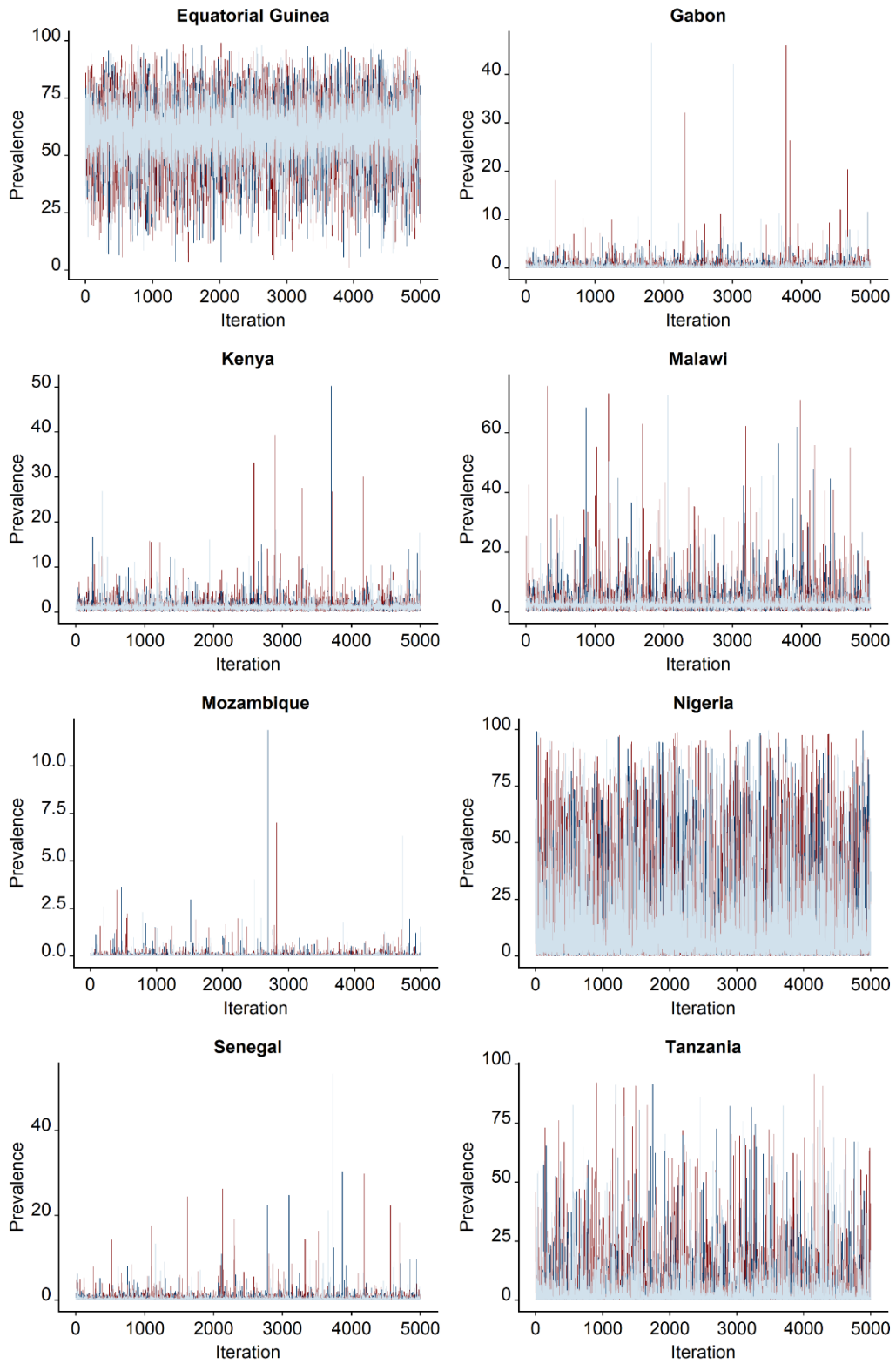


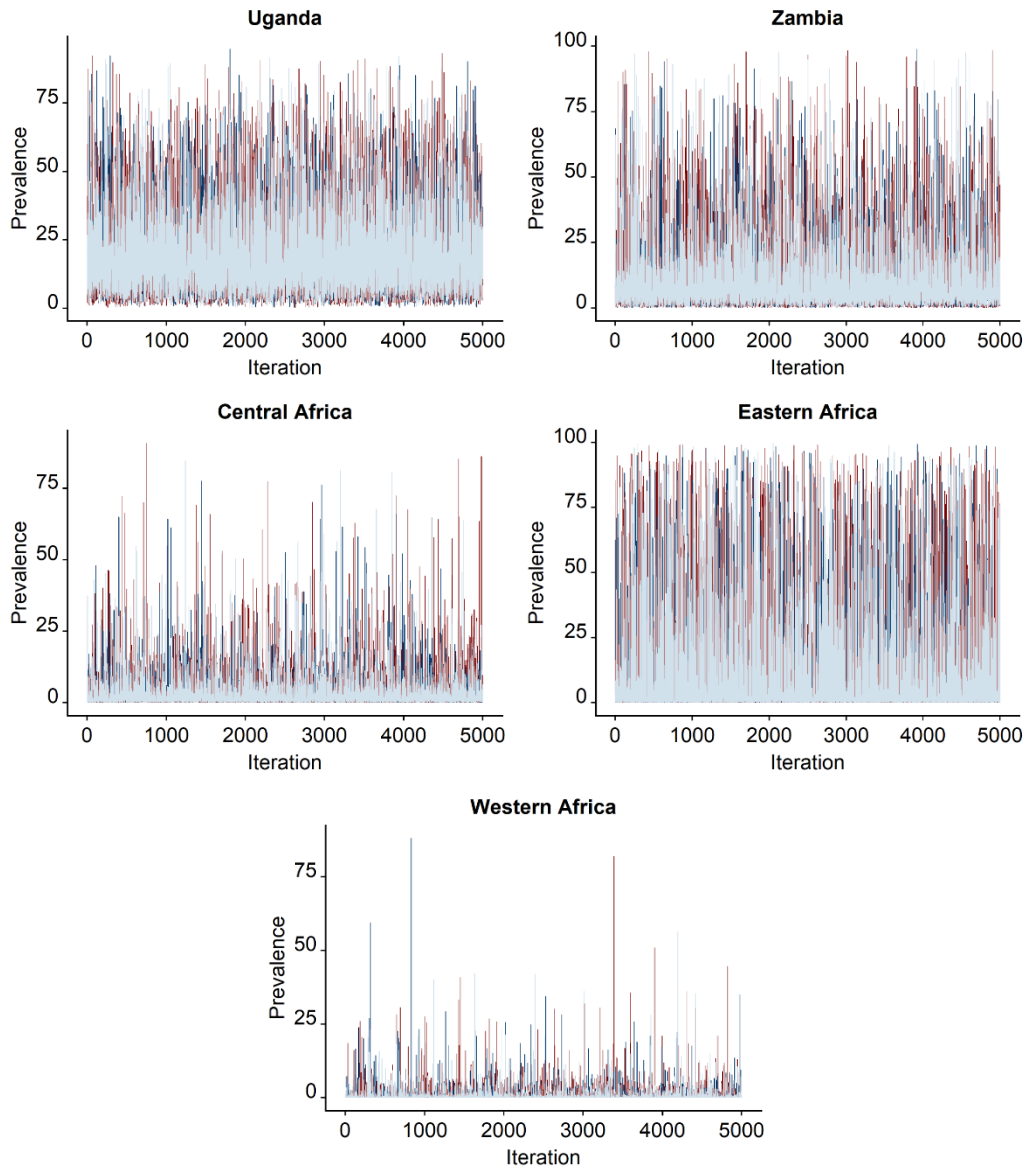






B.

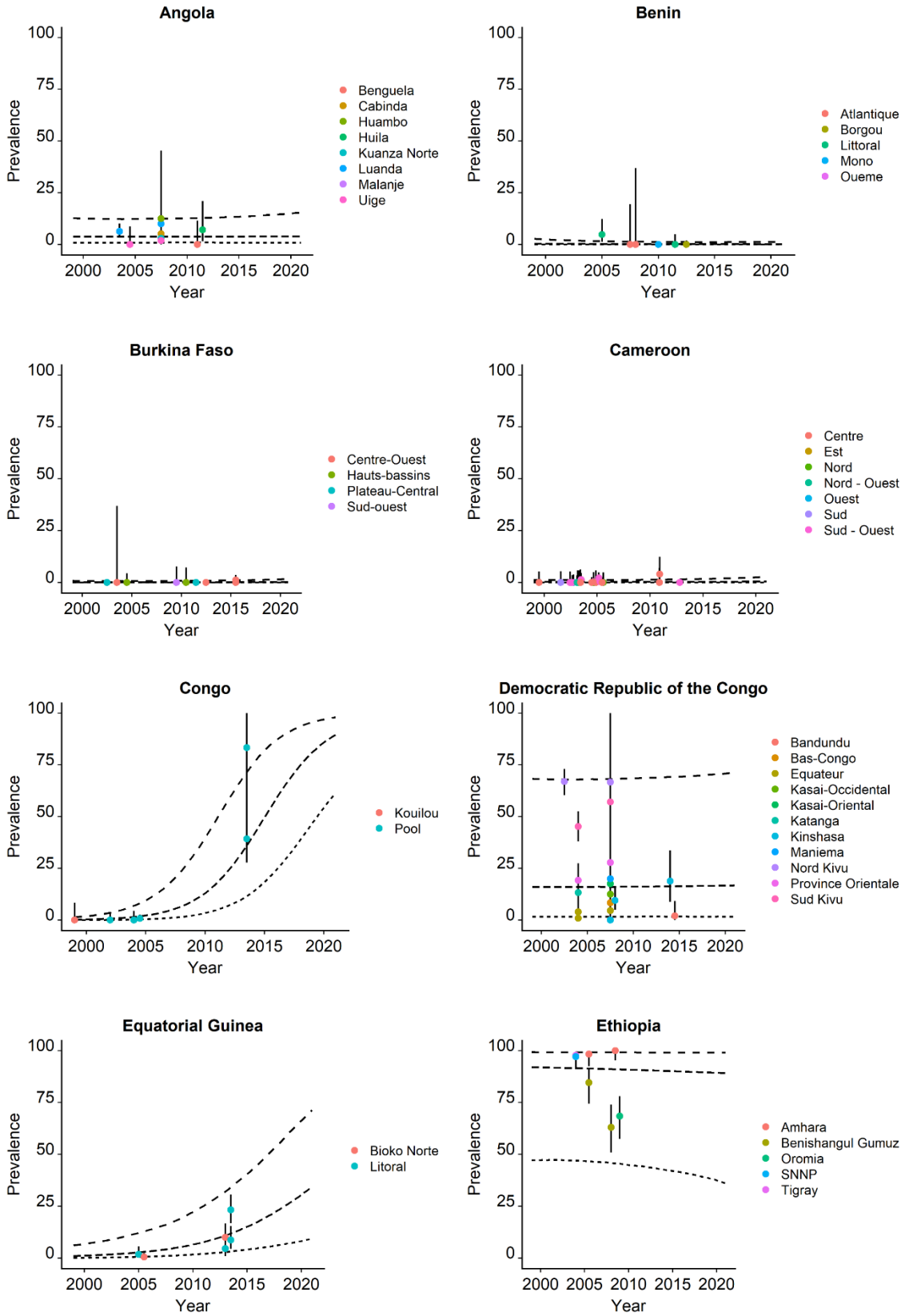


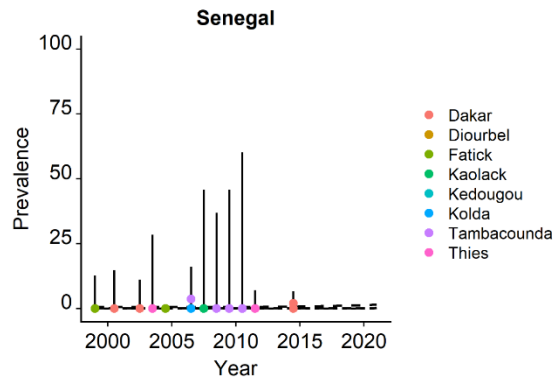
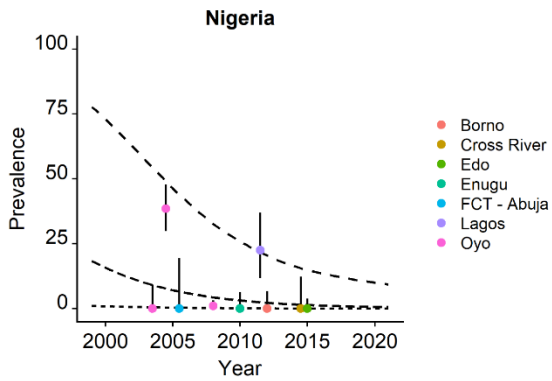
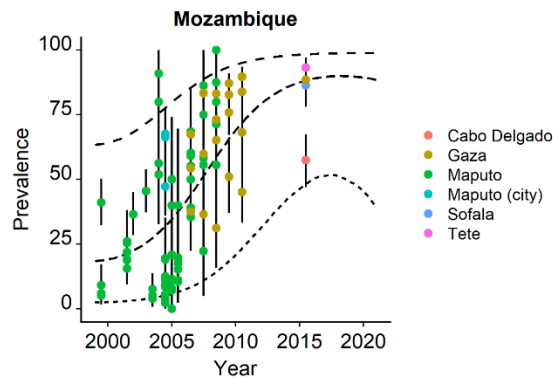
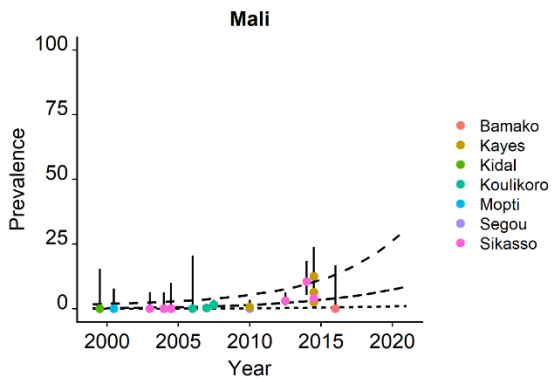
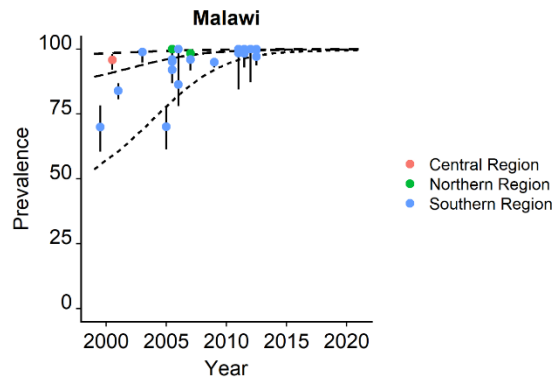
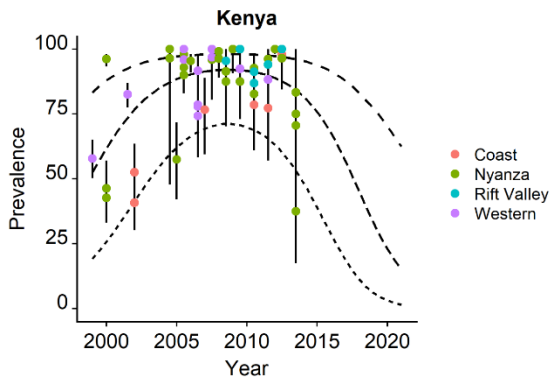
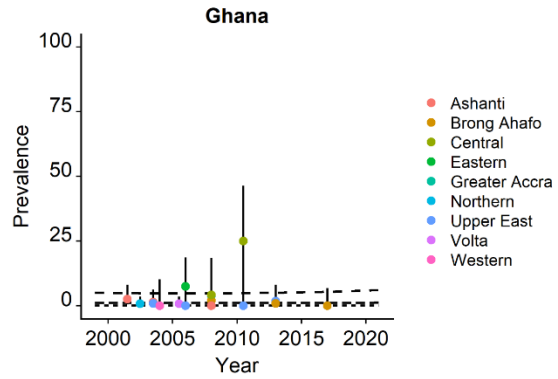
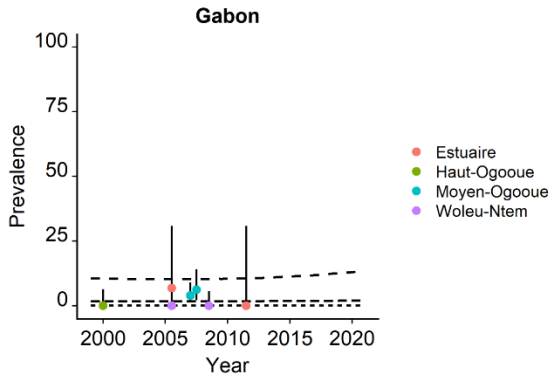


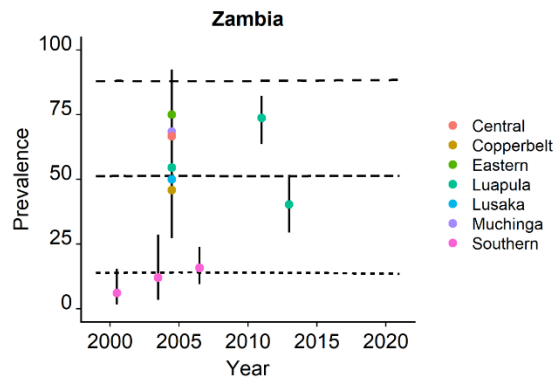
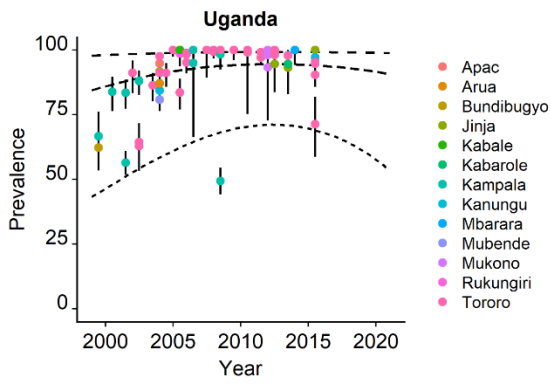
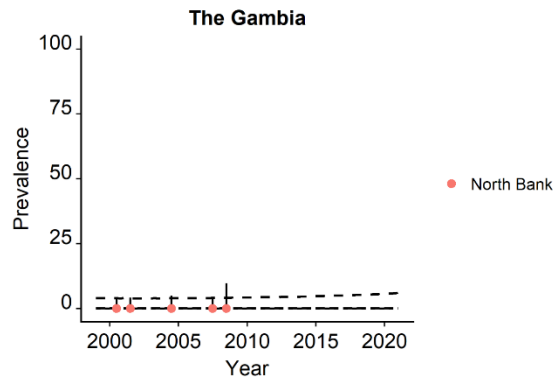
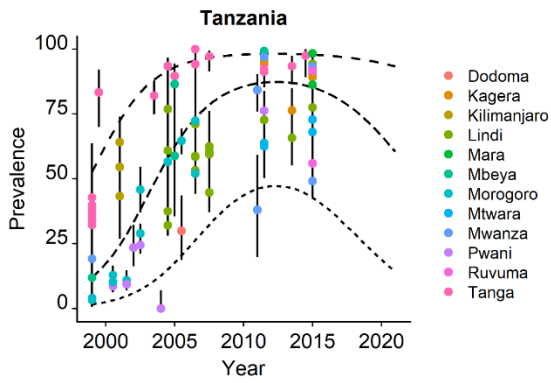
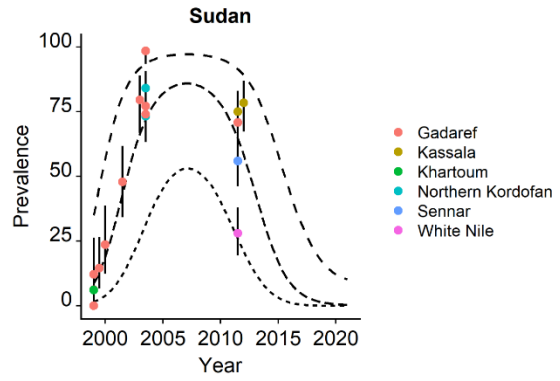
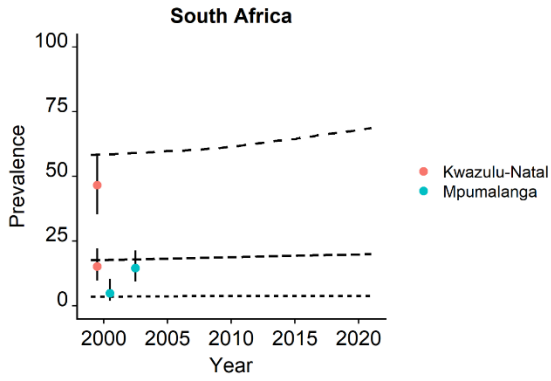
Supplement 3.4

Figure S10: National scale temporal trends in, and projections of, *P. falciparum* resistance to sulfadoxine-pyrimethamine. The upper and lower lines denote upper and lower bounds of the 95% uncertainty interval, respectively and the middle, the median of the posterior distribution. The estimates are population-level resistance levels per respective geography. The points and vertical bars indicate point estimates from each survey with respective uncertainty interval, whereas the colors denote the administrative level one of the sites where the patients were recruited, and clinical samples collected. The full list of site-years is provided in supplement 1.3. Posterior probability distribution of prevalence per survey is given in supplement 3.5. (A) Mid-level *P. falciparum* resistance to sulfadoxine-pyrimethamine. (B) High-level *P. falciparum* resistance to sulfadoxine-pyrimethamine.

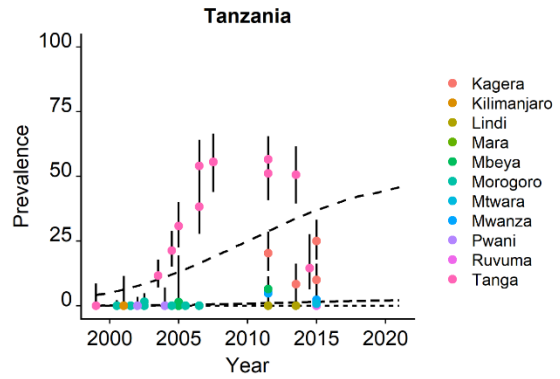
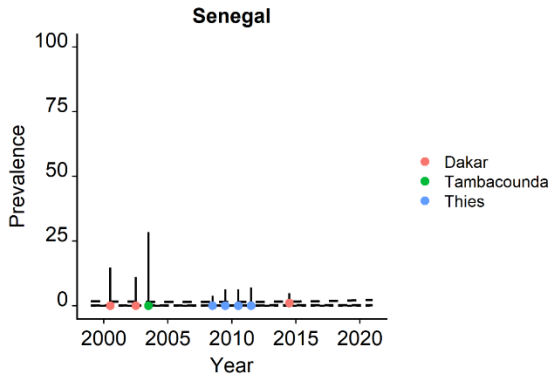
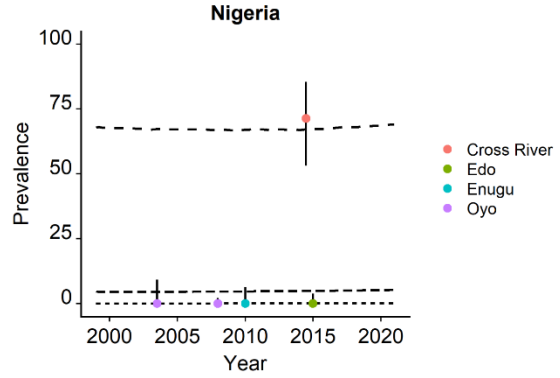
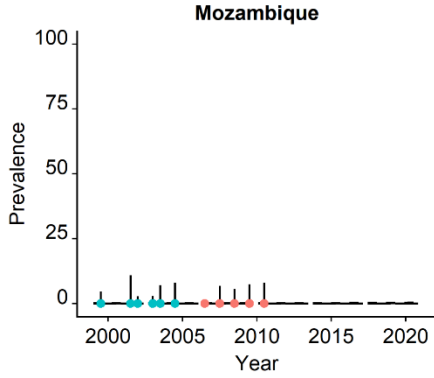
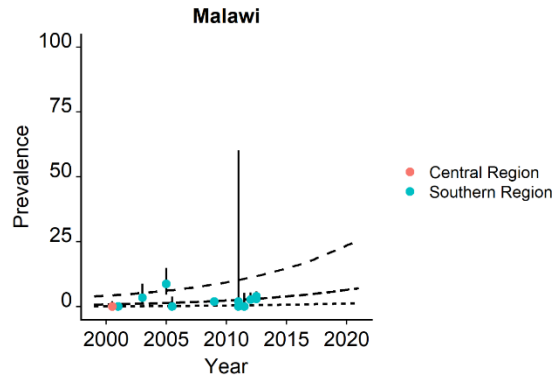
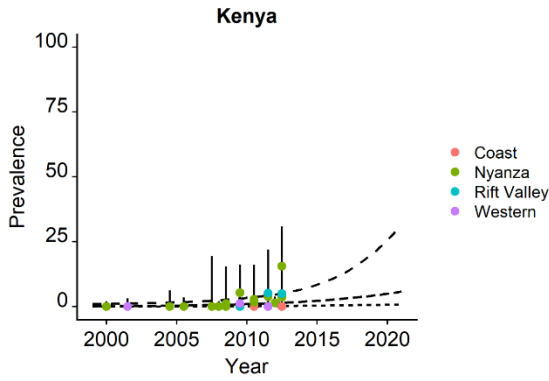
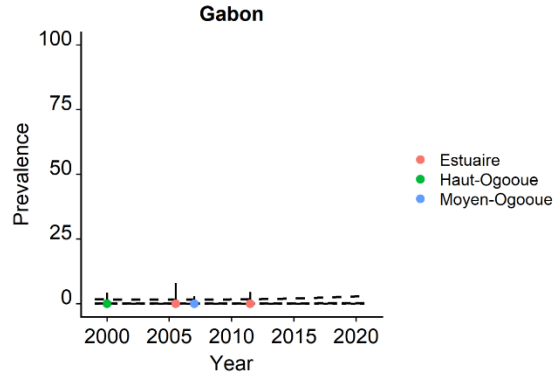
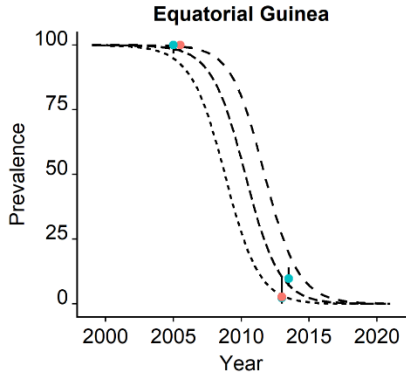
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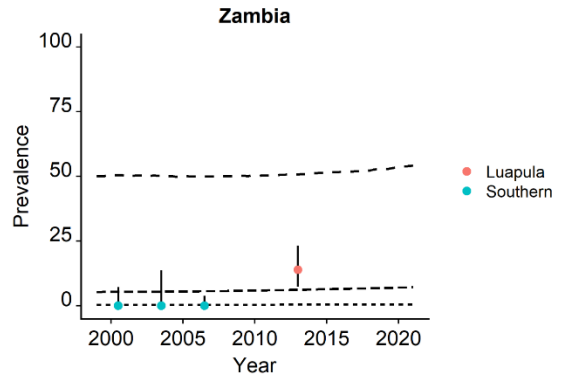
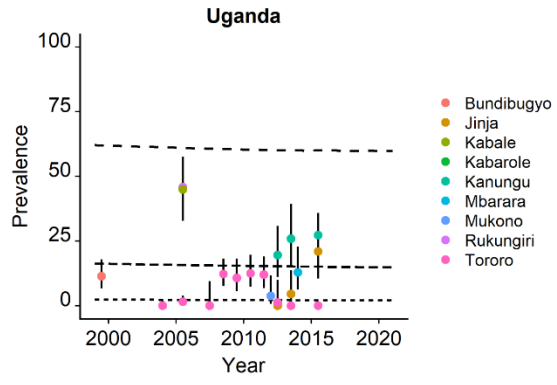






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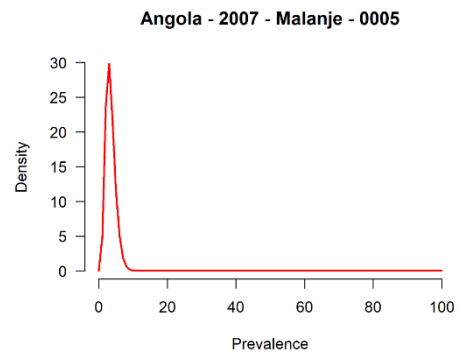
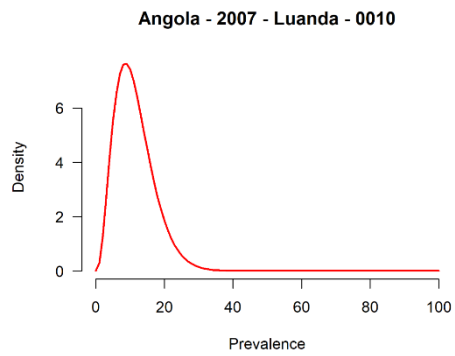
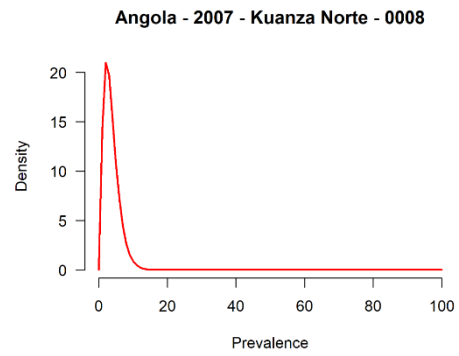
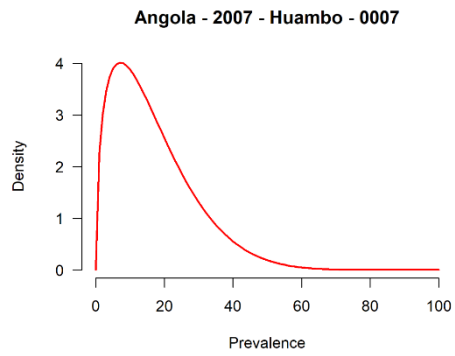
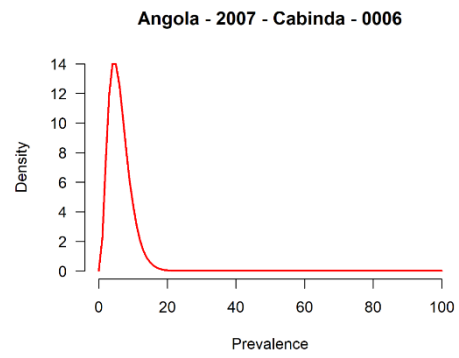
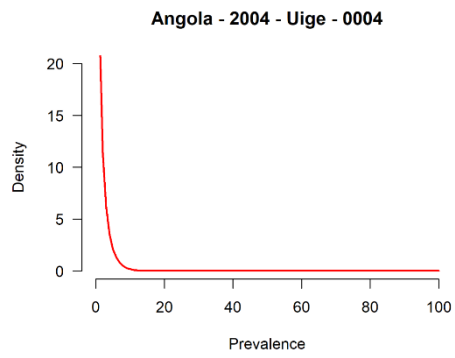
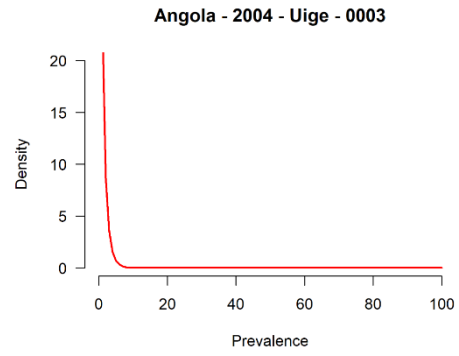
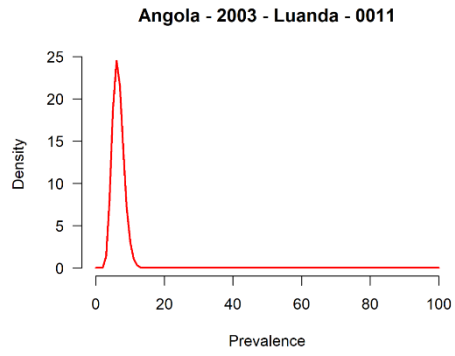


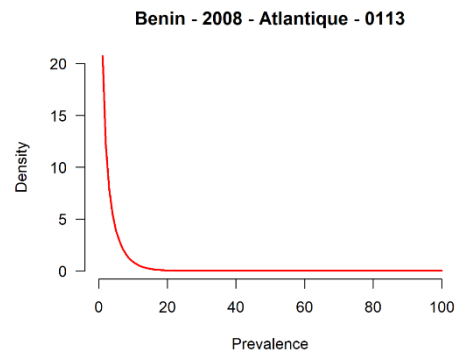
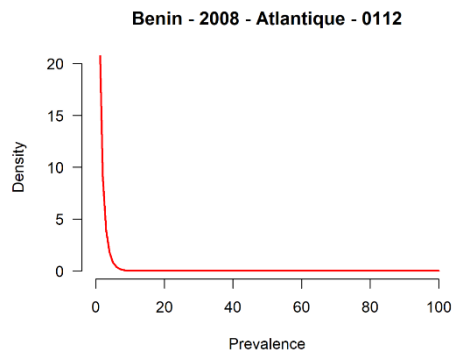
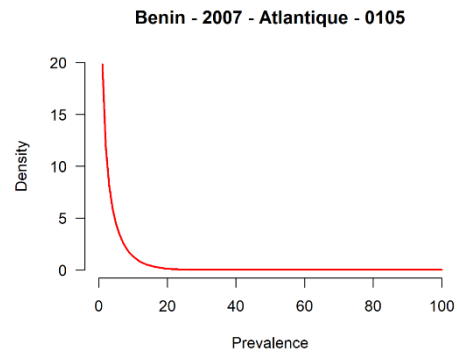
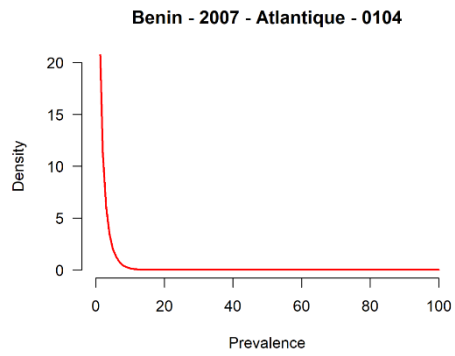
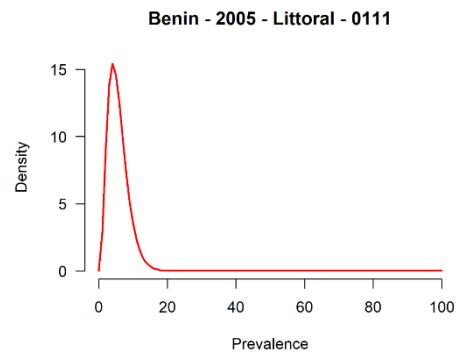
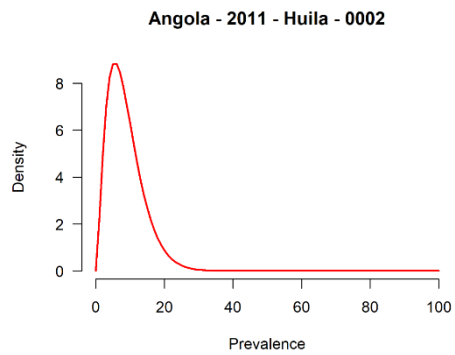
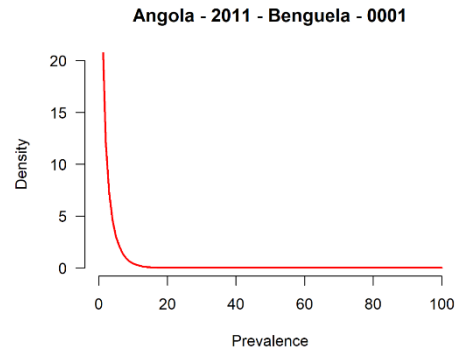
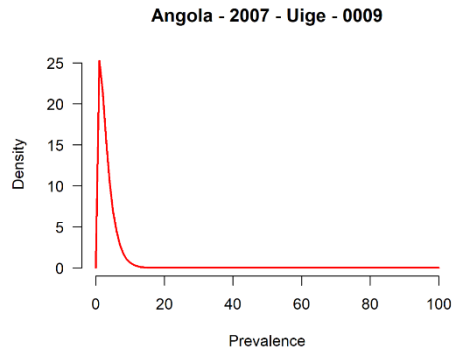


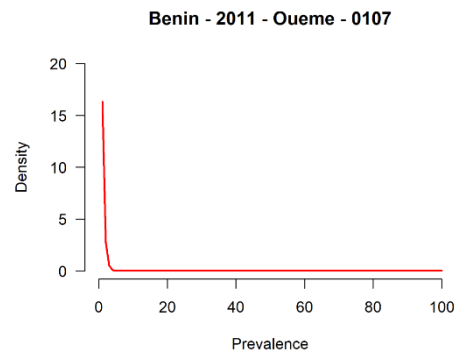
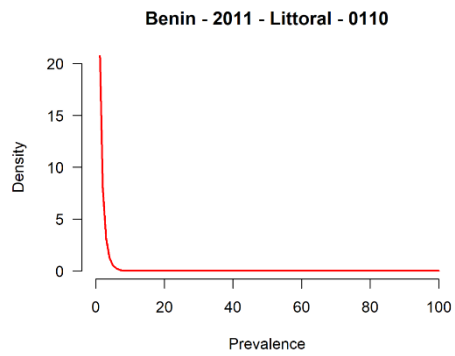
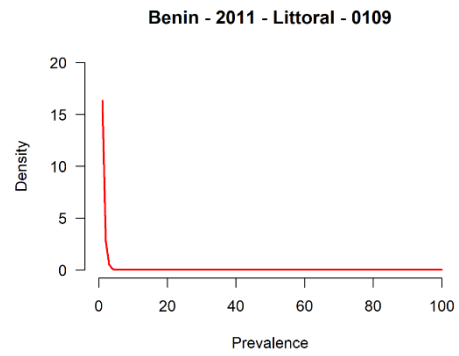
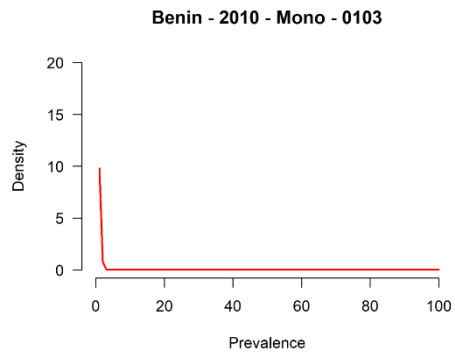
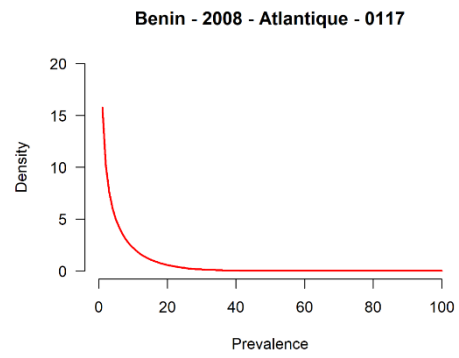
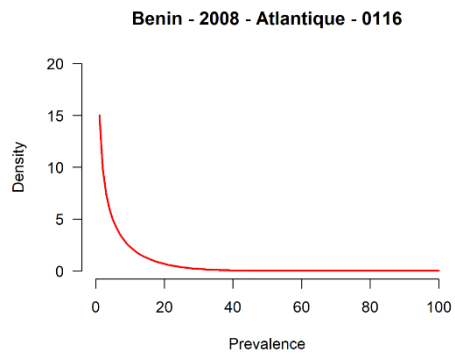
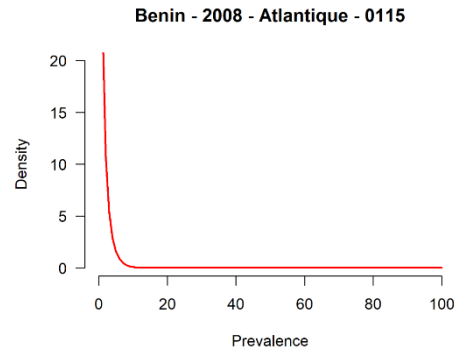
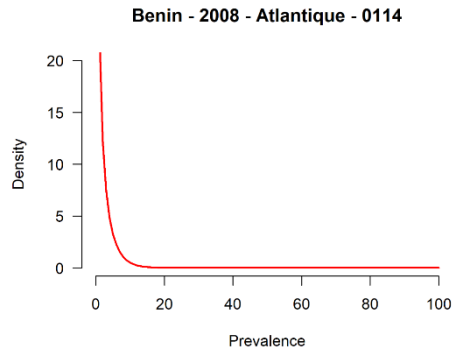
Supplement 3.5

Figure S11: Posterior probability distribution of prevalence per survey. To illustrate in depth the patterns in each survey, below I provide the posterior probability distribution of prevalence for each site-year of data. The title of each graph below is comprised of country name-sampling year-subnational geography-data record. Further details of each data point are provided in Table S3. Here I cover 30 and 38 malaria endemic countries for sulfadoxine-pyrimethamine, respectively. CAR and DRC denote Central African Republic and the Democratic Republic of the Congo, respectively. For further details, see supplement 2.5. (A) Mid-level resistance. (B) High-level resistance.

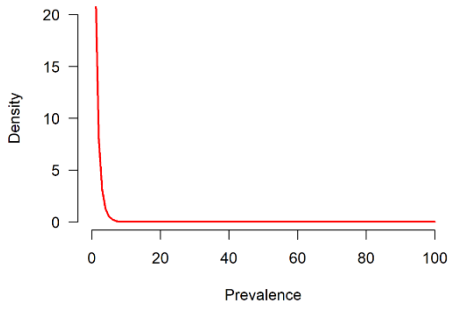
A.



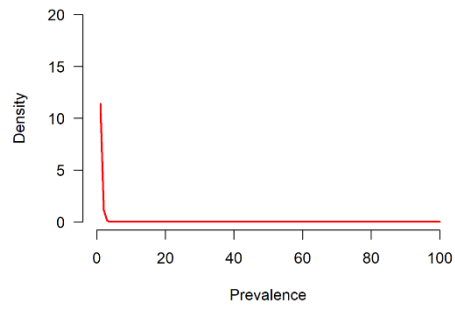




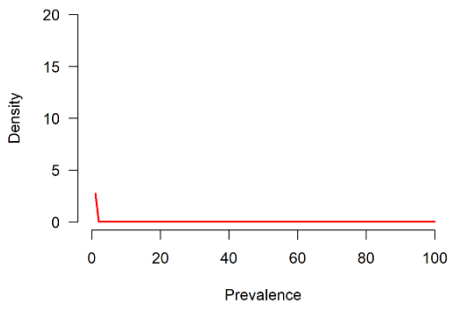
Benin - 2011 - Oueme - 0108



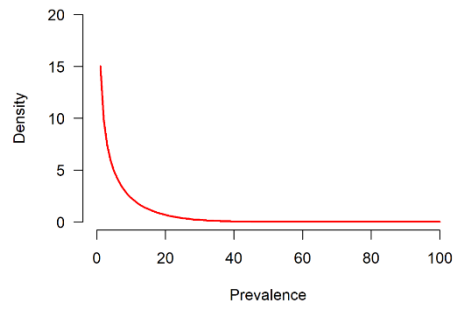
Benin - 2012 - Borgou - 0106



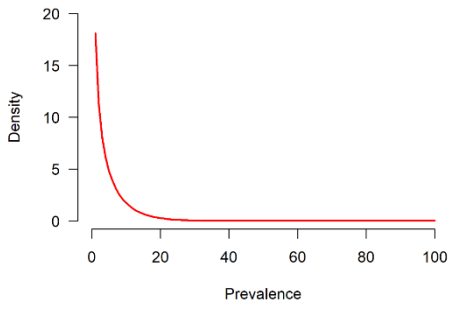
Burkina Faso - 2002 - Plateau-Central - 0126



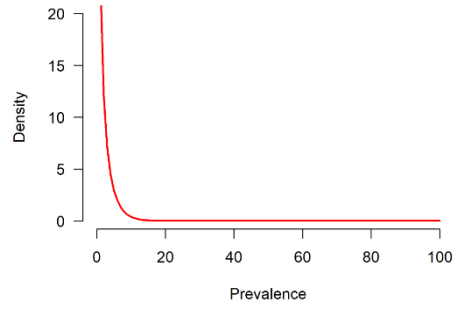
Burkina Faso - 2003 - Centre-Ouest - 0127



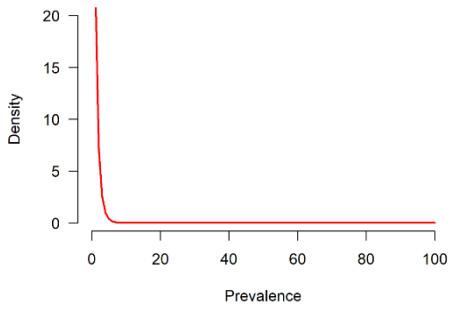
Burkina Faso - 2003 - Centre-Ouest - 0128



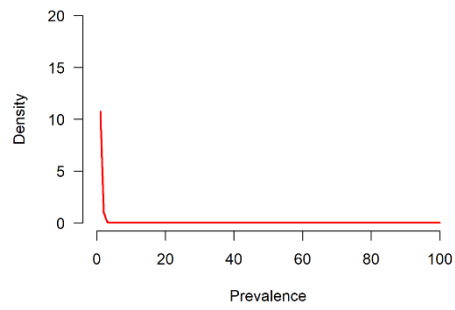
Burkina Faso - 2003 - Centre-Ouest - 0129



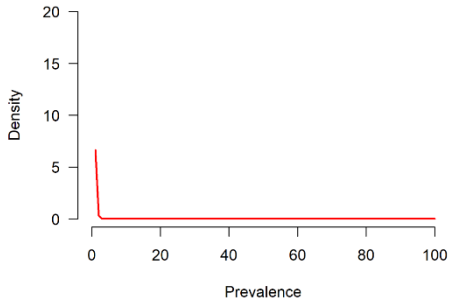
Burkina Faso - 2004 - Hauts-bassins - 0130



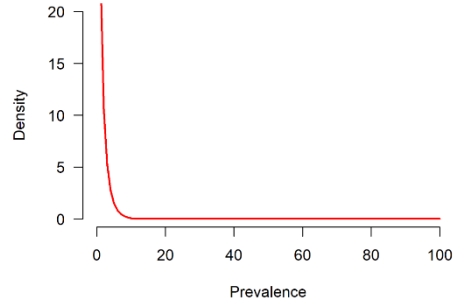
Burkina Faso - 2004 - Hauts-bassins - 0131



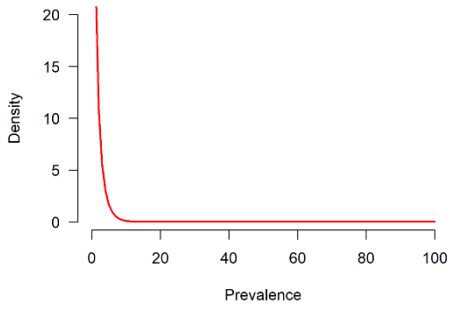
Burkina Faso - 2009 - Sud-ouest - 0122



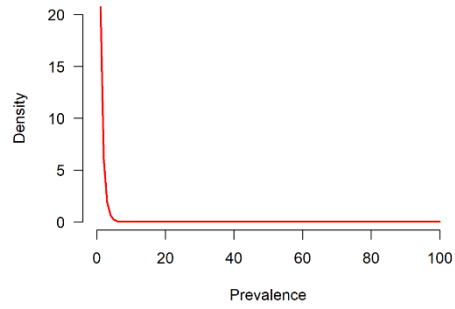
Burkina Faso - 2009 - Sud-ouest - 0123



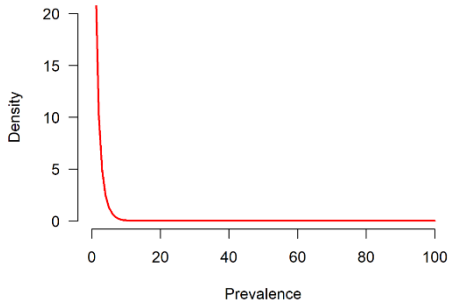
Burkina Faso - 2009 - Sud-ouest - 0124



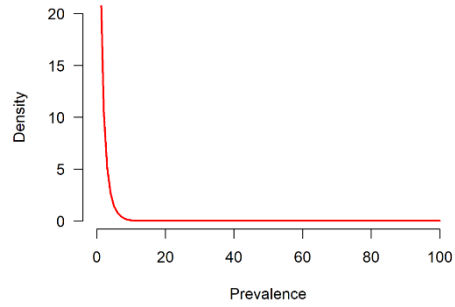
Burkina Faso - 2009 - Sud-ouest - 0125



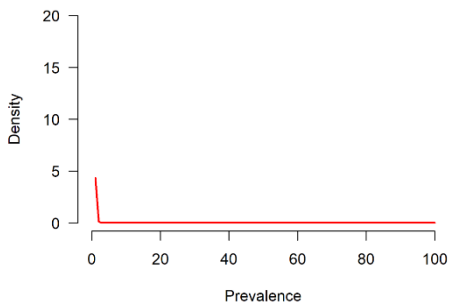
Burkina Faso - 2010 - Hauts-bassins - 0133



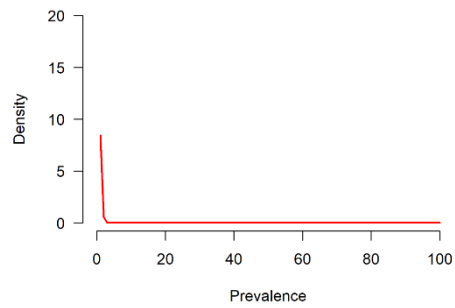
Burkina Faso - 2010 - Hauts-bassins - 0134



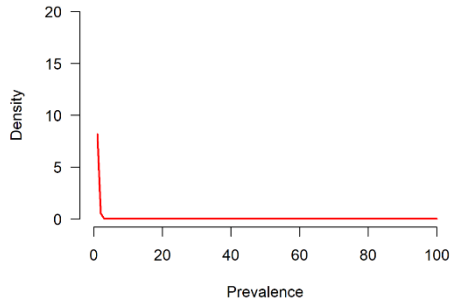
Burkina Faso - 2011 - Plateau-Central - 0132



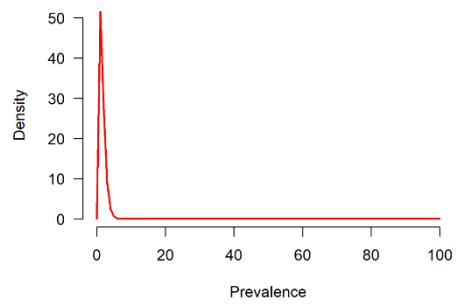
Burkina Faso - 2012 - Centre-Ouest - 0121



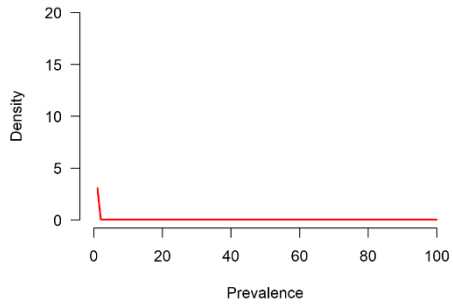
Burkina Faso - 2012 - Hauts-bassins - 0119



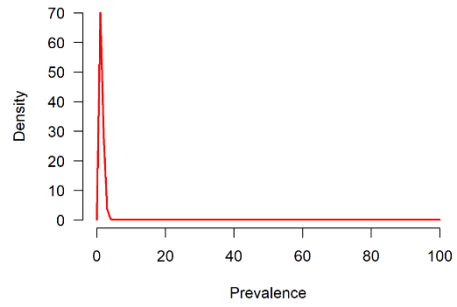
Burkina Faso - 2015 - Centre-Ouest - 0135



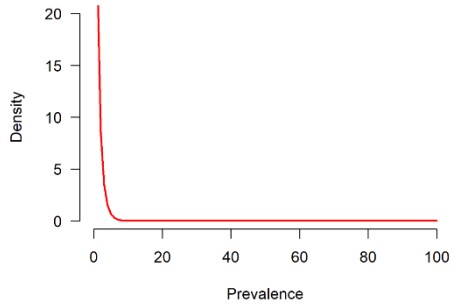
Burkina Faso - 2015 - Centre-Ouest - 0136



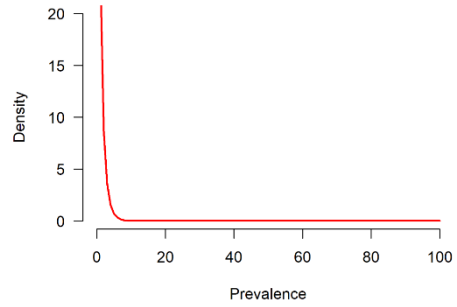
Burkina Faso - 2015 - Centre-Ouest - 0137



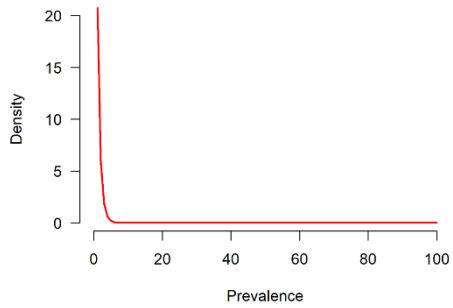
Cameroon - 1999 - Centre - 0145



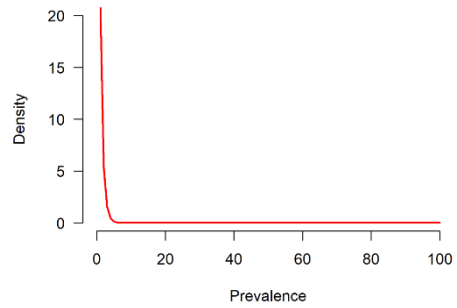
Cameroon - 2001 - Sud - 0146

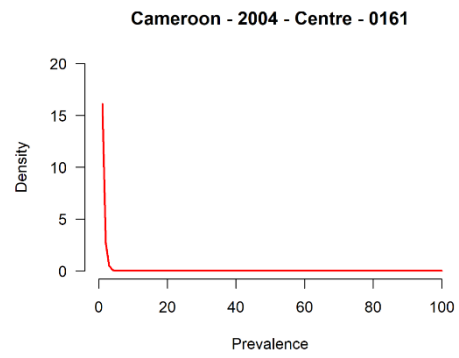
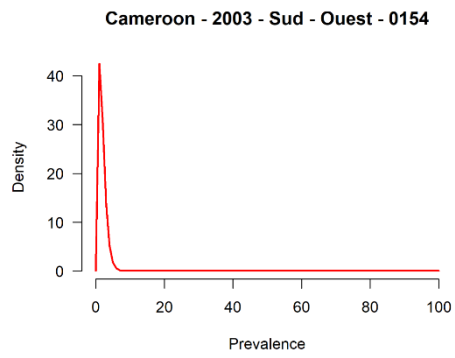
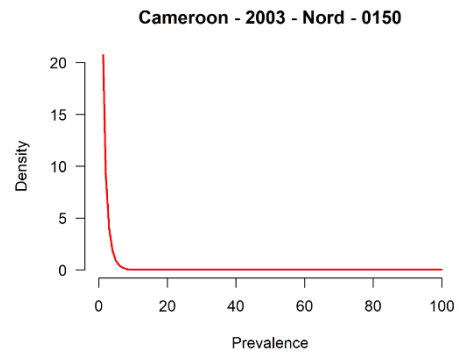
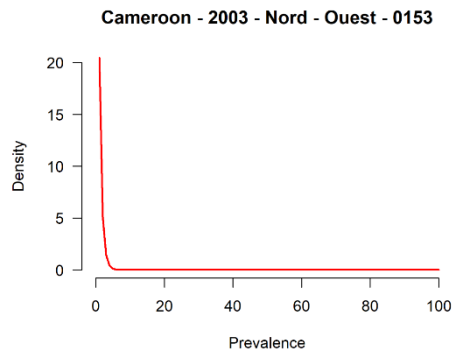
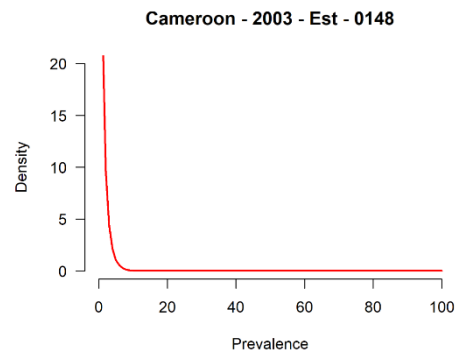
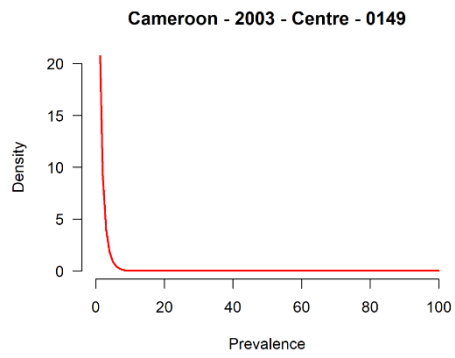
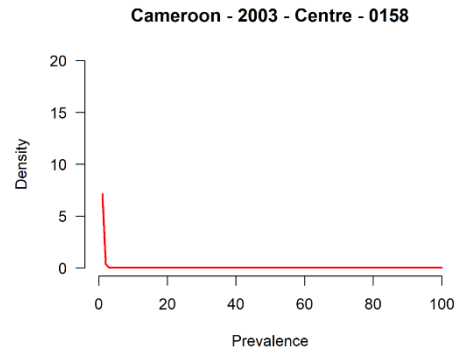
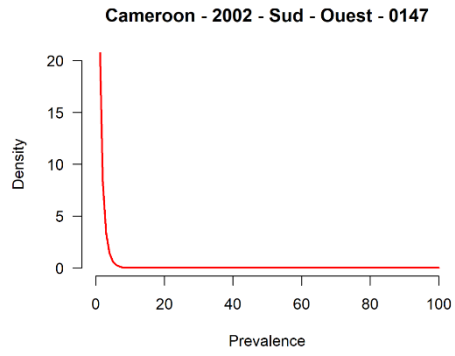


Cameroon - 2002 - Ouest - 0151

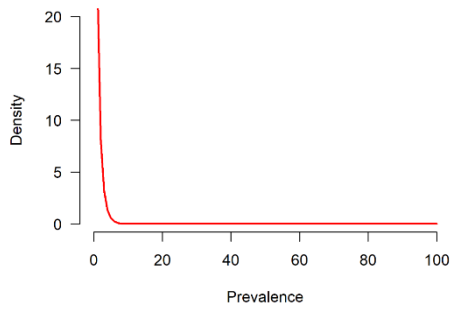


Cameroon - 2002 - Sud - Ouest - 0152

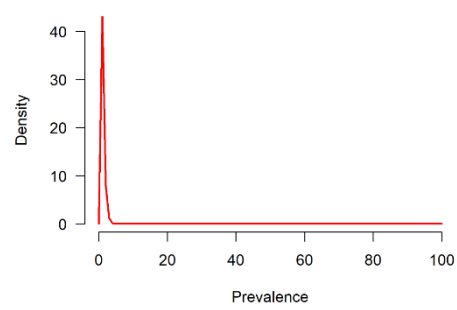




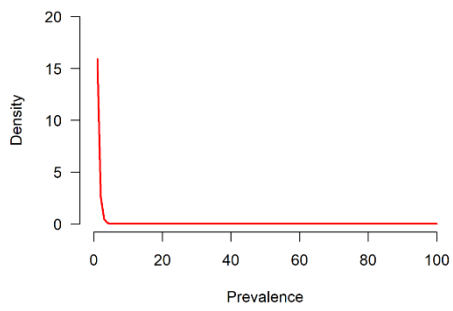
Cameroon - 2004 - Nord - 0160



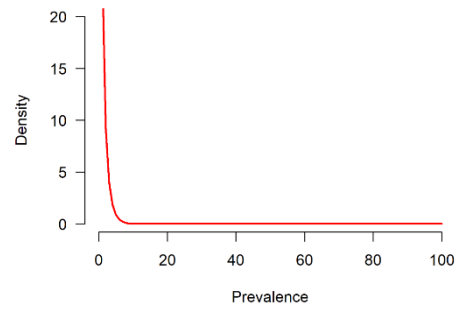
Cameroon - 2004 - Sud - Ouest - 0159



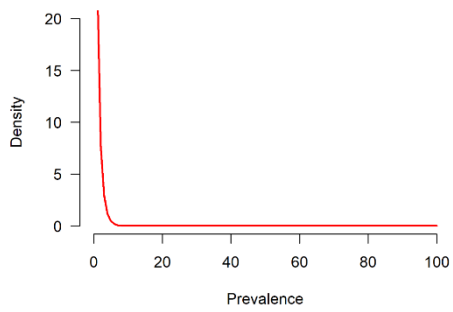
Cameroon - 2005 - Centre - 0157



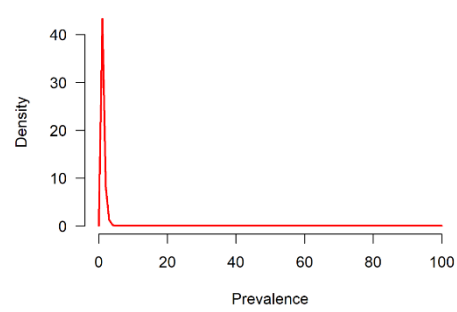
Cameroon - 2005 - Centre - 0162



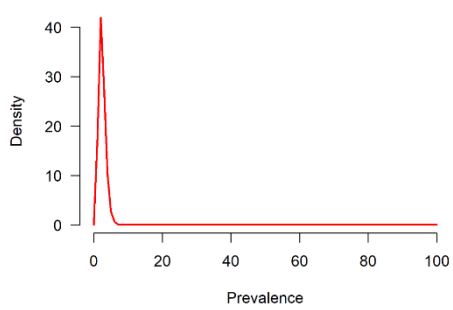
Cameroon - 2005 - Nord - 0156



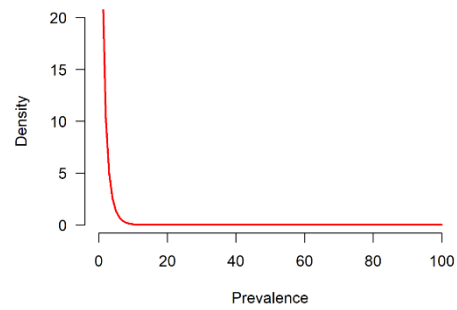
Cameroon - 2005 - Sud - Ouest - 0155



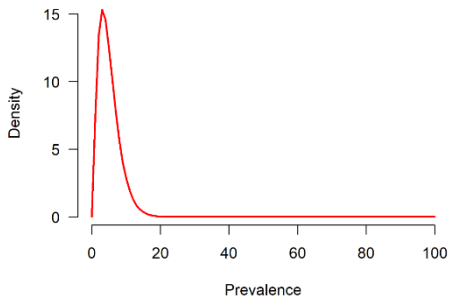
Cameroon - 2005 - Sud - Ouest - 0163



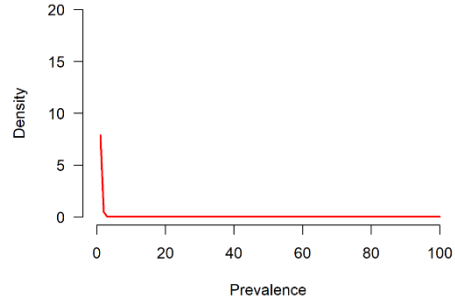
Cameroon - 2011 - Centre - 0141



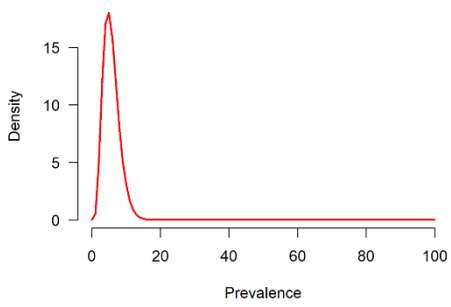
Cameroon - 2011 - Centre - 0142



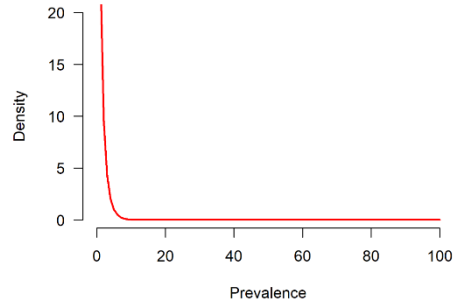
Cameroon - 2013 - Sud - Ouest - 0164



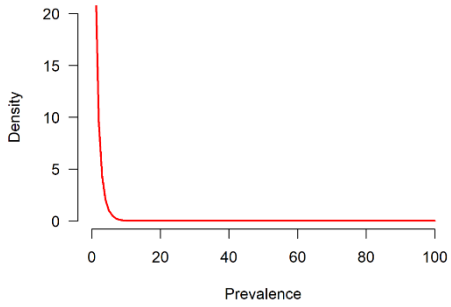
CAR - 2004 - Ombella-mpoko - 0175



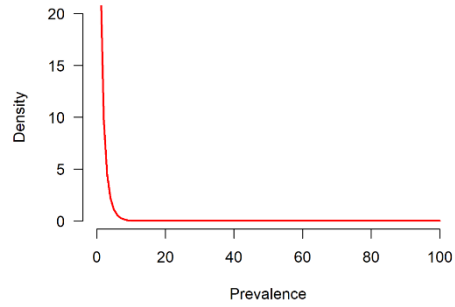
CAR - 2010 - Ombella-mpoko - 0176



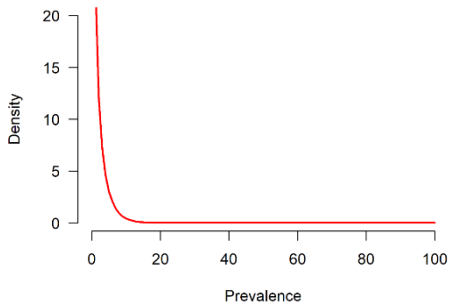
CAR - 2010 - Ombella-mpoko - 0177



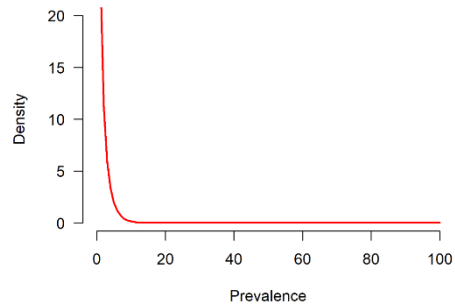
CAR - 2010 - Ombella-mpoko - 0178



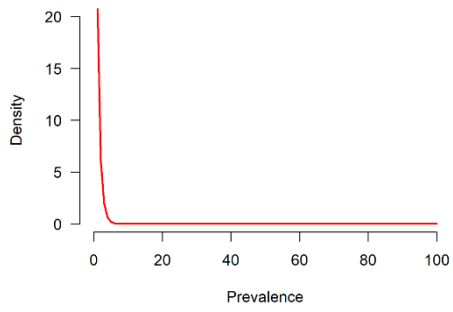
Chad - 2015 - Mayo-Dala - 0139



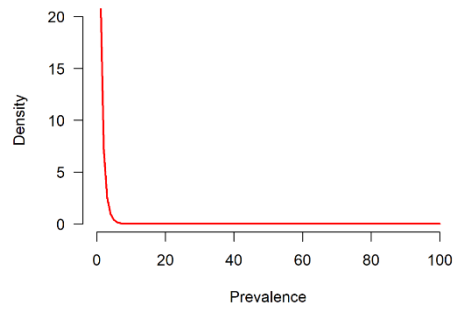
Congo - 1999 - Kouilou - 0182



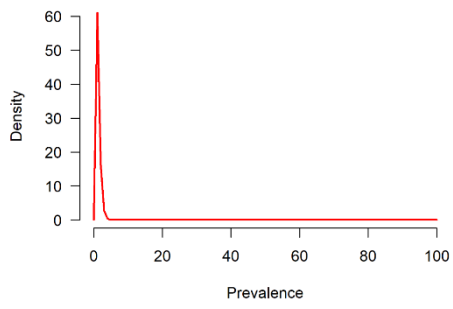
Congo - 2002 - Pool - 0183



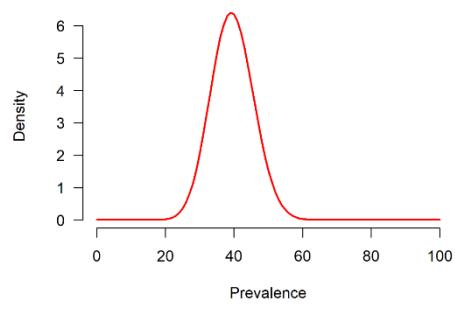
Congo - 2004 - Pool - 0184



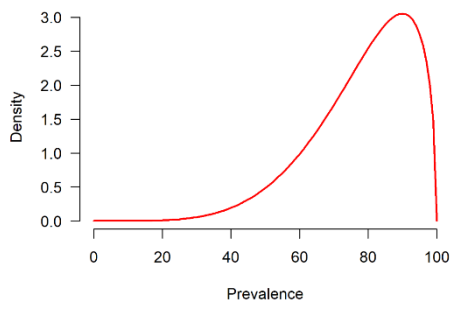
Congo - 2004 - Pool - 0185



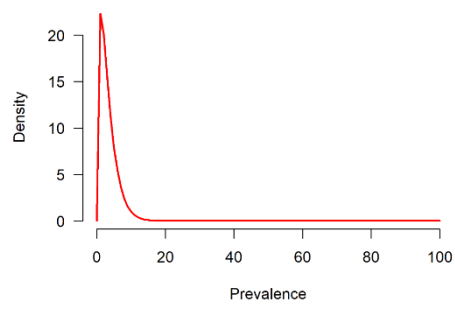
Congo - 2013 - Pool - 0180



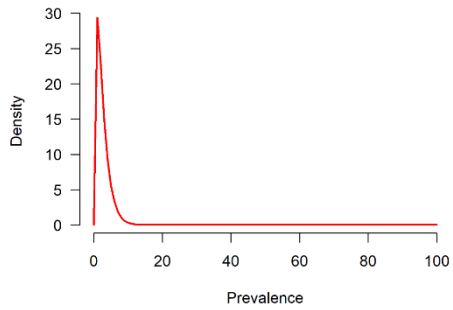
Congo - 2013 - Pool - 0181



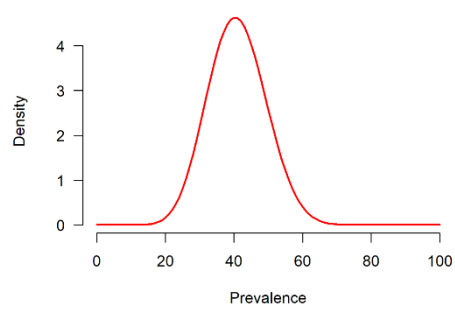
Djibouti - 1998 - Djibouti - 0208



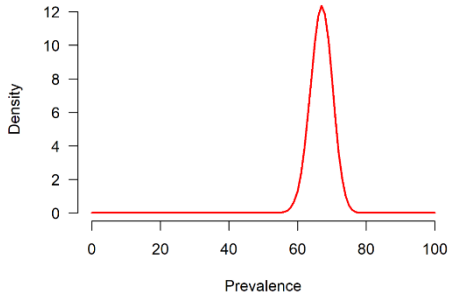
Djibouti - 1999 - Djibouti - 0209



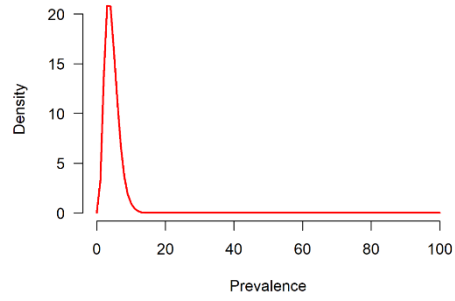
Djibouti - 2002 - Djibouti - 0210



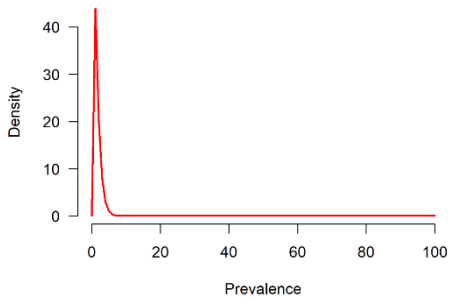
DRC - 2002 - Nord Kivu - 0188



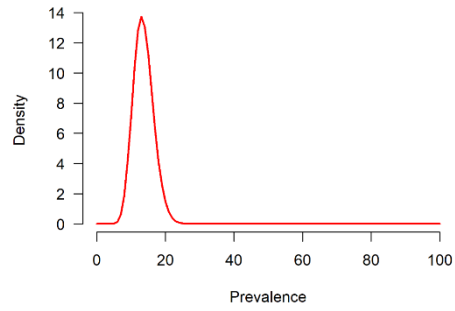
DRC - 2004 - Equateur - 0193



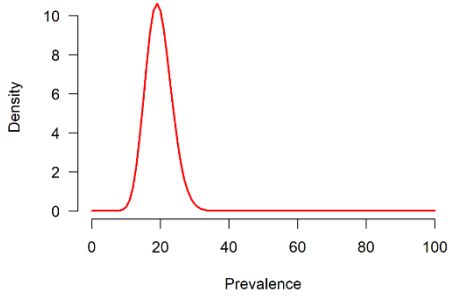
DRC - 2004 - Equateur - 0194



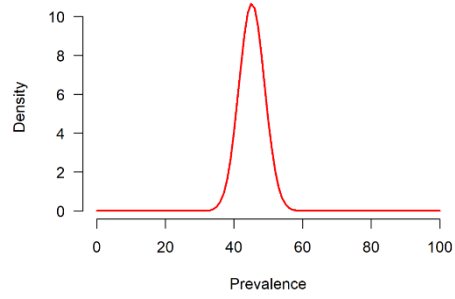
DRC - 2004 - Katanga - 0192



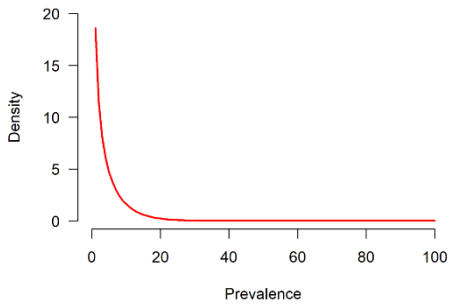
DRC - 2004 - Province Orientale - 0191



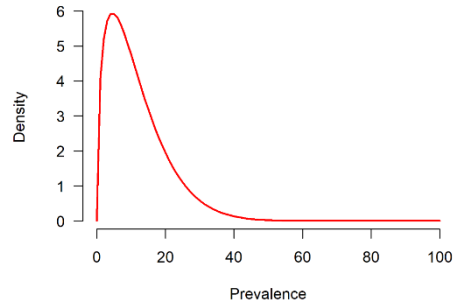
DRC - 2004 - Sud Kivu - 0195

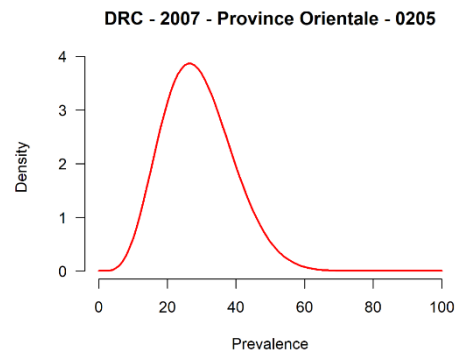
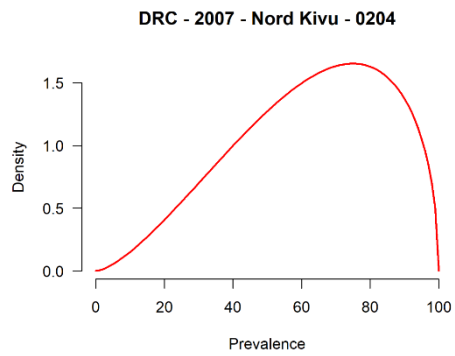
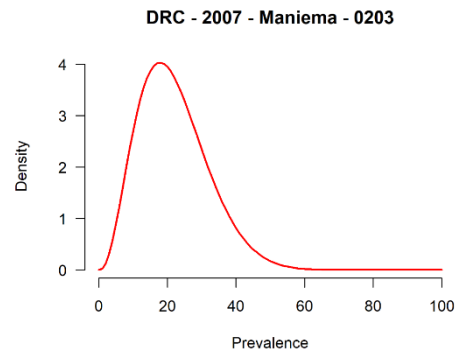
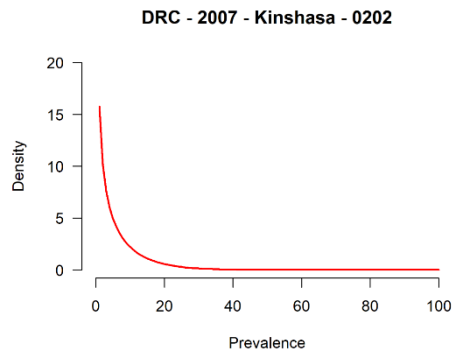
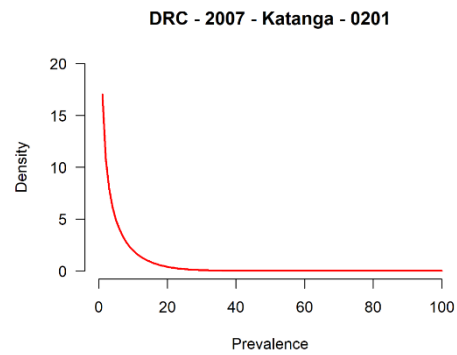
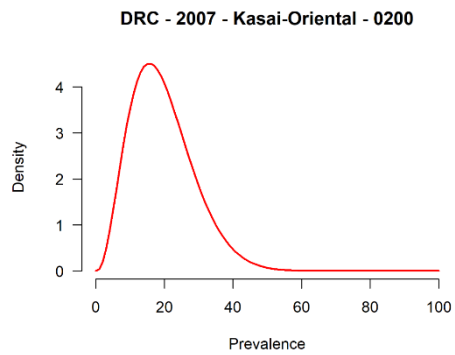
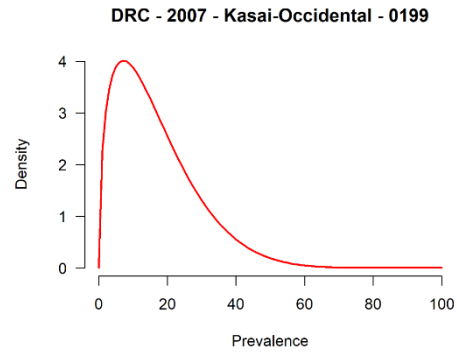
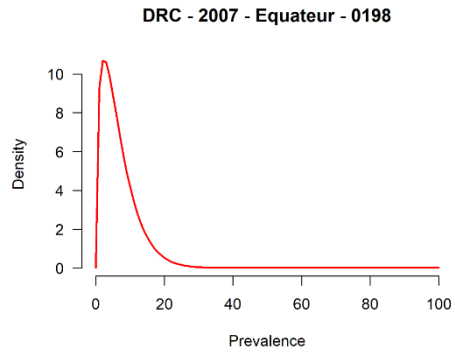


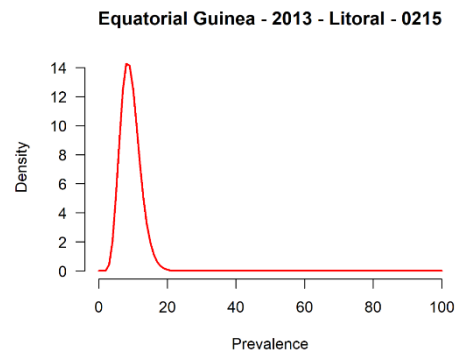
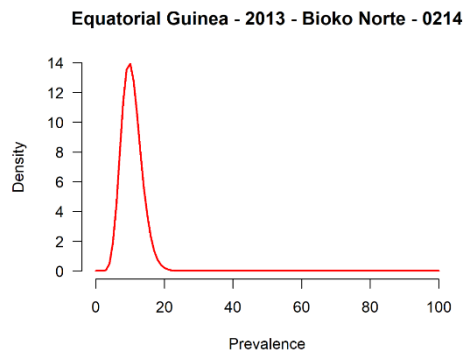
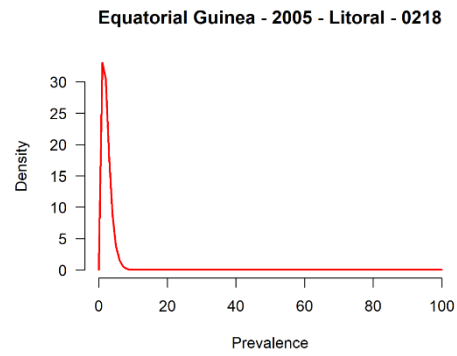
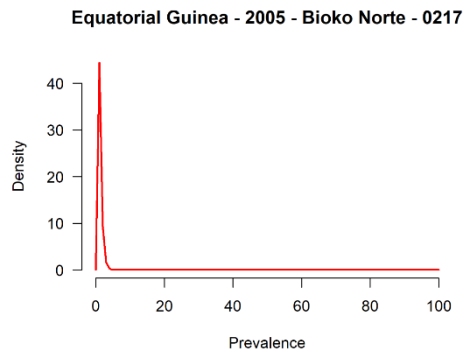
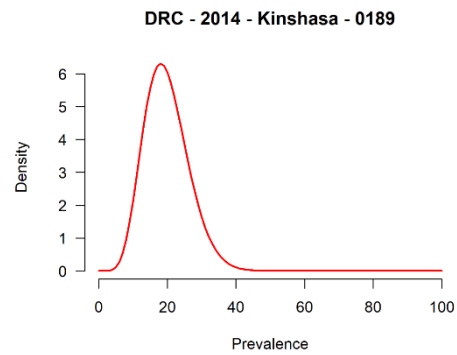
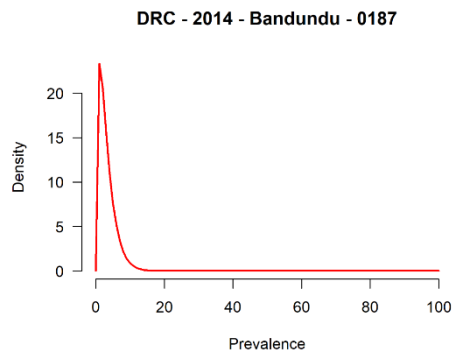
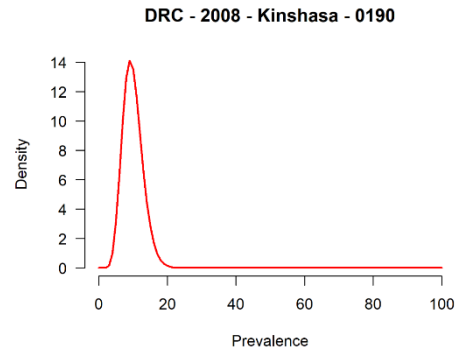
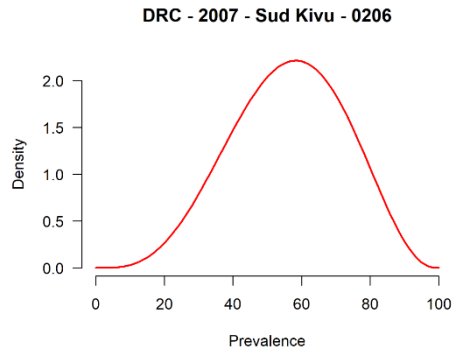
DRC - 2007 - Bandundu - 0196



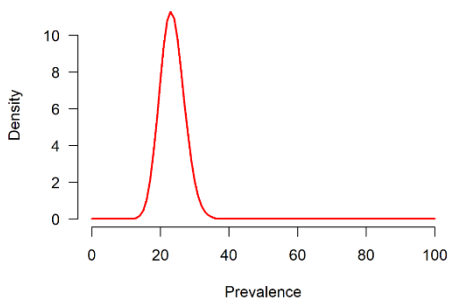
DRC - 2007 - Bas-Congo - 0197



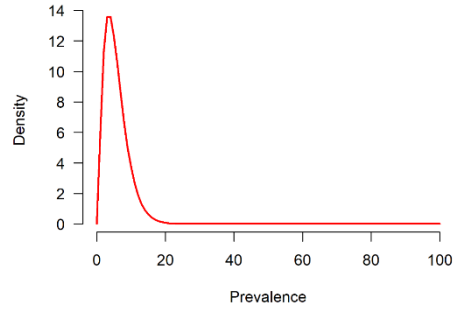




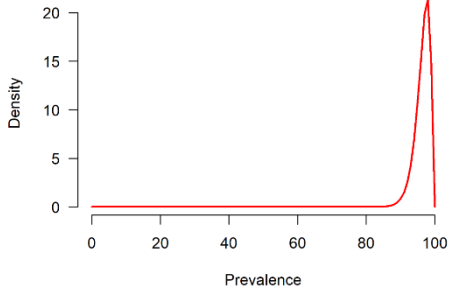
Equatorial Guinea - 2013 - Litoral - 0216



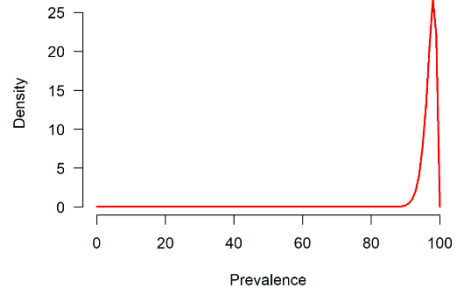
Equatorial Guinea - 2013 - Litoral - 0213



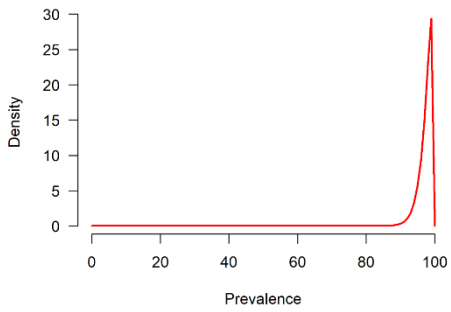
Ethiopia - 2004 - SNNP - 0227



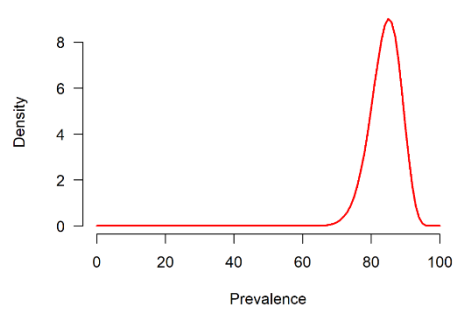
Ethiopia - 2004 - Tigray - 0226



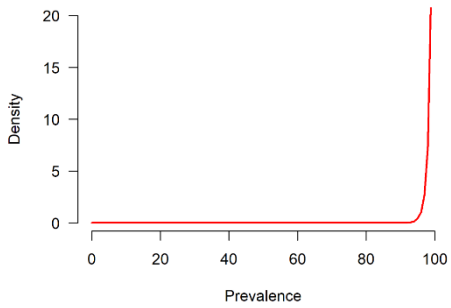
Ethiopia - 2005 - Amhara - 0222



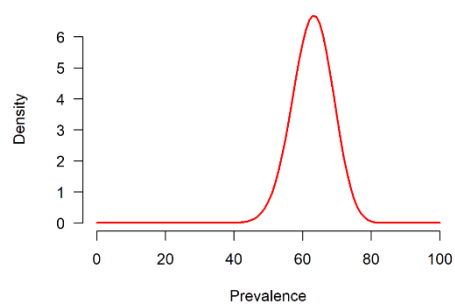
Ethiopia - 2005 - Benishangul Gumuz - 0221



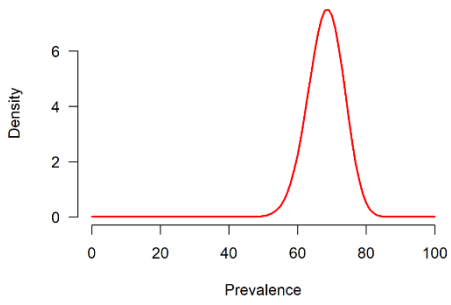
Ethiopia - 2008 - Amhara - 0223



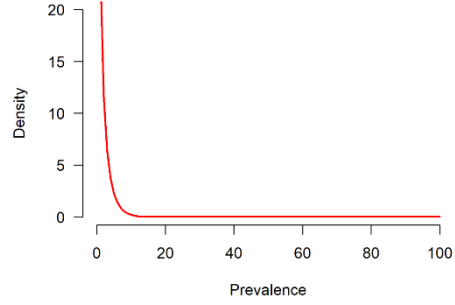
Ethiopia - 2008 - Benishangul Gumuz - 0220



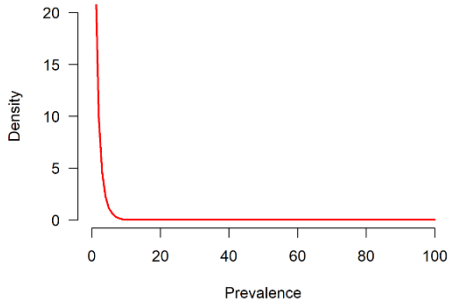
Ethiopia - 2009 - Oromia - 0224



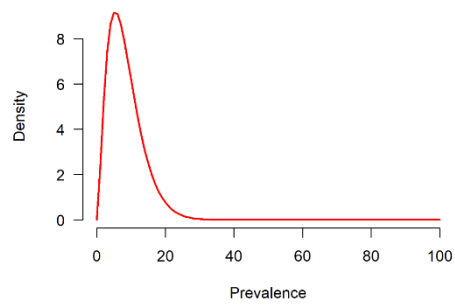
Gabon - 1998 - Haut-Ogooue - 0233



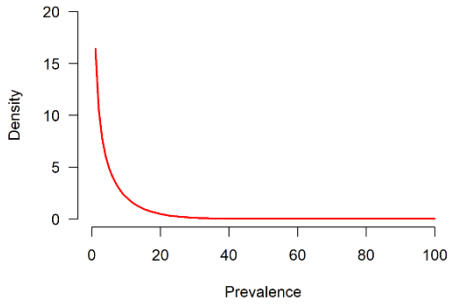
Gabon - 2000 - Haut-Ogooue - 0234



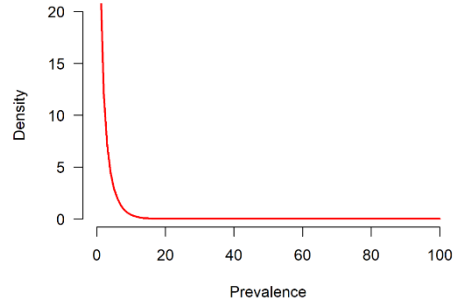
Gabon - 2005 - Estuaire - 0236



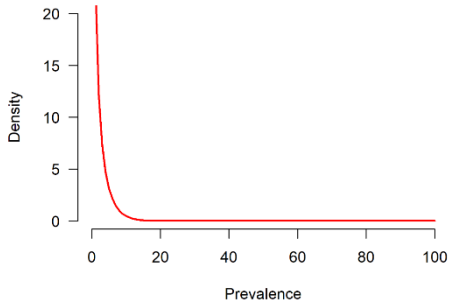
Gabon - 2005 - Estuaire - 0238



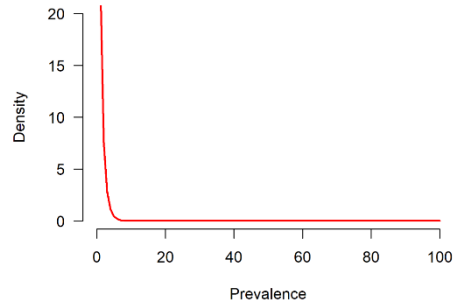
Gabon - 2005 - Estuaire - 0240

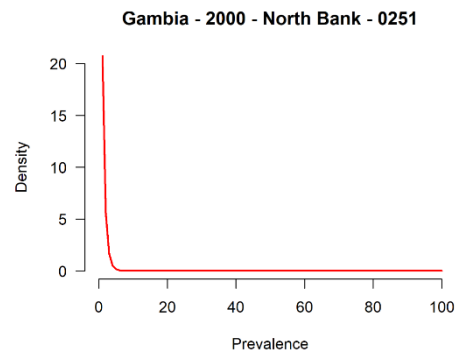
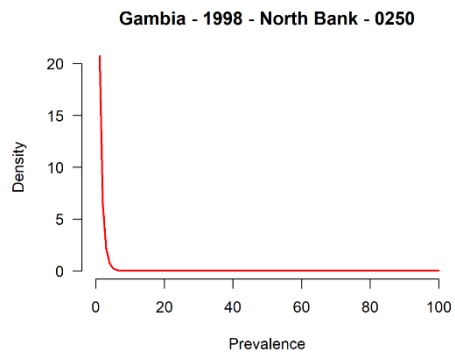
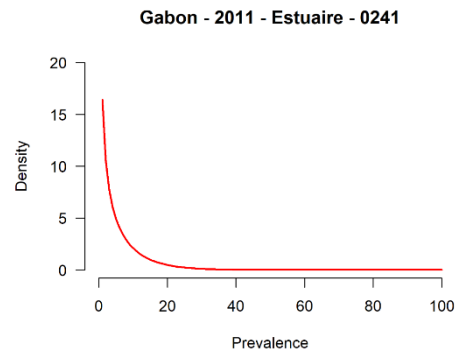
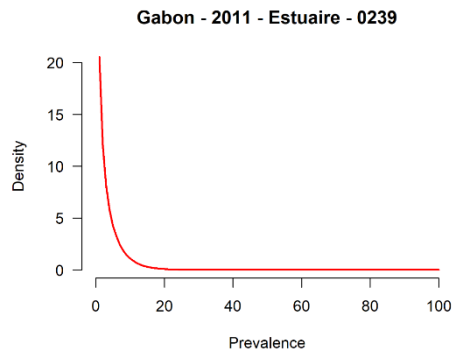
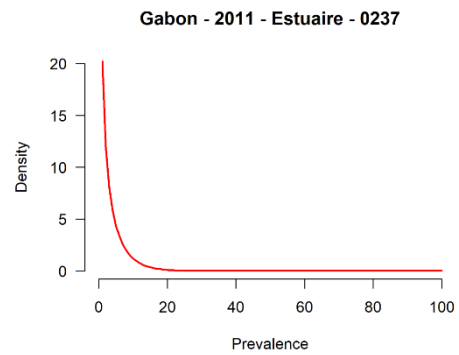
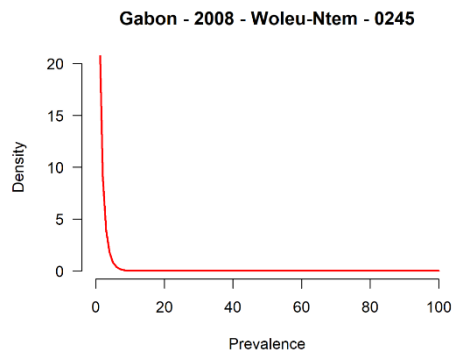
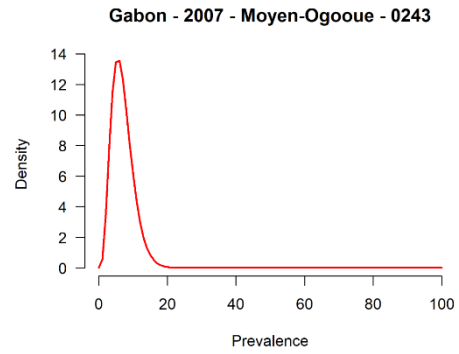
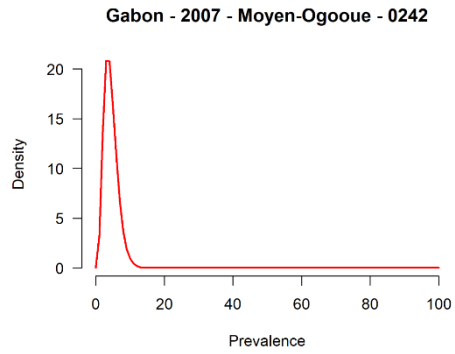


Gabon - 2005 - Woleu-Ntem - 0244

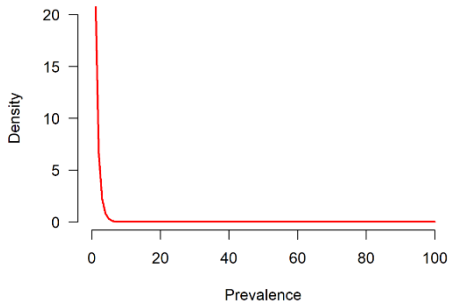


Gabon - 2005 - Woleu-Ntem - 0235

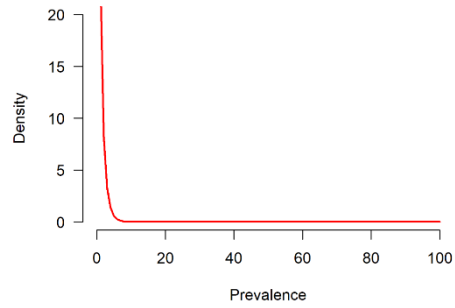




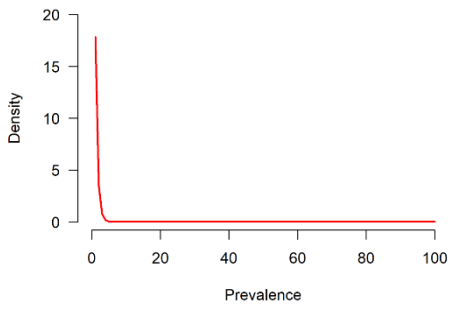
Gambia - 2001 - North Bank - 0255



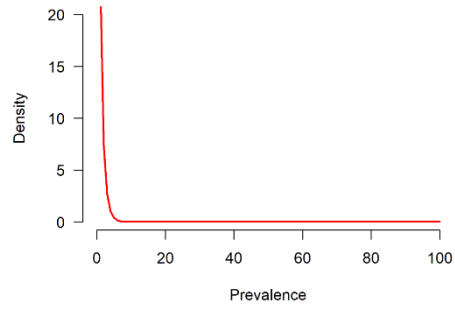
Gambia - 2004 - North Bank - 0252



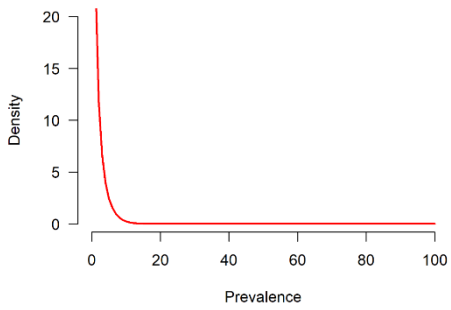
Gambia - 2004 - North Bank - 0256



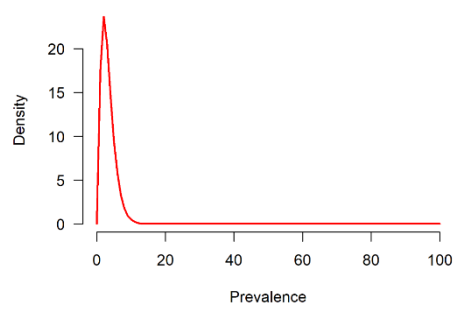
Gambia - 2007 - North Bank - 0253



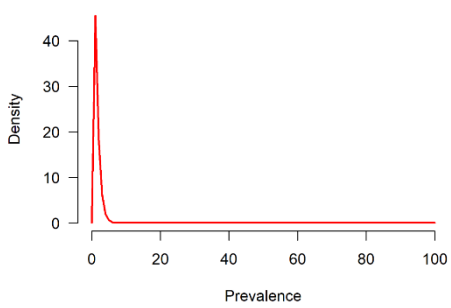
Gambia - 2008 - North Bank - 0254



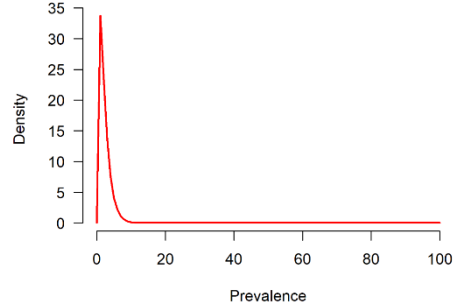
Ghana - 2001 - Ashanti - 0259



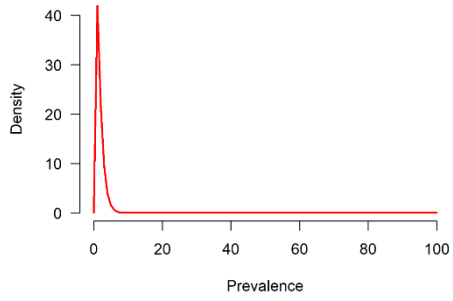
Ghana - 2002 - Northern - 0258



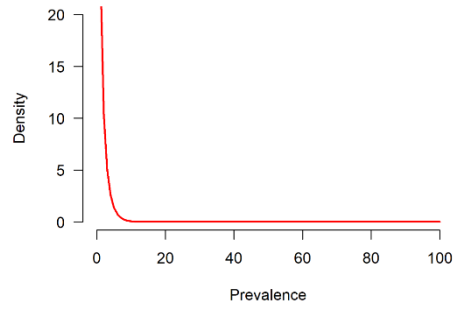
Ghana - 2003 - Ashanti - 0260



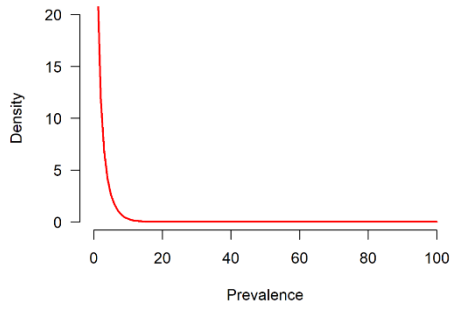
Ghana - 2003 - Upper East - 0261



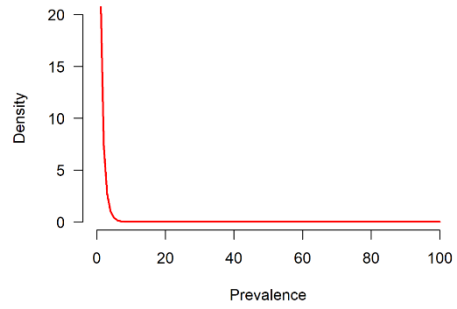
Ghana - 2004 - Brong Ahafo - 0266



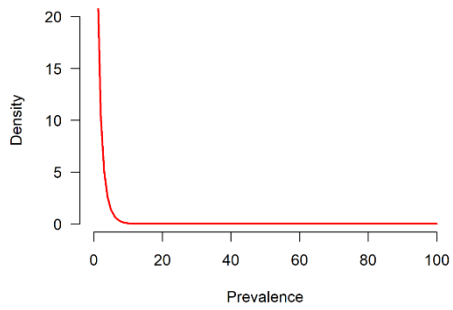
Ghana - 2004 - Upper East - 0278



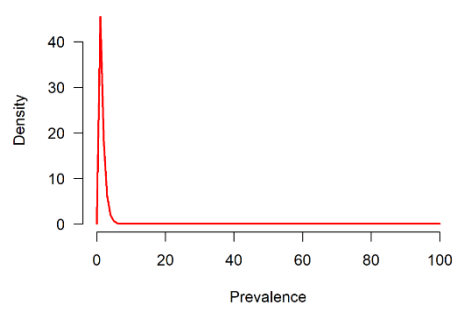
Ghana - 2004 - Volta - 0284



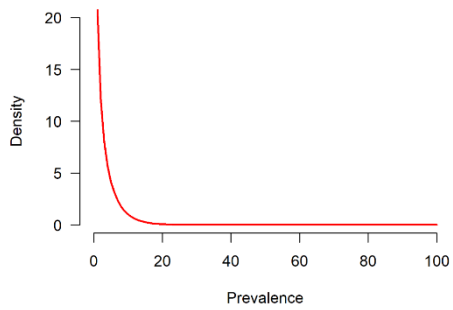
Ghana - 2004 - Western - 0286



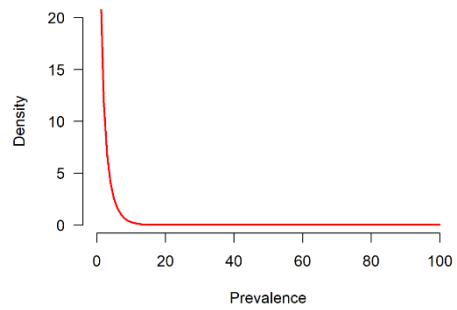
Ghana - 2005 - Volta - 0262

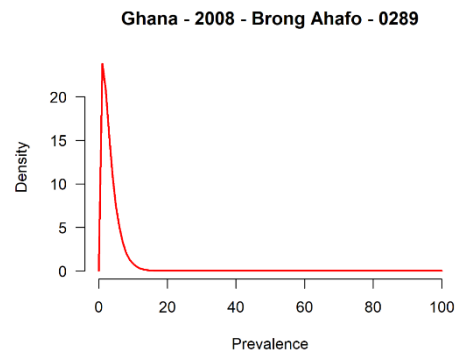
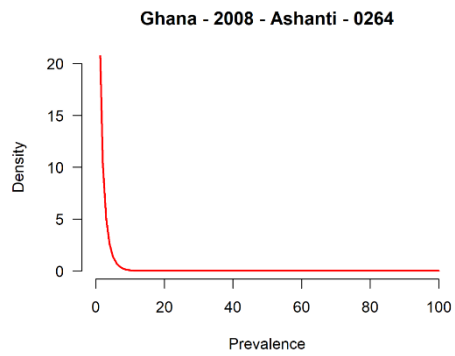
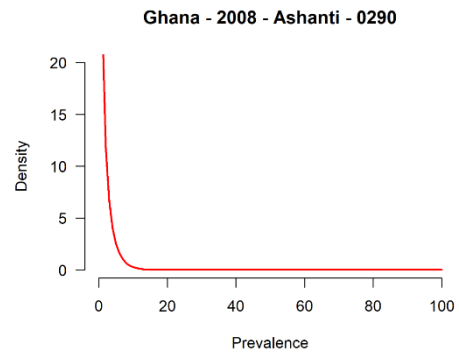
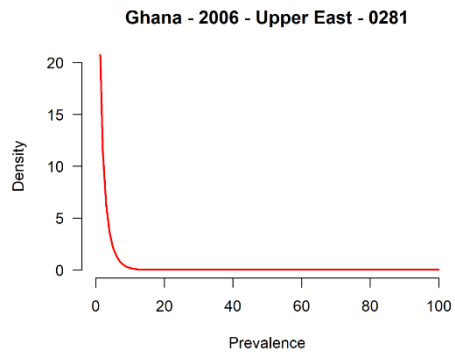
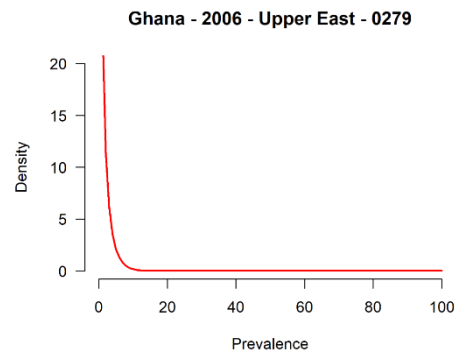
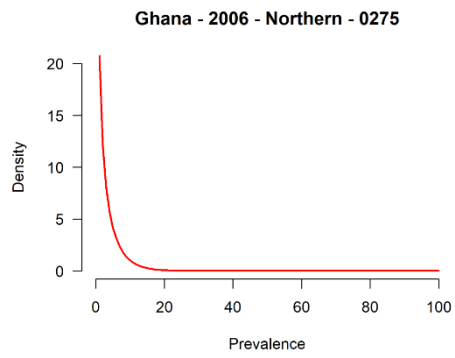
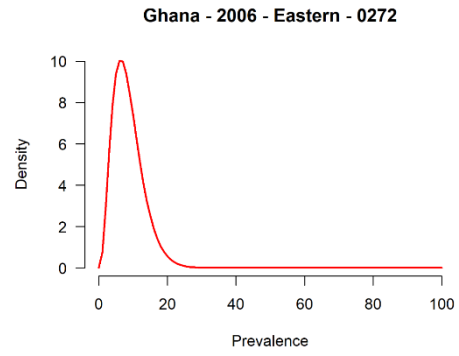
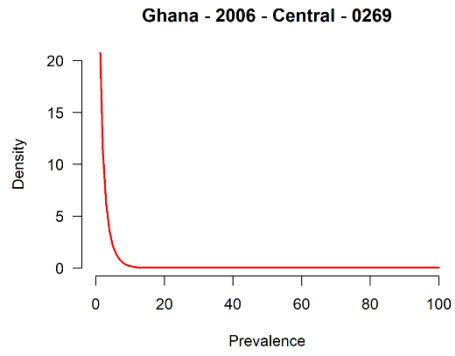


Ghana - 2006 - Ashanti - 0263

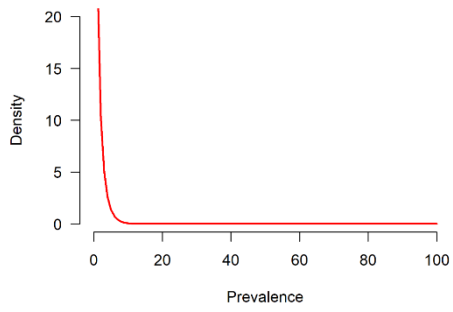


Ghana - 2006 - Brong Ahafo - 0267

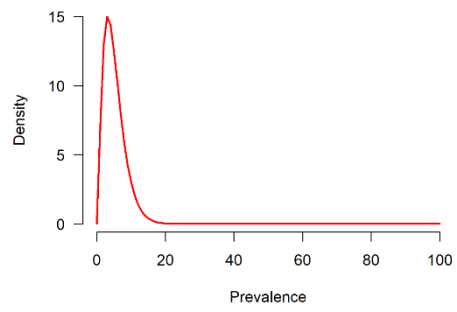




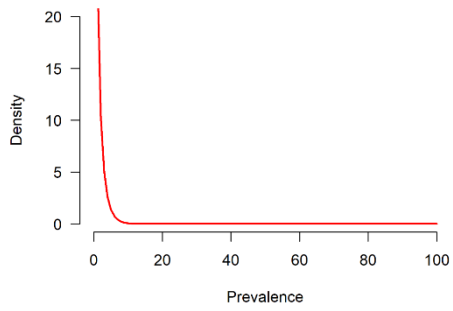
Ghana - 2008 - Brong Ahafo - 0268



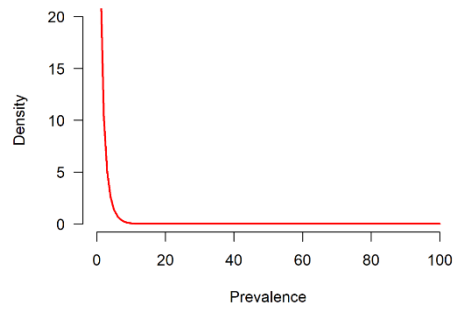
Ghana - 2008 - Central - 0291



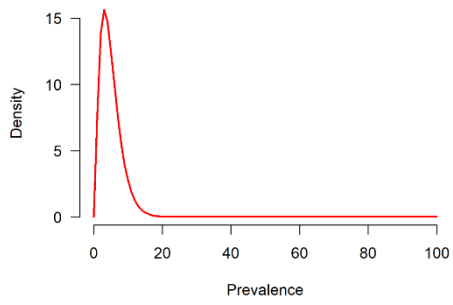
Ghana - 2008 - Central - 0270



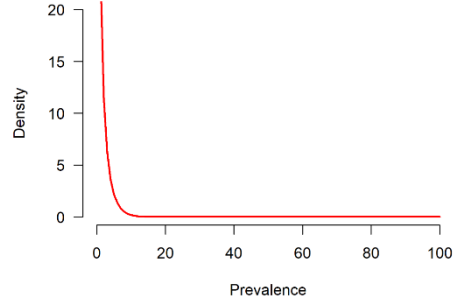
Ghana - 2008 - Eastern - 0273



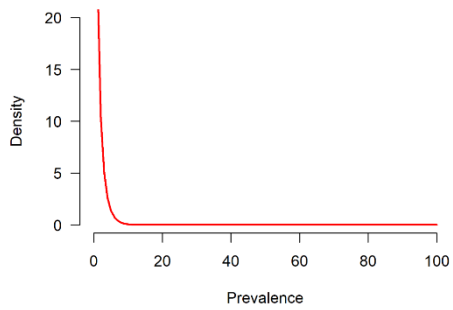
Ghana - 2008 - Northern - 0276



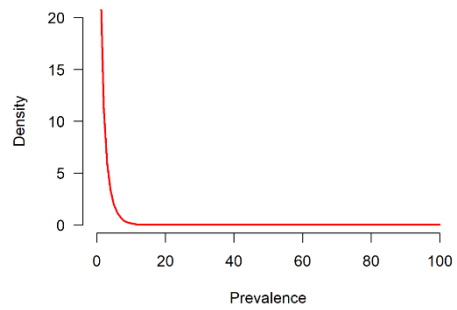
Ghana - 2008 - Upper East - 0288

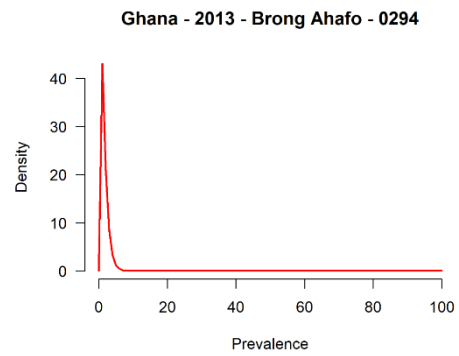
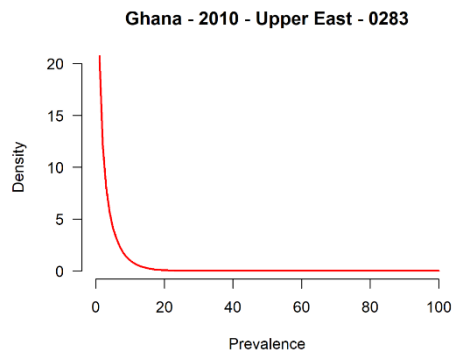
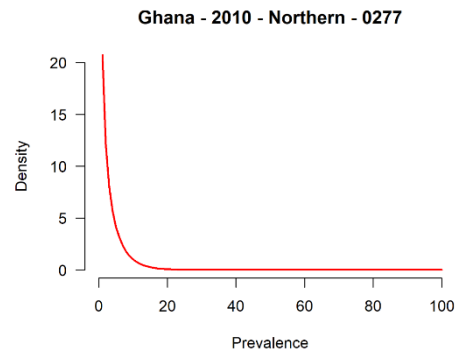
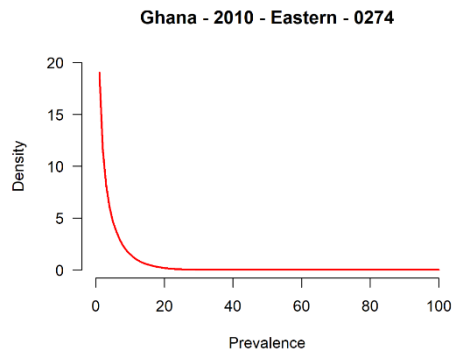
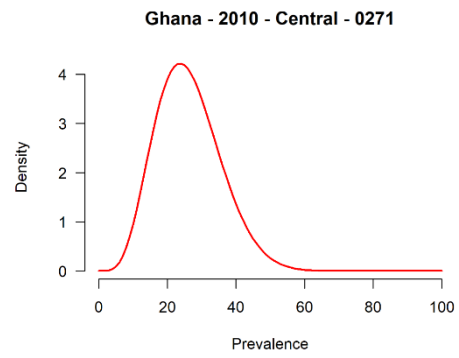
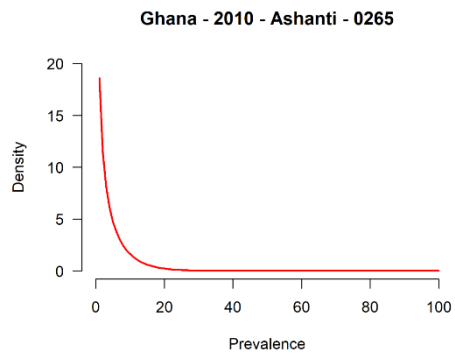
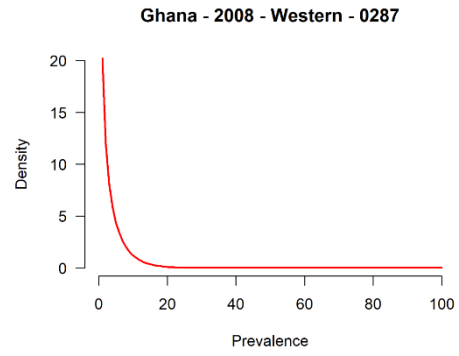
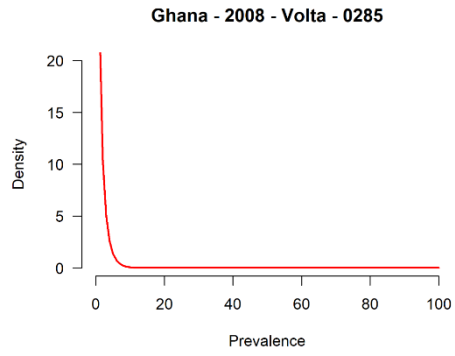


Ghana - 2008 - Upper East - 0280

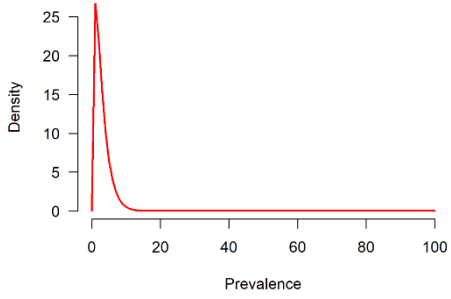


Ghana - 2008 - Upper East - 0282

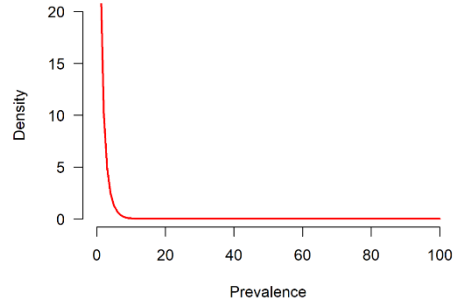




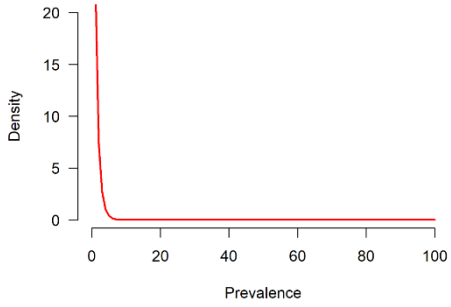
Ghana - 2013 - Upper East - 0293



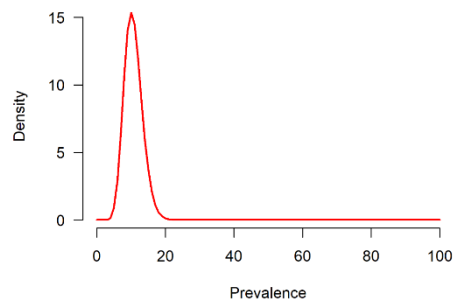
Ghana - 2017 - Brong Ahafo - 0295



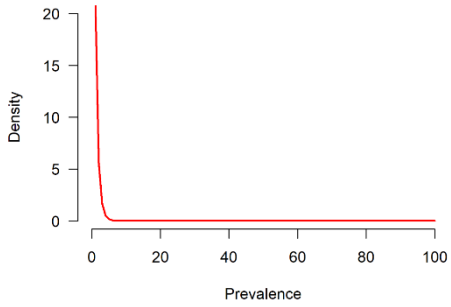
Ghana - 2017 - Greater Accra - 0292



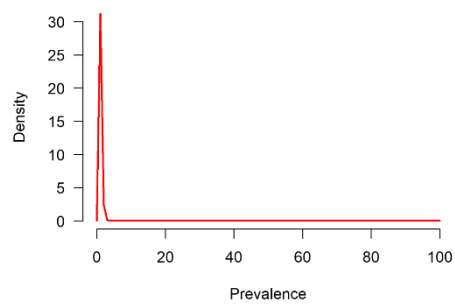
Guinea - 2004 - N'Zerekore - 0304



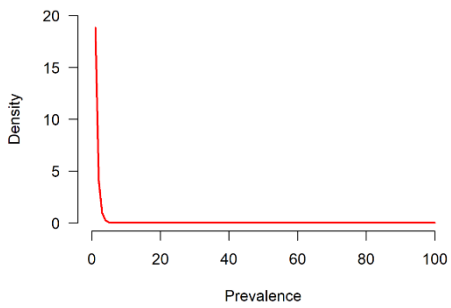
Guinea-Bissau - 2001 - Tombali - 0302



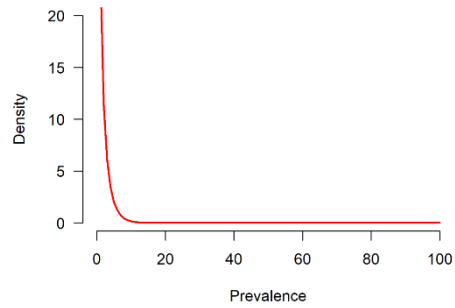
Guinea-Bissau - 2016 - Bissau Autonomous Sector - 0303



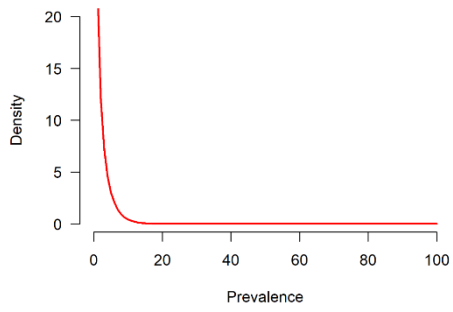
Ivory Coast - 2001 - Abidjan - 0306



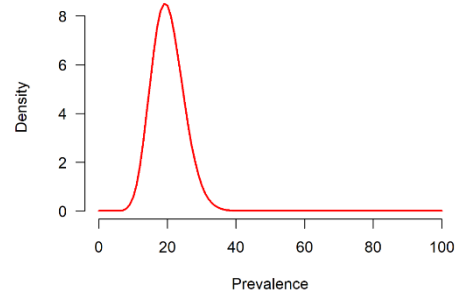
Ivory Coast - 2005 - Comoe - 0307



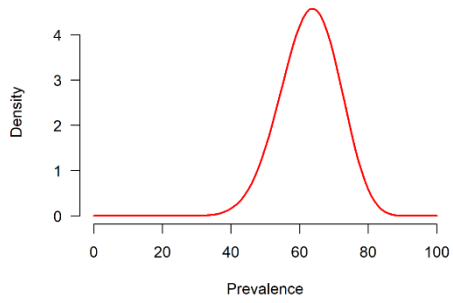
Ivory Coast - 2005 - Lagunes - 0308



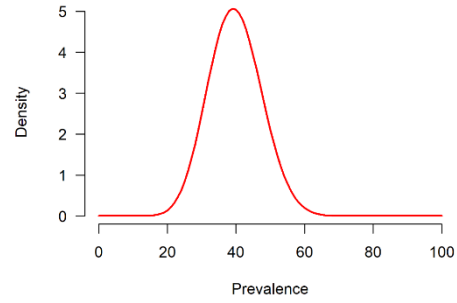
Kenya - 1998 - Coast - 0375



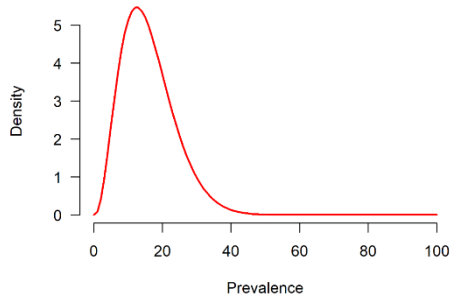
Kenya - 1998 - Coast - 0376



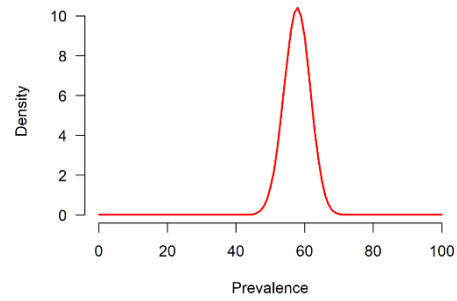
Kenya - 1998 - Coast - 0338



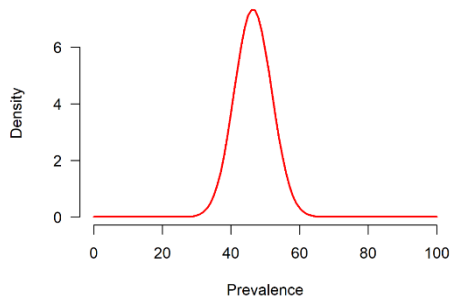
Kenya - 1998 - Western - 0339



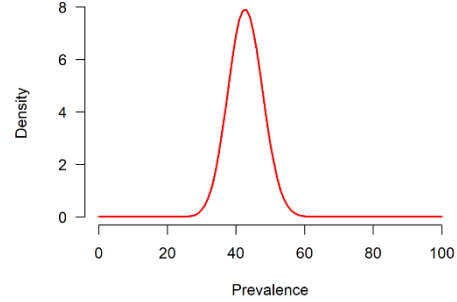
Kenya - 1999 - Western - 0374



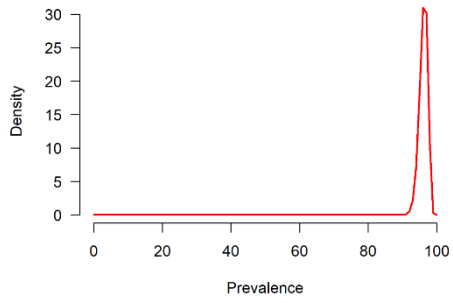
Kenya - 2000 - Nyanza - 0355



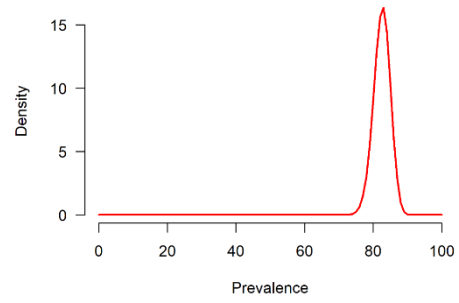
Kenya - 2000 - Nyanza - 0358



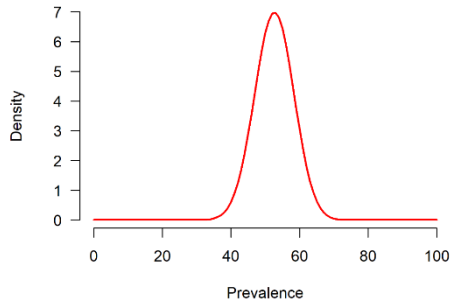
Kenya - 2000 - Nyanza - 0367



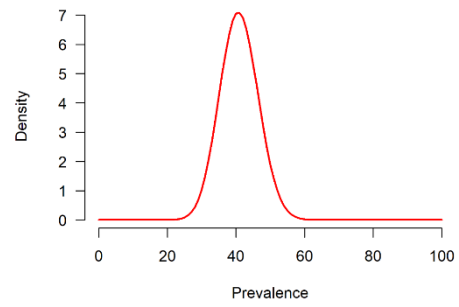
Kenya - 2001 - Western - 0315



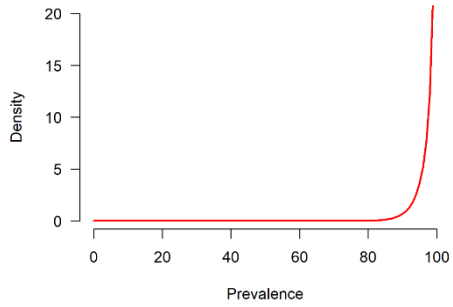
Kenya - 2002 - Coast - 0362



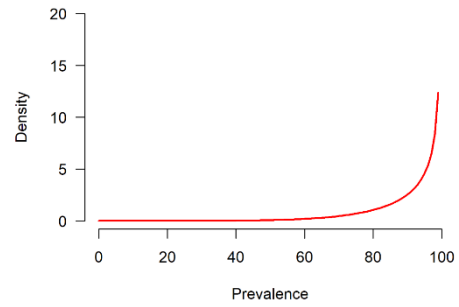
Kenya - 2002 - Coast - 0363



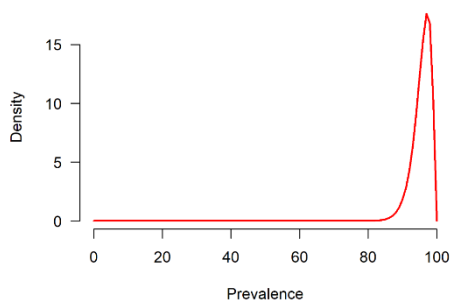
Kenya - 2004 - Nyanza - 0364



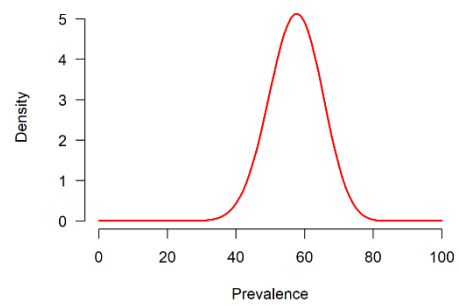
Kenya - 2004 - Nyanza - 0365



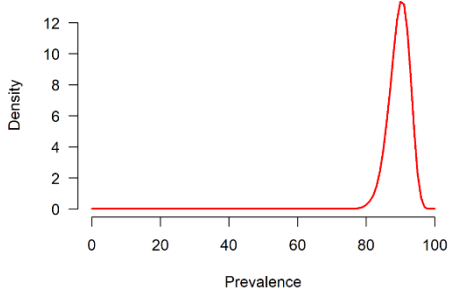
Kenya - 2004 - Nyanza - 0366



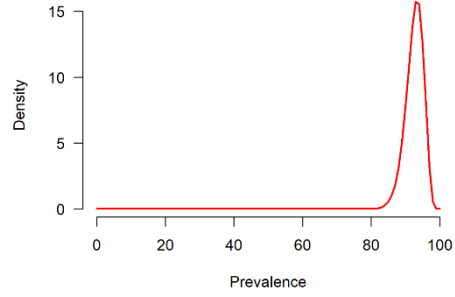
Kenya - 2005 - Nyanza - 0368



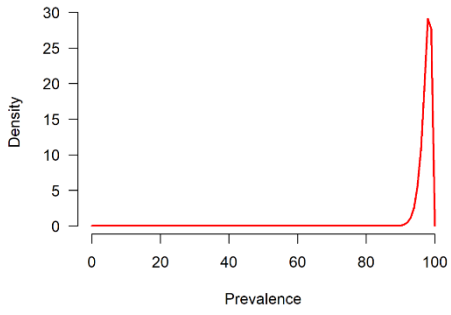
Kenya - 2005 - Nyanza - 0344



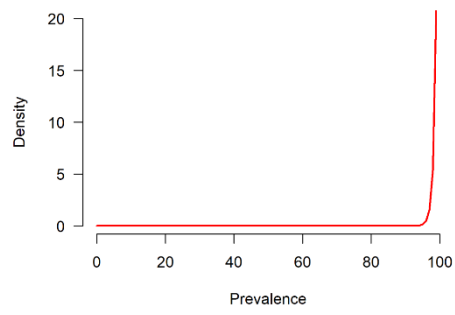
Kenya - 2005 - Nyanza - 0345



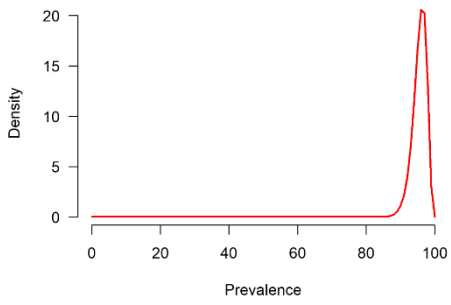
Kenya - 2005 - Nyanza - 0346



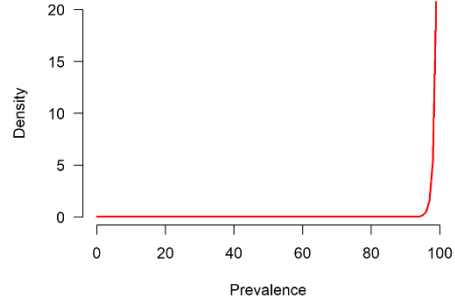
Kenya - 2005 - Nyanza - 0347



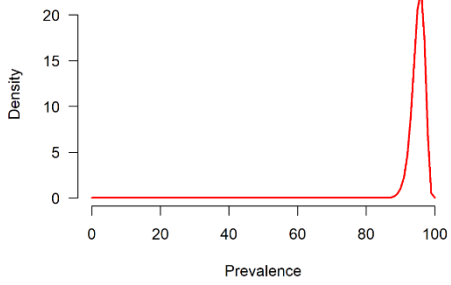
Kenya - 2005 - Western - 0348



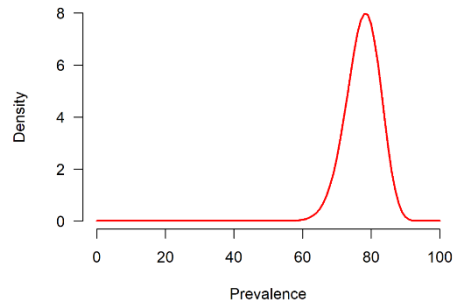
Kenya - 2005 - Western - 0349



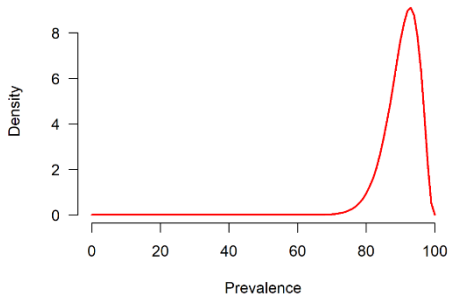
Kenya - 2006 - Nyanza - 0350



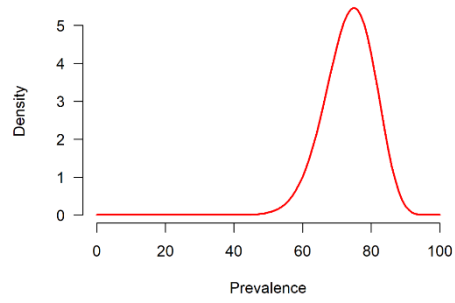
Kenya - 2006 - Western - 0351



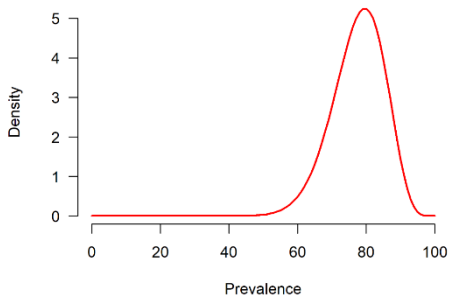
Kenya - 2006 - Western - 0352



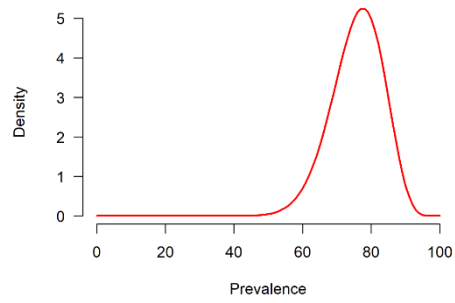
Kenya - 2006 - Western - 0353



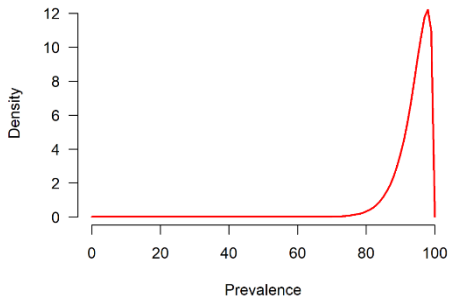
Kenya - 2006 - Western - 0354



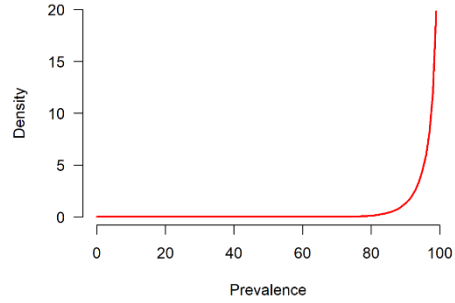
Kenya - 2007 - Coast - 0361



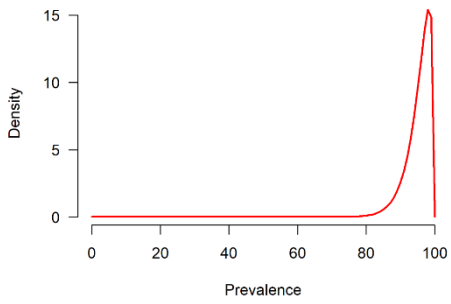
Kenya - 2007 - Nyanza - 0311



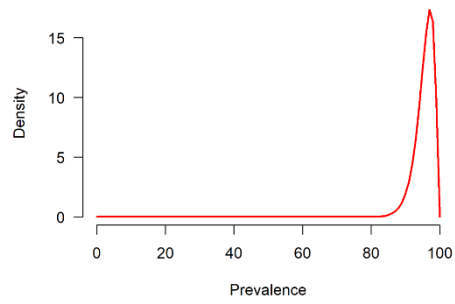
Kenya - 2007 - Western - 0312



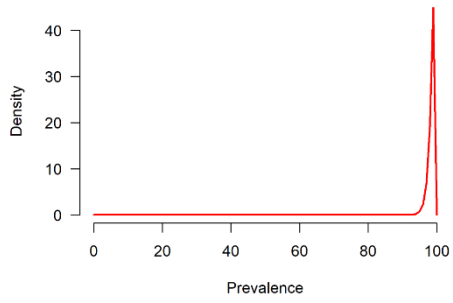
Kenya - 2007 - Western - 0313



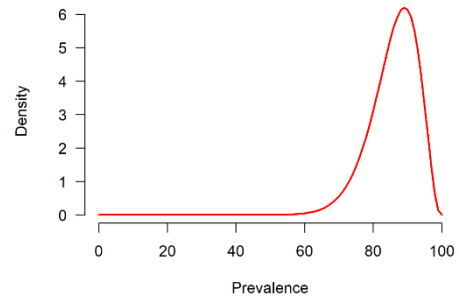
Kenya - 2008 - Nyanza - 0356



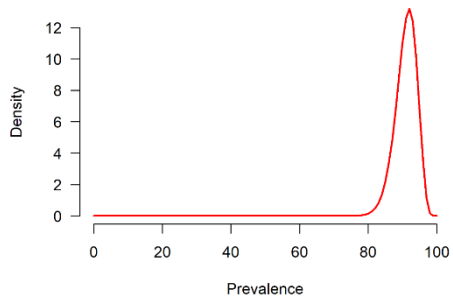
Kenya - 2008 - Nyanza - 0359



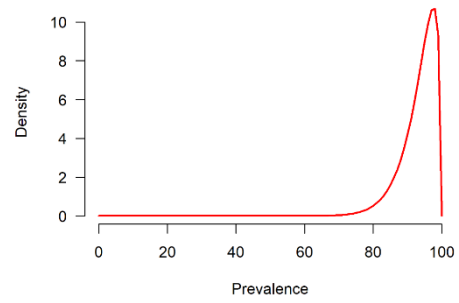
Kenya - 2008 - Nyanza - 0320



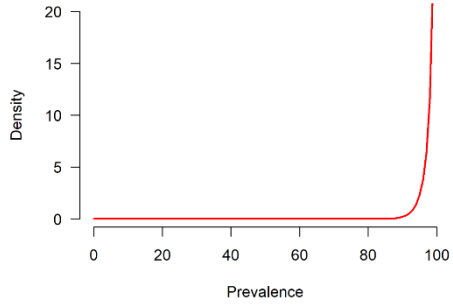
Kenya - 2008 - Nyanza - 0324



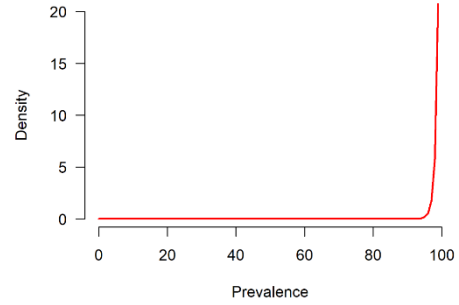
Kenya - 2008 - Rift Valley - 0327



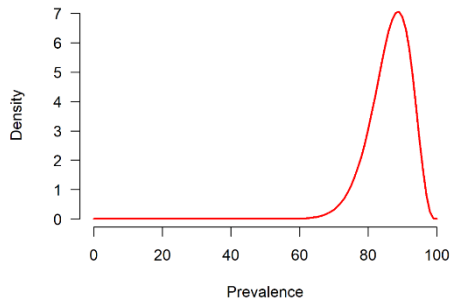
Kenya - 2009 - Nyanza - 0357



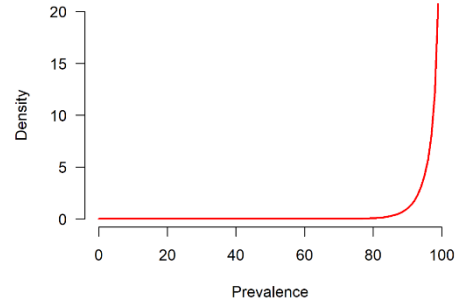
Kenya - 2009 - Nyanza - 0360

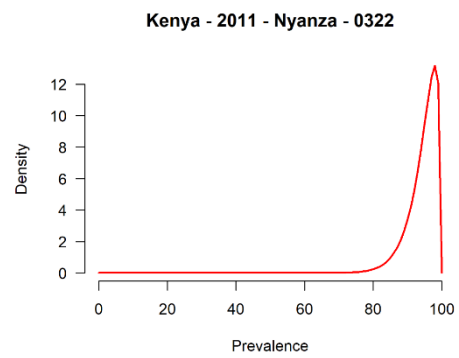
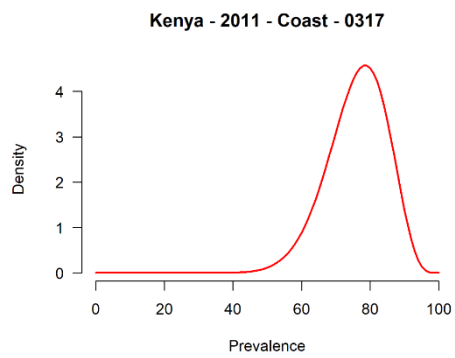
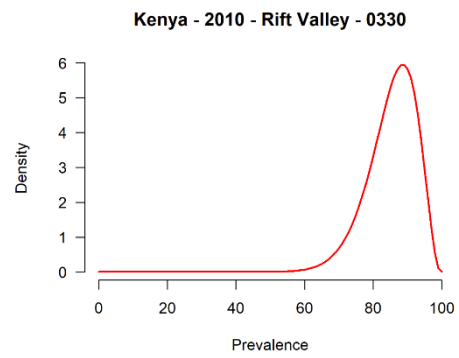
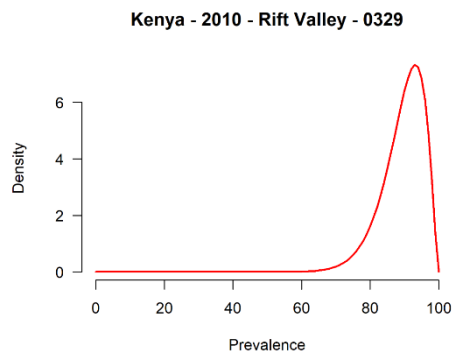
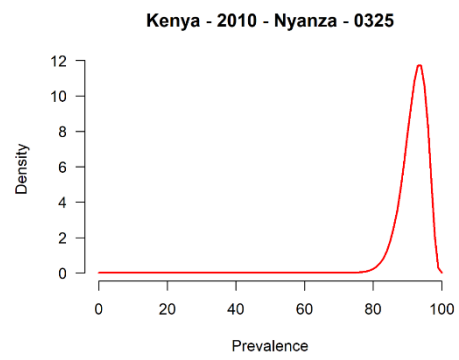
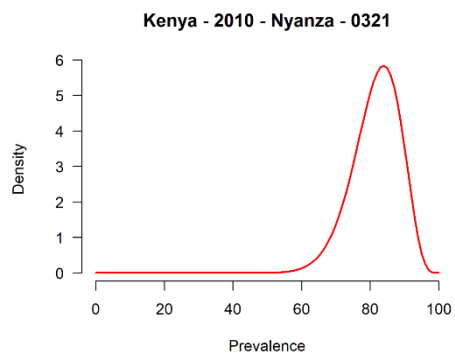
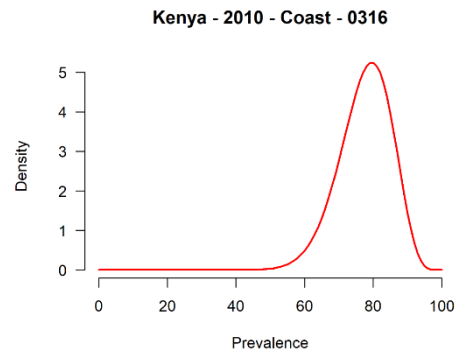
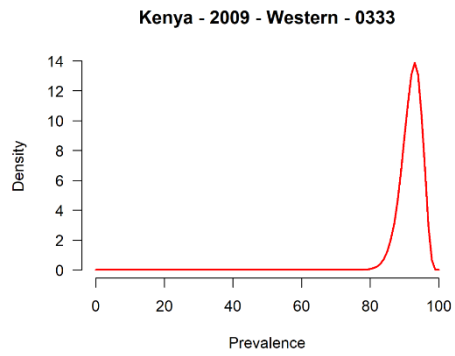


Kenya - 2009 - Nyanza - 0319

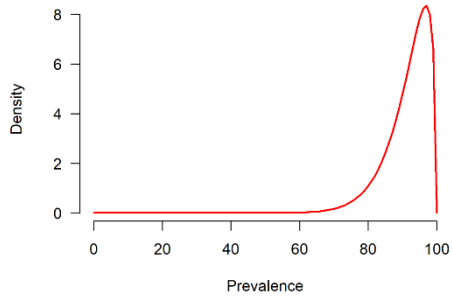


Kenya - 2009 - Rift Valley - 0328

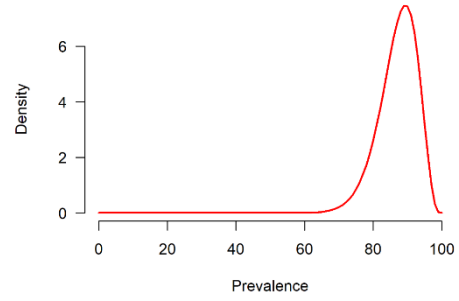




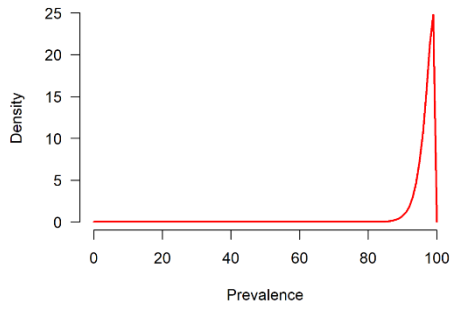
Kenya - 2011 - Rift Valley - 0331



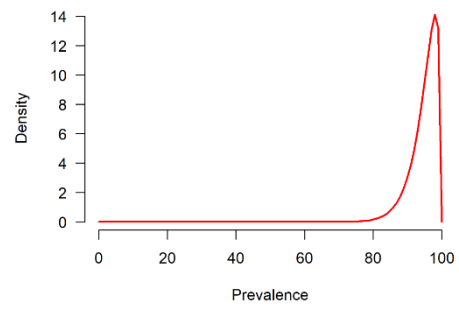
Kenya - 2011 - Western - 0334



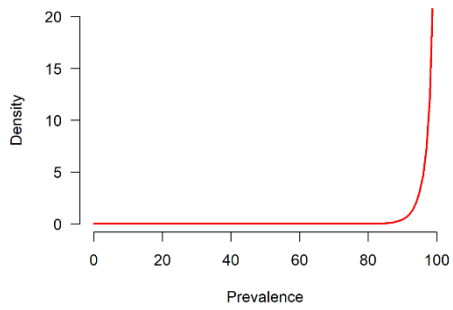
Kenya - 2012 - Coast - 0318



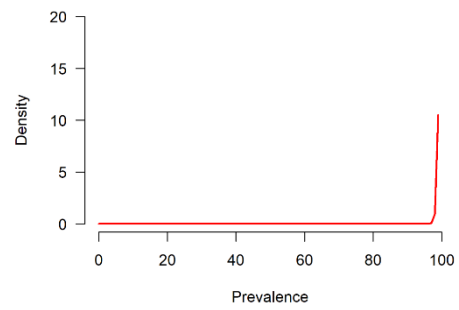
Kenya - 2012 - Nyanza - 0323



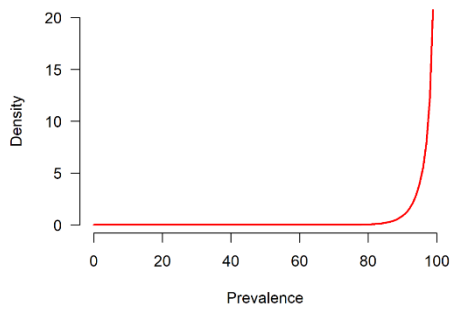
Kenya - 2012 - Nyanza - 0326



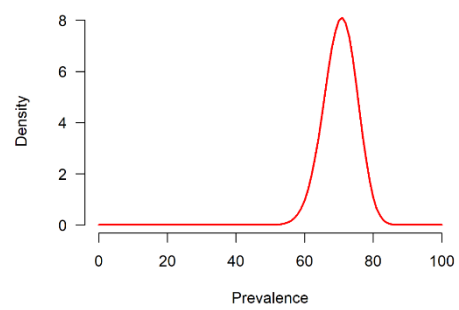
Kenya - 2012 - Nyanza - 0335

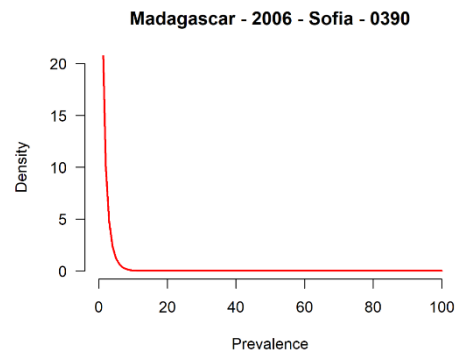
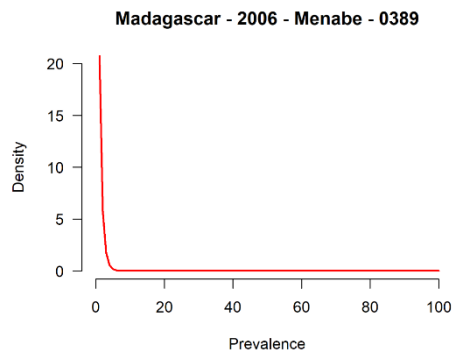
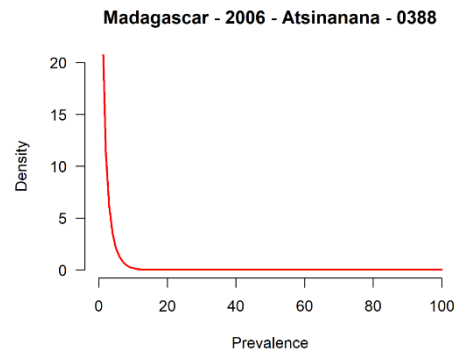
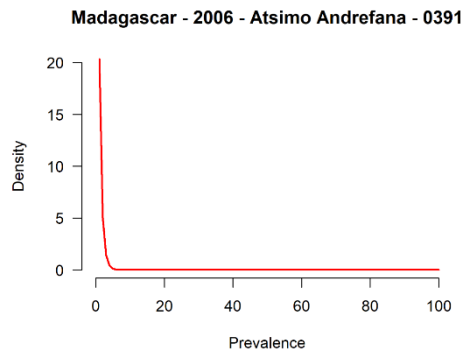
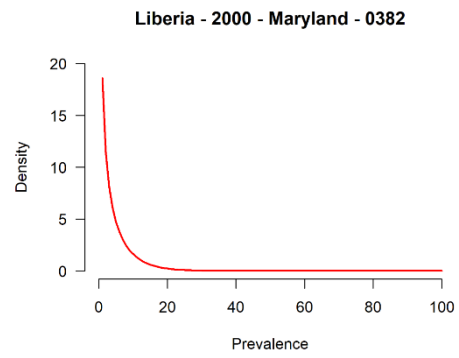
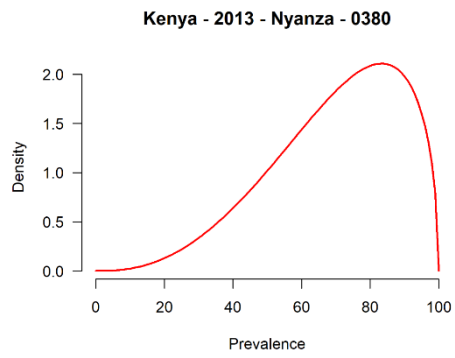
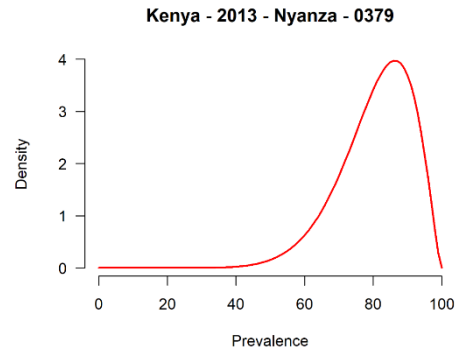
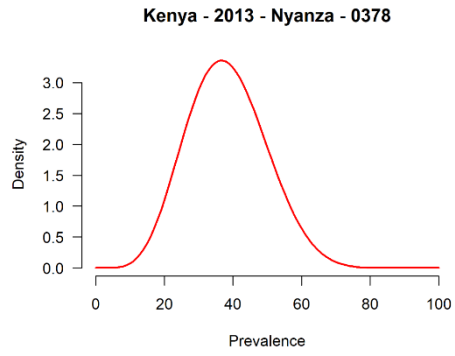


Kenya - 2012 - Rift Valley - 0332

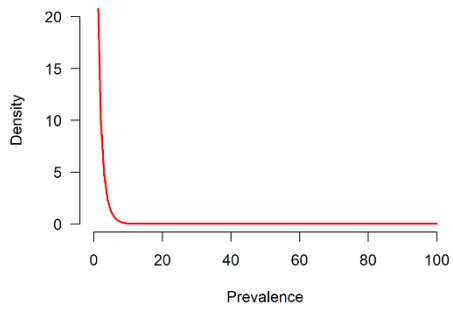


Kenya - 2013 - Nyanza - 0377

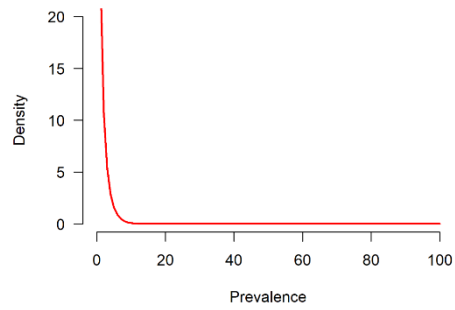




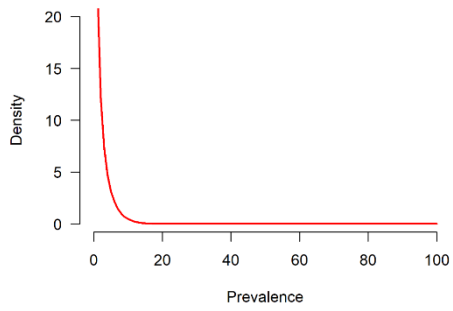
Madagascar - 2007 - Atsimo Andrefana - 0397



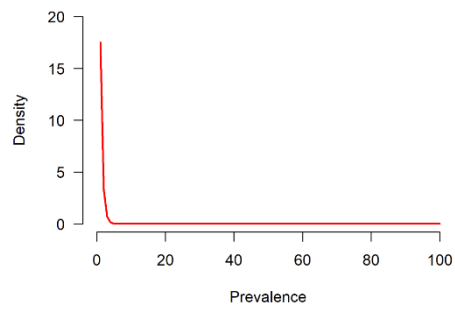
Madagascar - 2007 - Atsimo Atsinanana - 0396



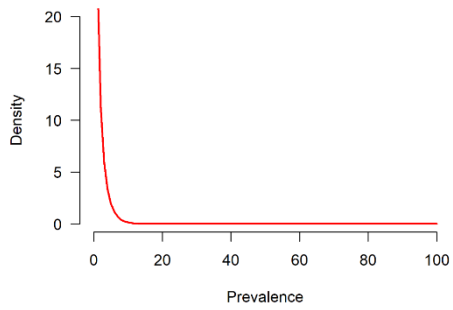
Madagascar - 2007 - Atsinanana - 0392



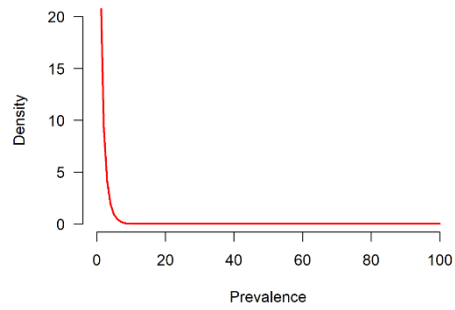
Madagascar - 2007 - Menabe - 0393



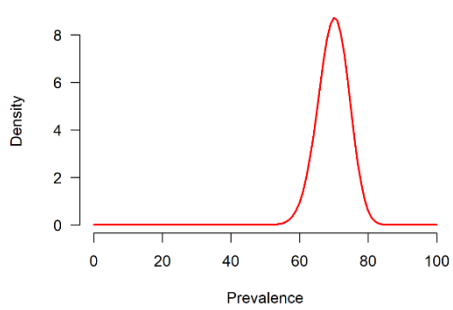
Madagascar - 2007 - Sava - 0394



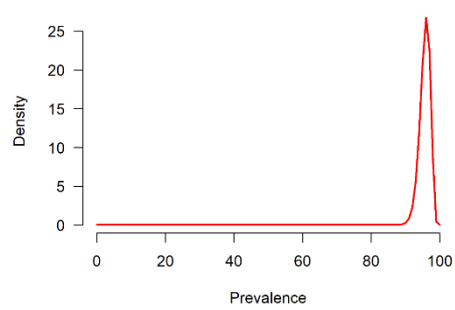
Madagascar - 2007 - Sofia - 0395



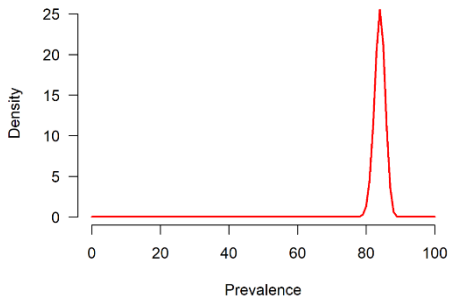
Malawi - 1999 - Southern Region - 0411



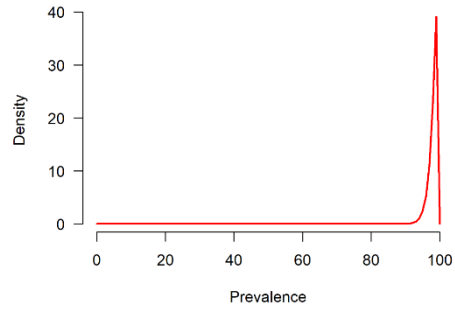
Malawi - 2000 - Central Region - 0415



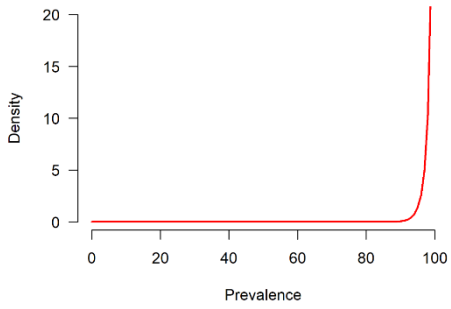
Malawi - 2001 - Southern Region - 0412



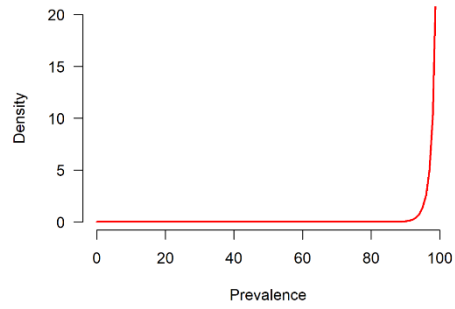
Malawi - 2003 - Southern Region - 0416



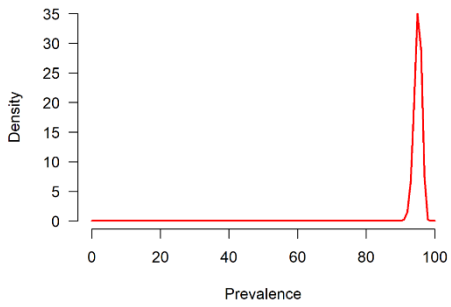
Malawi - 2005 - Central Region - 0419



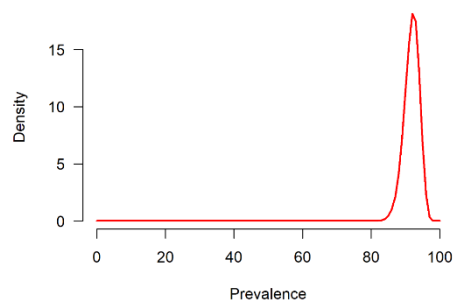
Malawi - 2005 - Northern Region - 0420



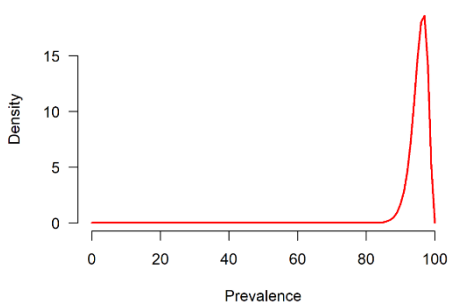
Malawi - 2005 - Southern Region - 0423



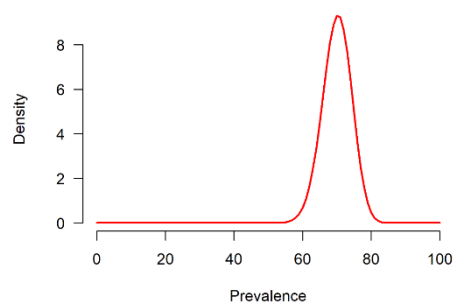
Malawi - 2005 - Southern Region - 0424



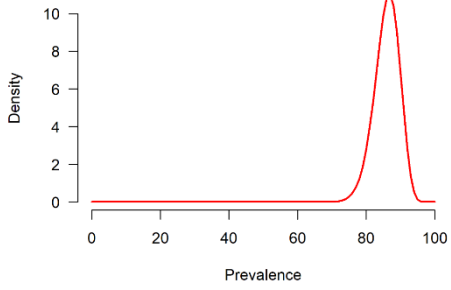
Malawi - 2005 - Southern Region - 0418



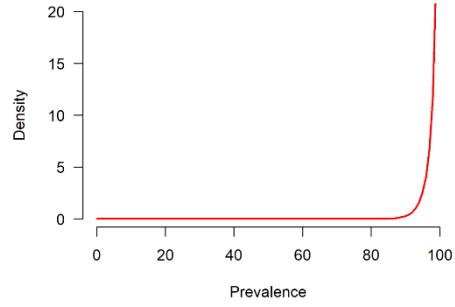
Malawi - 2005 - Southern Region - 0417



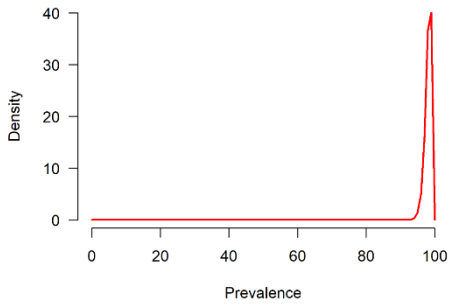
Malawi - 2006 - Southern Region - 0407



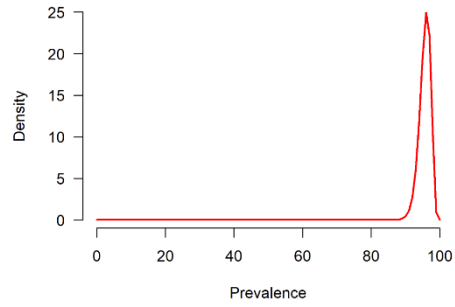
Malawi - 2006 - Southern Region - 0408



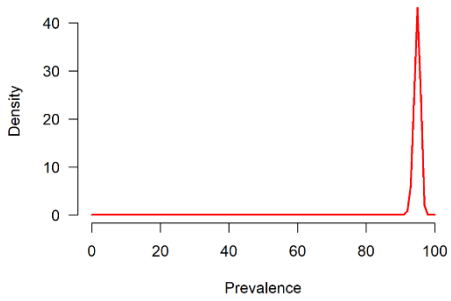
Malawi - 2007 - Northern Region - 0421



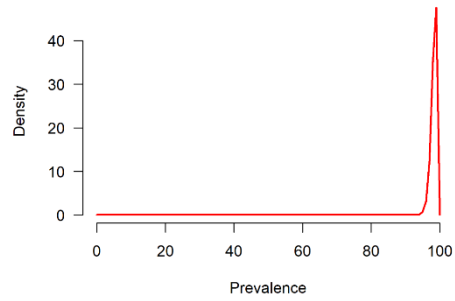
Malawi - 2007 - Southern Region - 0422



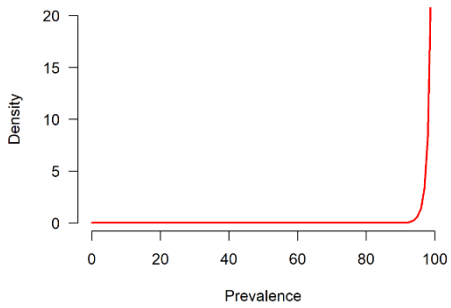
Malawi - 2009 - Southern Region - 0413



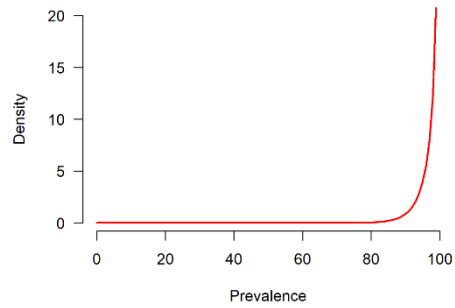
Malawi - 2011 - Southern Region - 0409



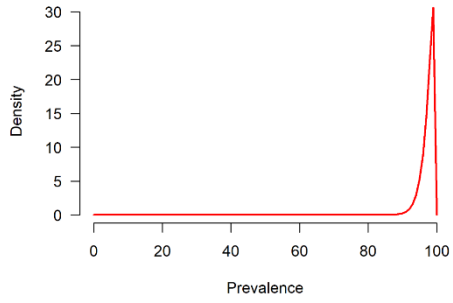
Malawi - 2011 - Southern Region - 0425



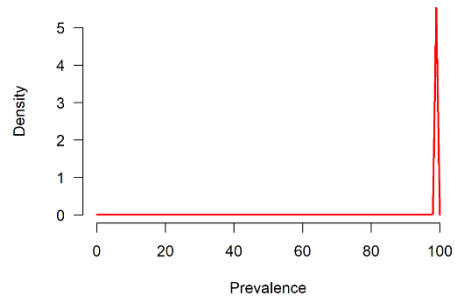
Malawi - 2011 - Southern Region - 0402



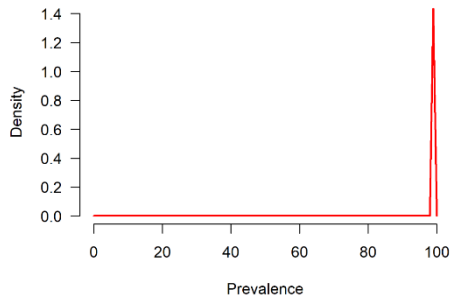
Malawi - 2011 - Southern Region - 0403



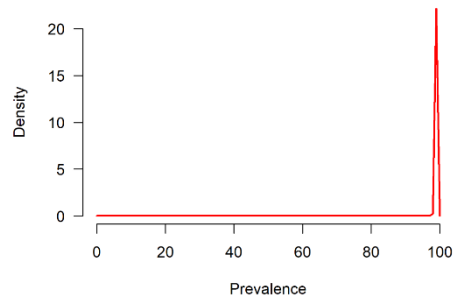
Malawi - 2012 - Southern Region - 0399



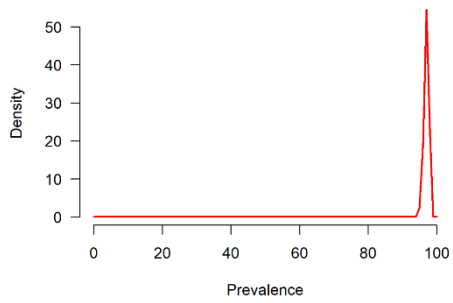
Malawi - 2012 - Southern Region - 0400



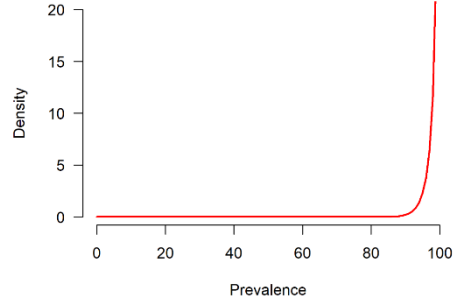
Malawi - 2012 - Southern Region - 0401



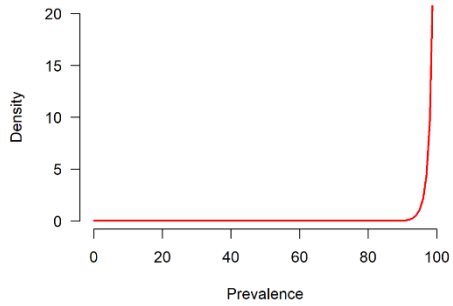
Malawi - 2012 - Southern Region - 0414



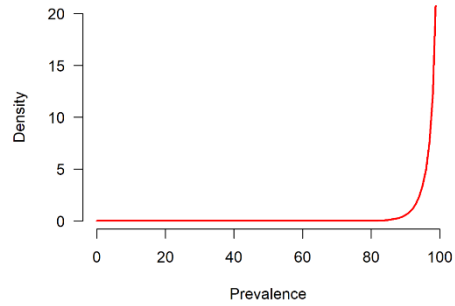
Malawi - 2012 - Southern Region - 0404

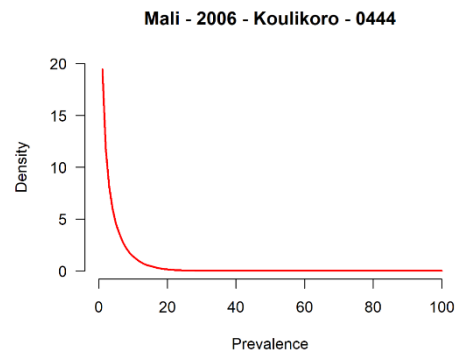
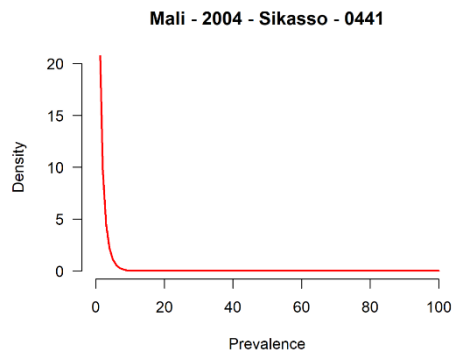
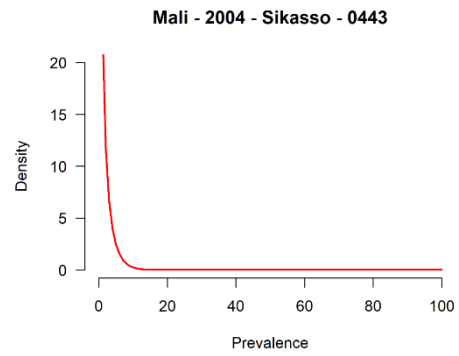
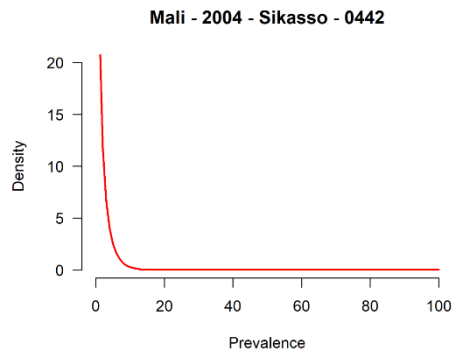
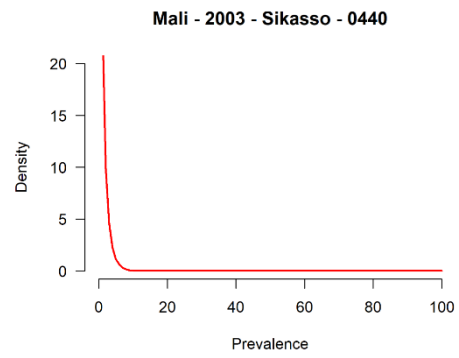
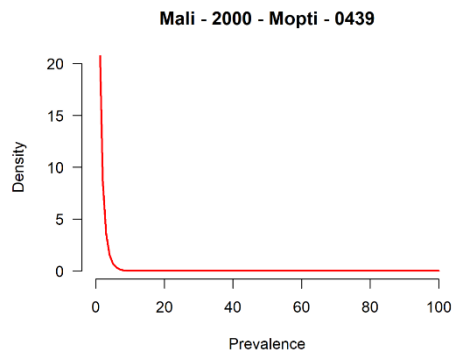
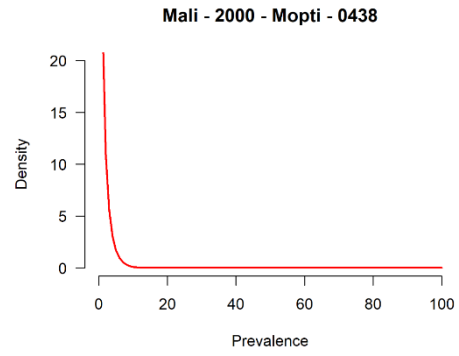
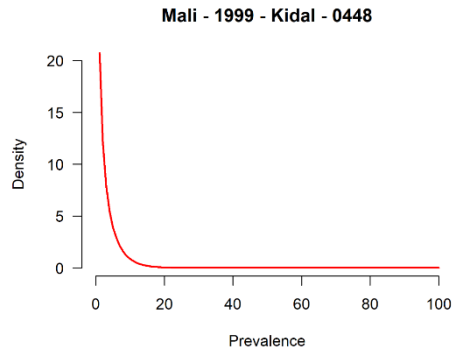


Malawi - 2012 - Southern Region - 0405

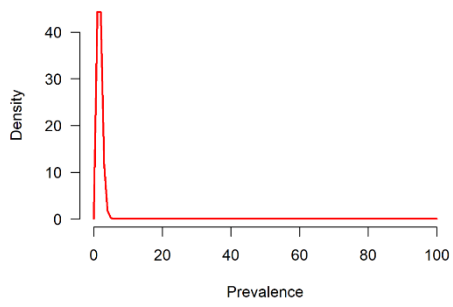


Malawi - 2012 - Southern Region - 0406

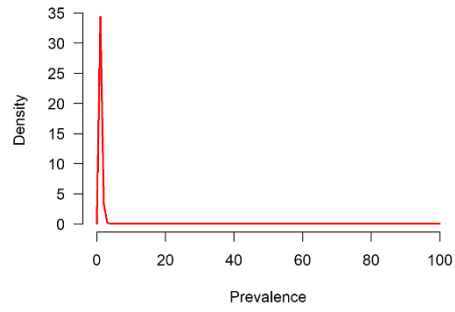




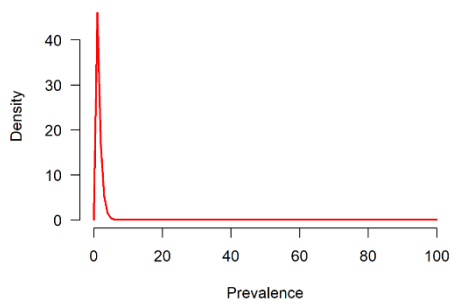
Mali - 2007 - Koulikoro - 0449



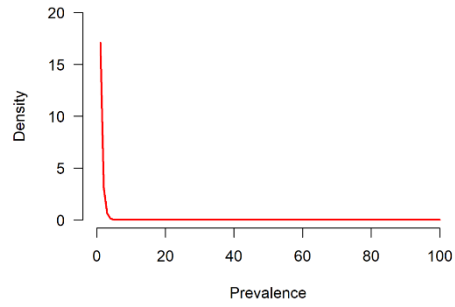
Mali - 2007 - Koulikoro - 0450



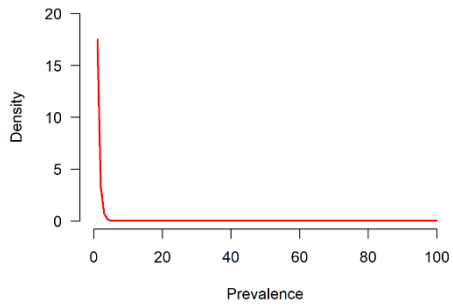
Mali - 2010 - Kayes - 0452



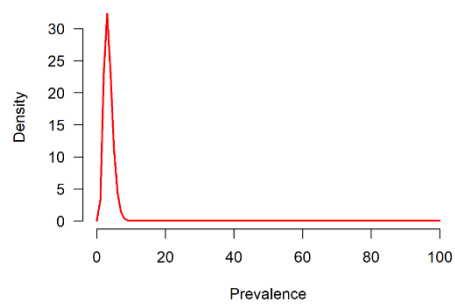
Mali - 2010 - Segou - 0451



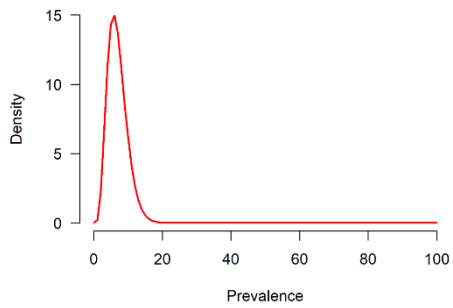
Mali - 2010 - Segou - 0435



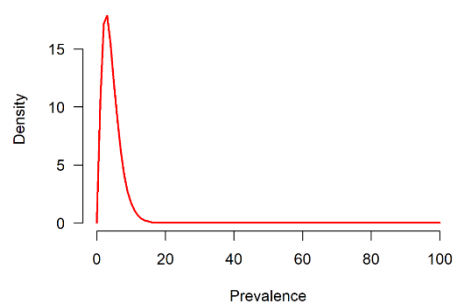
Mali - 2012 - Sikasso - 0434



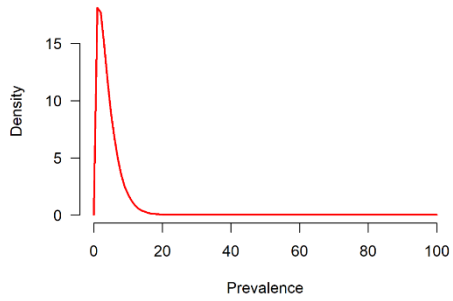
Mali - 2014 - Kayes - 0428



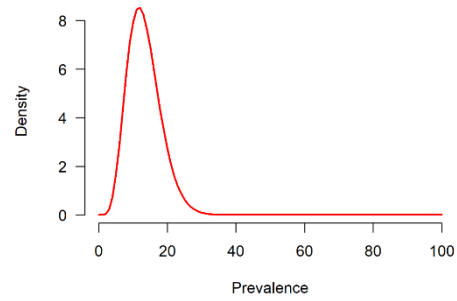
Mali - 2014 - Kayes - 0429



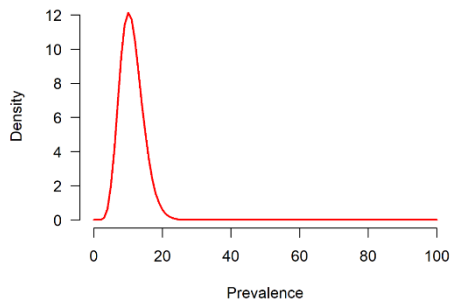
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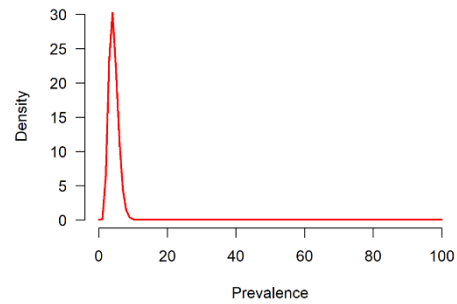
Mali - 2014 - Kayes - 0431



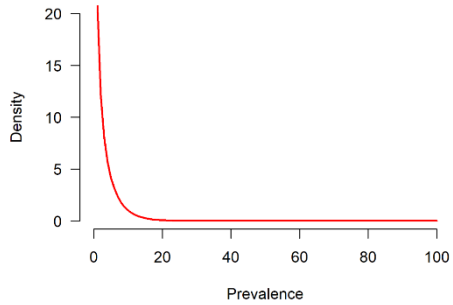
Mali - 2014 - Sikasso - 0432



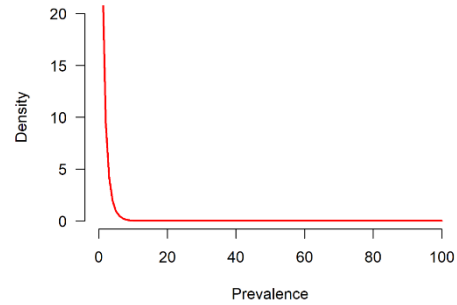
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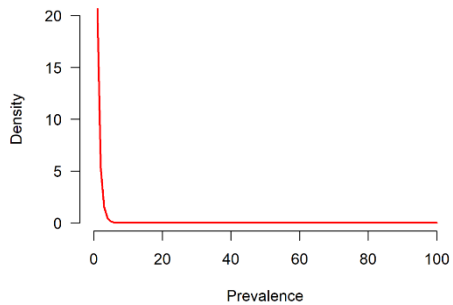
Mali - 2016 - Bamako - 0427



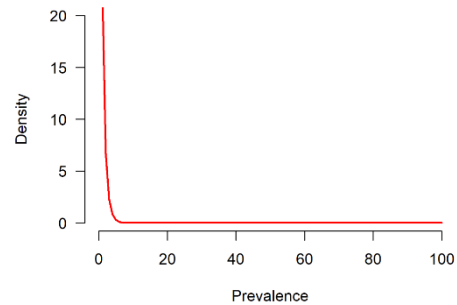
Mauritania - 1998 - Hodh el Gharbi - 0457



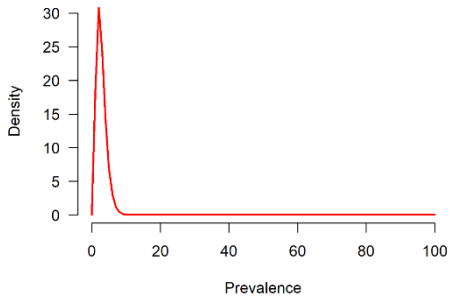
Mauritania - 1998 - Hodh el Gharbi - 0458



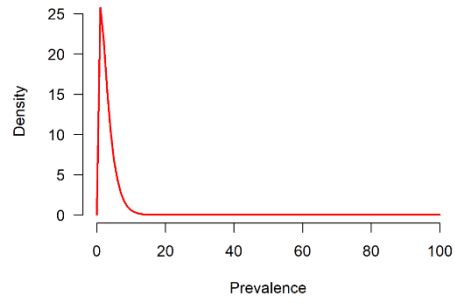
Mauritania - 2010 - Hodh el Gharbi - 0454



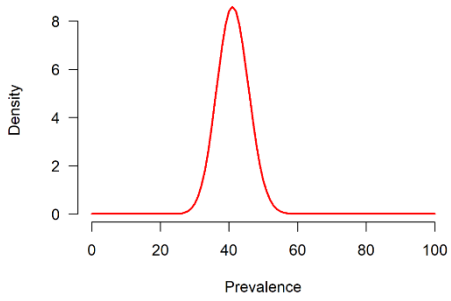
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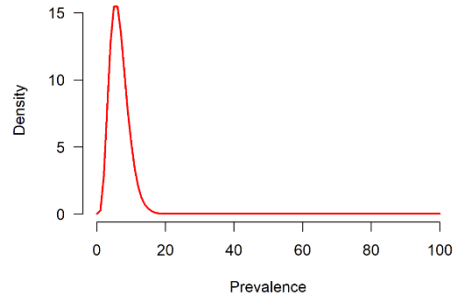
Mauritania - 2010 - Hodh el Gharbi - 0456



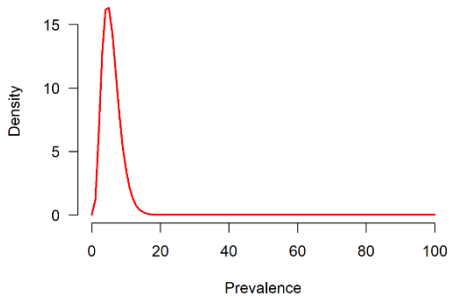
Mozambique - 1999 - Maputo - 0033



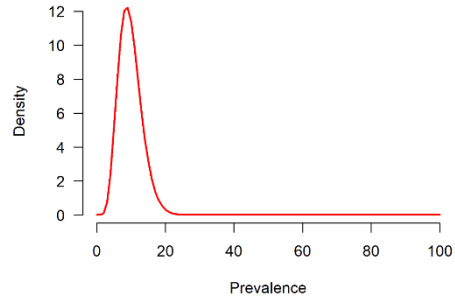
Mozambique - 1999 - Maputo - 0021



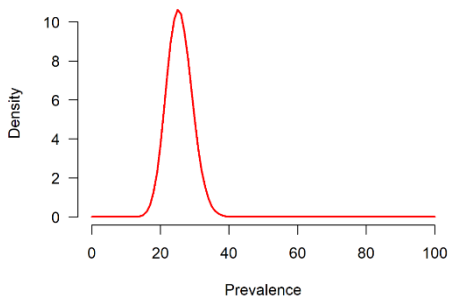
Mozambique - 1999 - Maputo - 0022



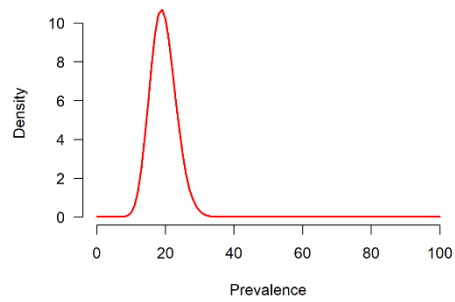
Mozambique - 1999 - Maputo - 0023



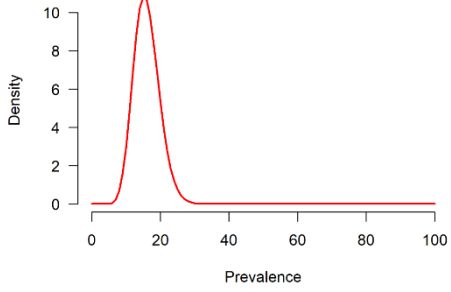
Mozambique - 2001 - Maputo - 0039



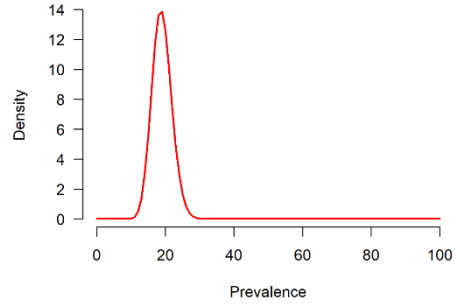
Mozambique - 2001 - Maputo - 0040



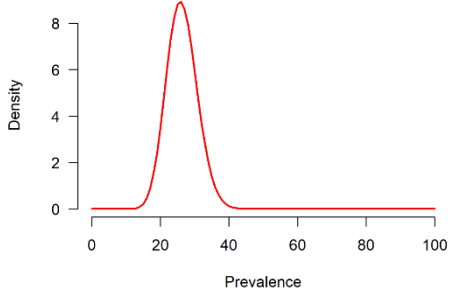
Mozambique - 2001 - Maputo - 0041



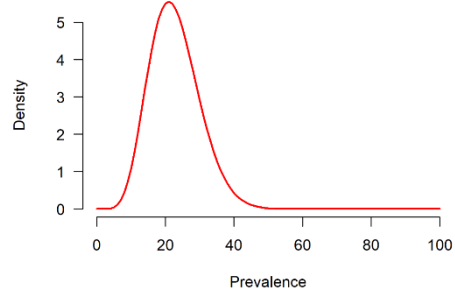
Mozambique - 2001 - Maputo - 0024



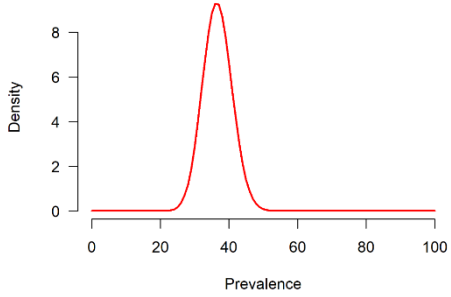
Mozambique - 2001 - Maputo - 0025



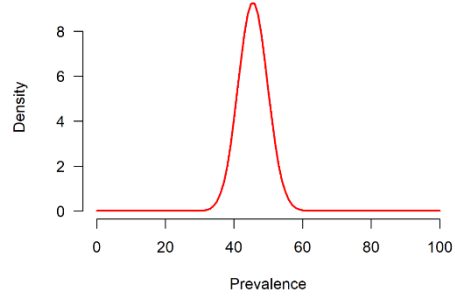
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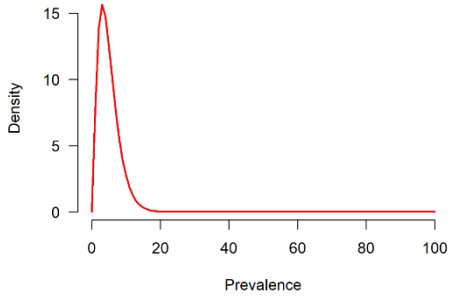
Mozambique - 2002 - Maputo - 0038



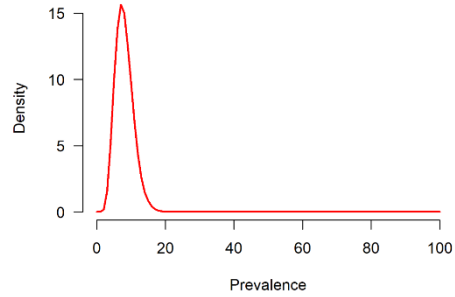
Mozambique - 2003 - Maputo - 0037



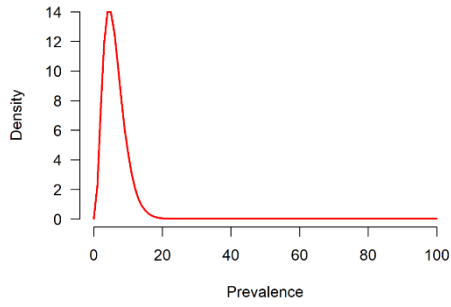
Mozambique - 2003 - Maputo - 0027



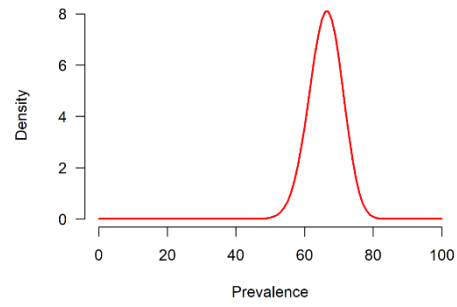
Mozambique - 2003 - Maputo - 0028



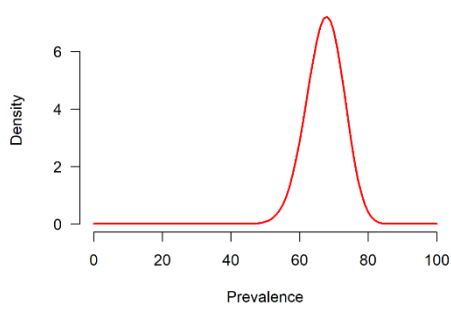
Mozambique - 2003 - Maputo - 0029



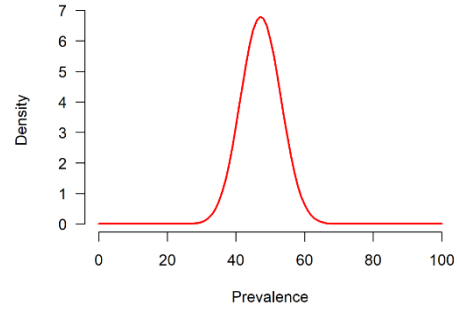
Mozambique - 2004 - Maputo city - 0034



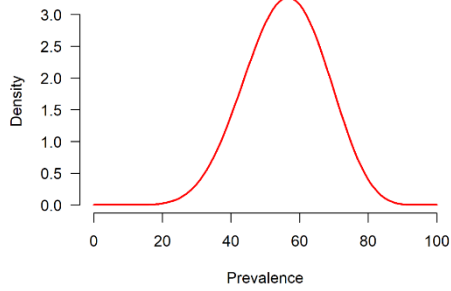
Mozambique - 2004 - Maputo city - 0035



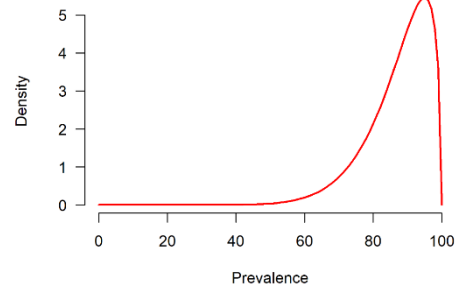
Mozambique - 2004 - Maputo city - 0036



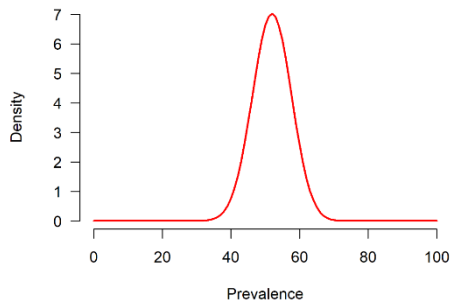
Mozambique - 2004 - Maputo - 0013



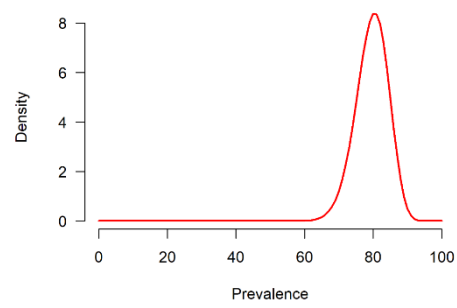
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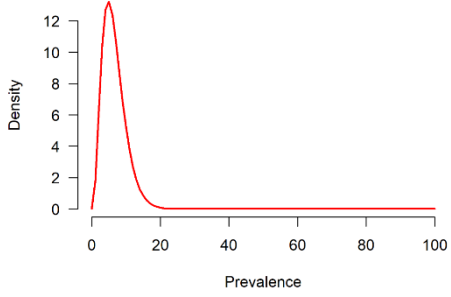
Mozambique - 2004 - Maputo - 0015



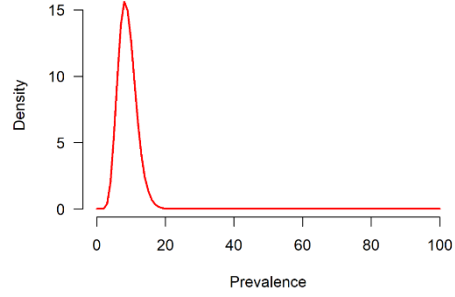
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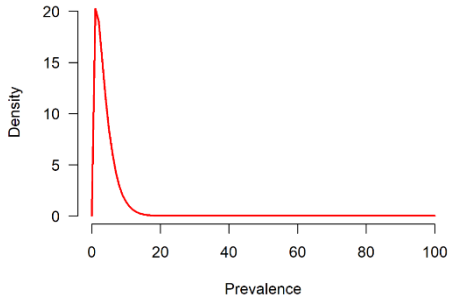
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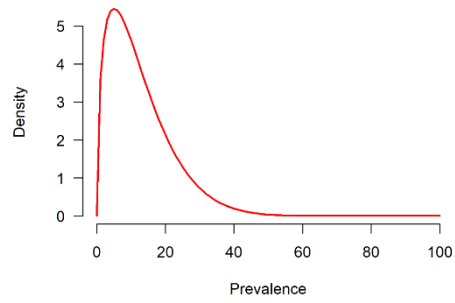
Mozambique - 2004 - Maputo - 0031



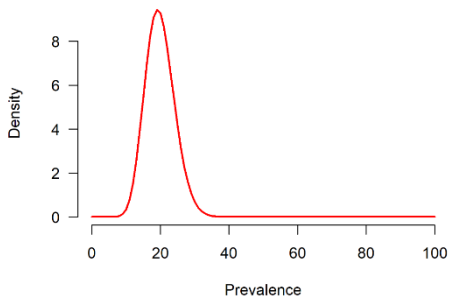
Mozambique - 2004 - Maputo - 0032



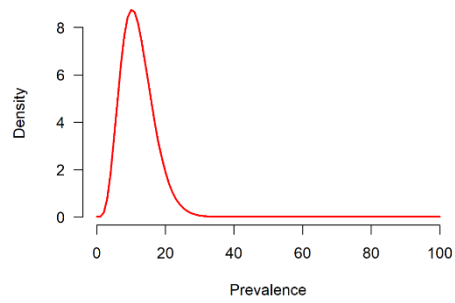
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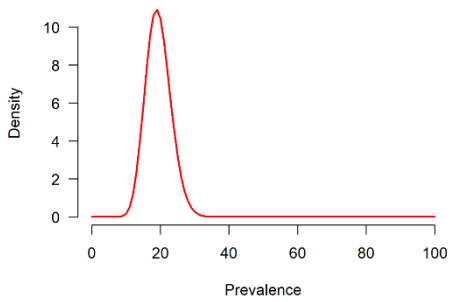
Mozambique - 2004 - Maputo - 0050



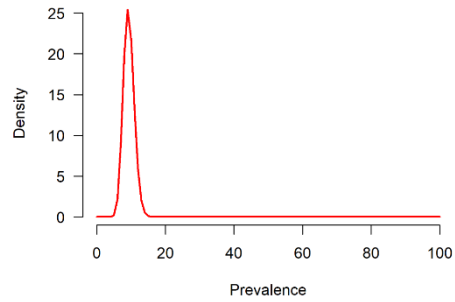
Mozambique - 2004 - Maputo - 0051



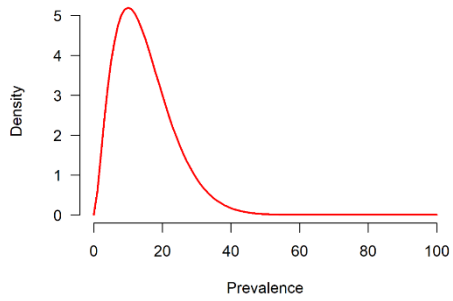
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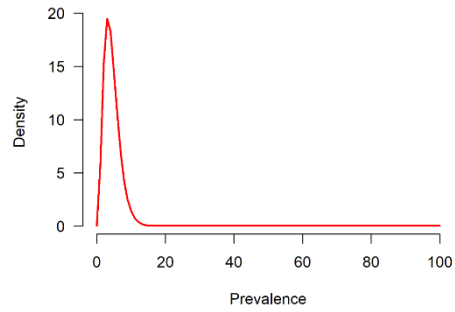
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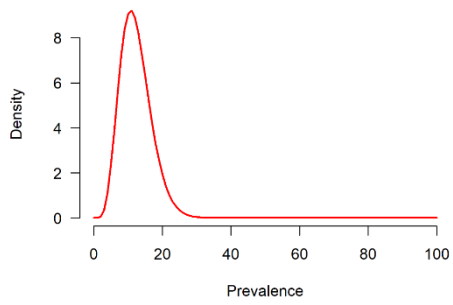
Mozambique - 2004 - Maputo - 0066



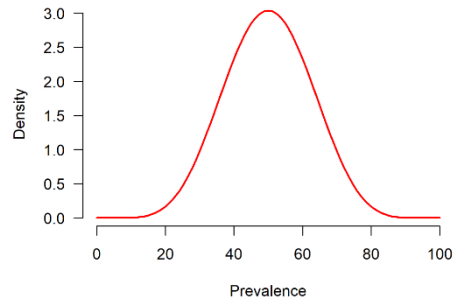
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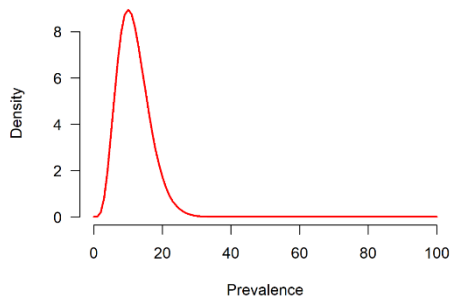
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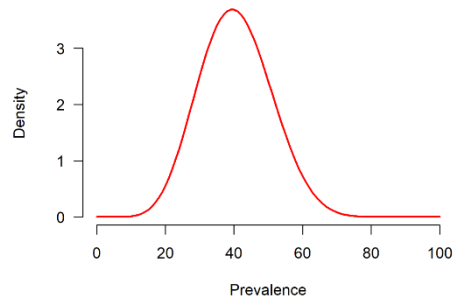
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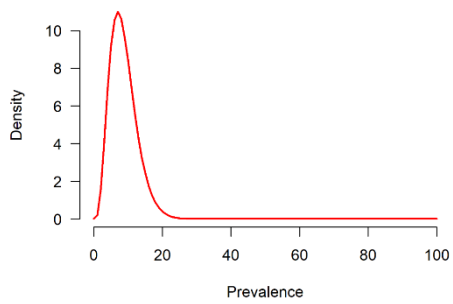
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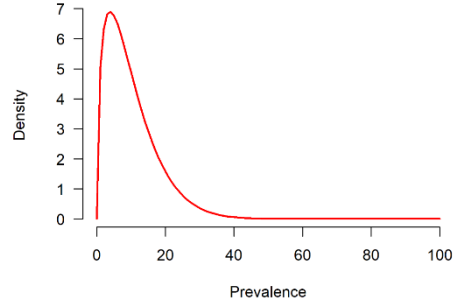
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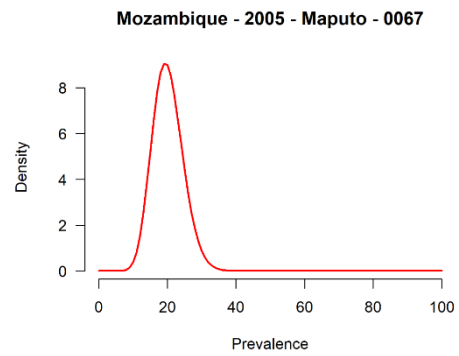
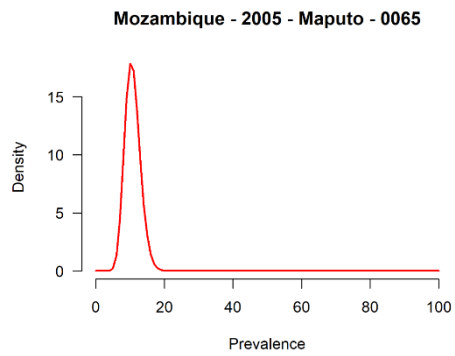
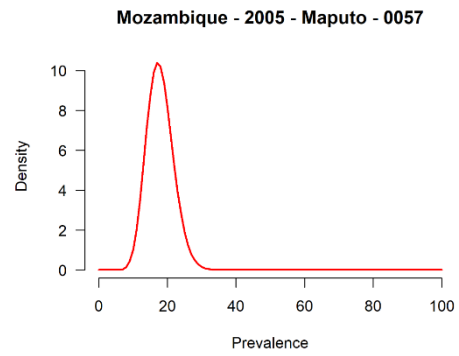
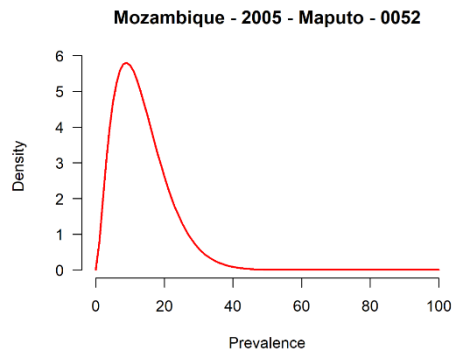
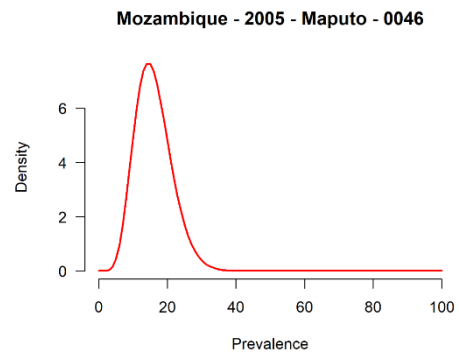
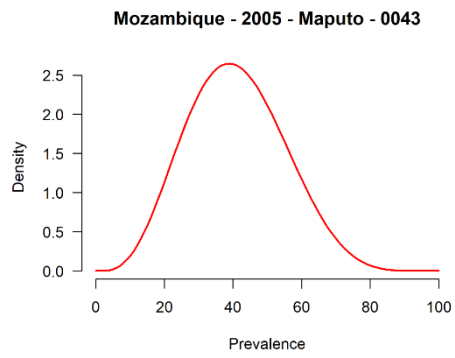
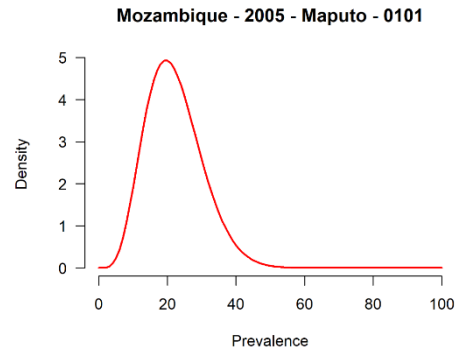
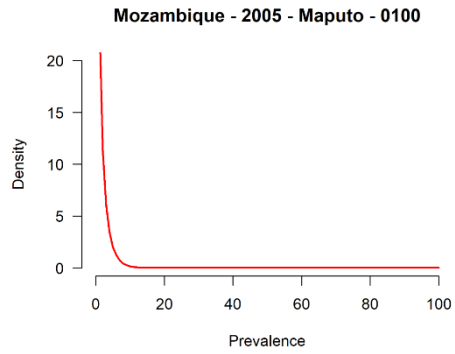


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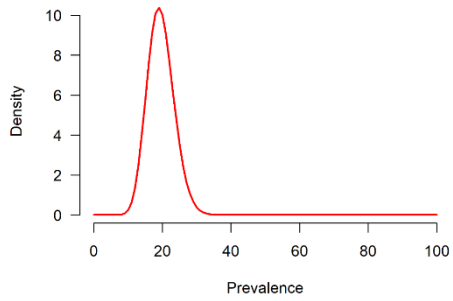


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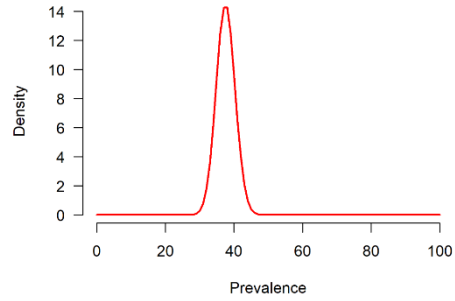




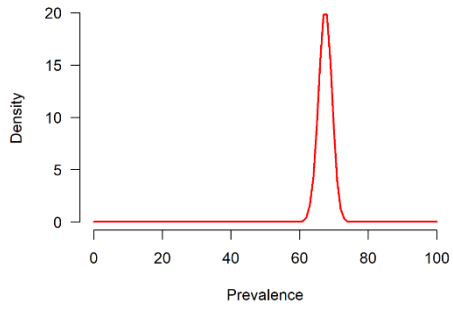
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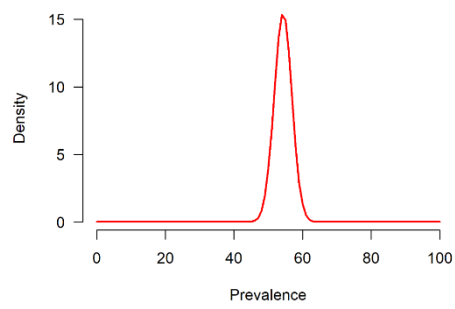
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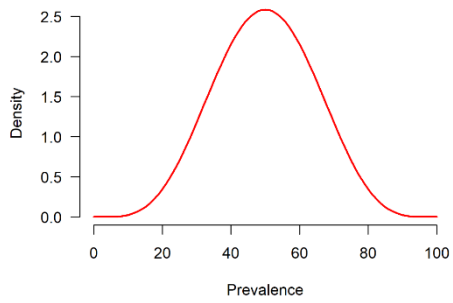
Mozambique - 2006 - Gaza - 0077



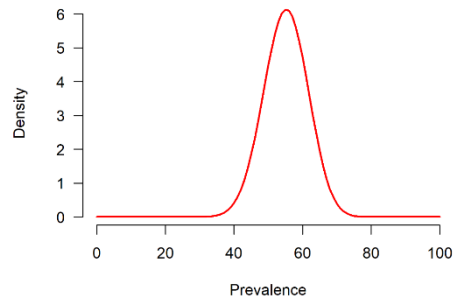
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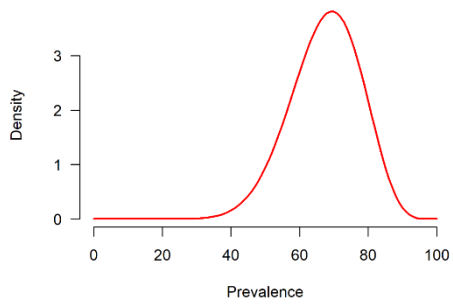
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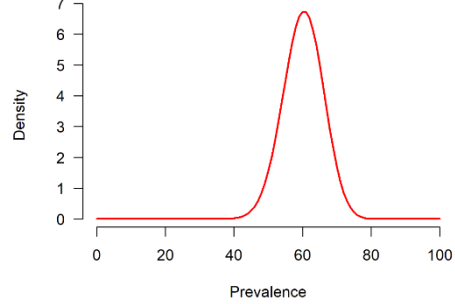
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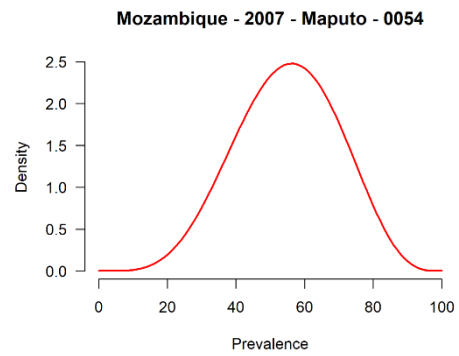
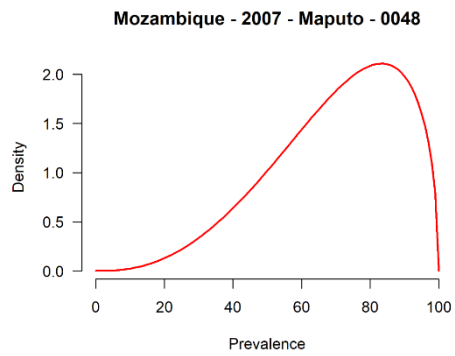
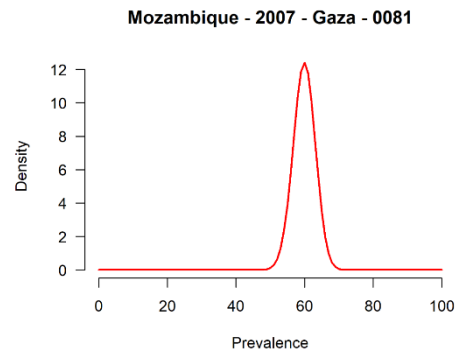
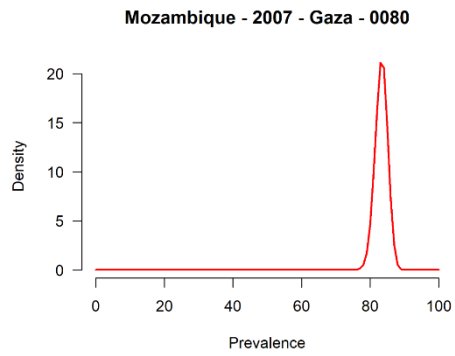
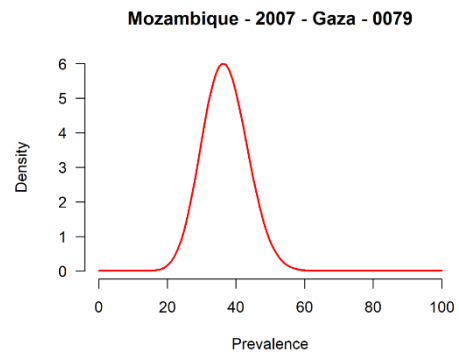
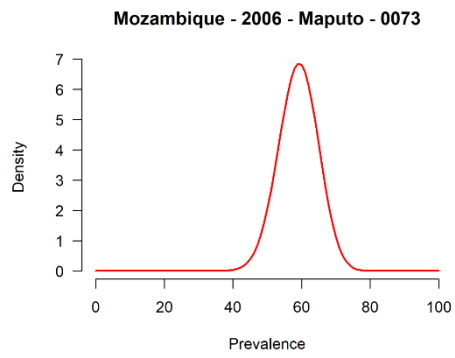
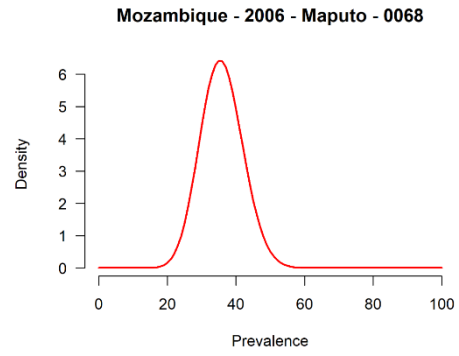
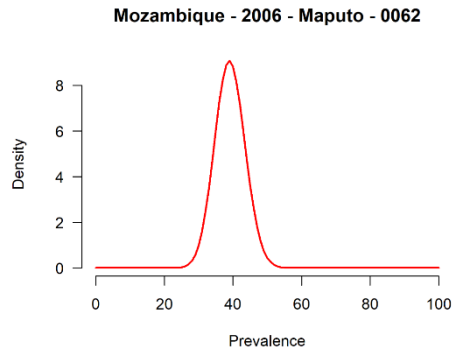


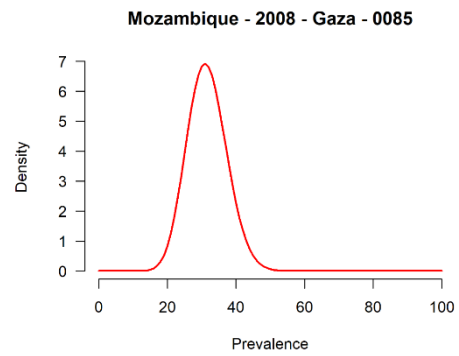
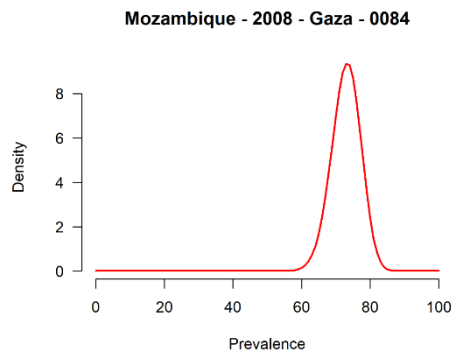
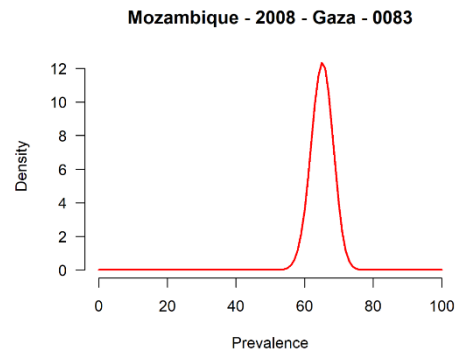
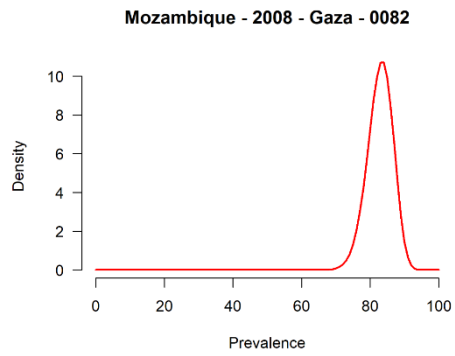
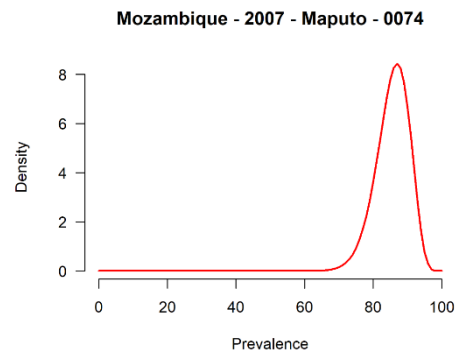
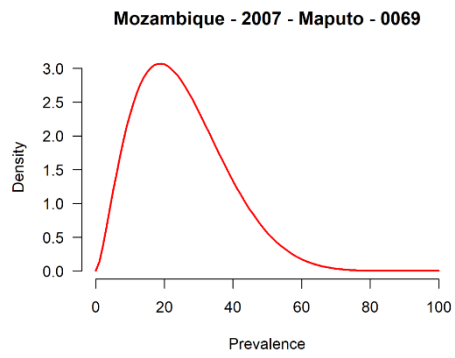
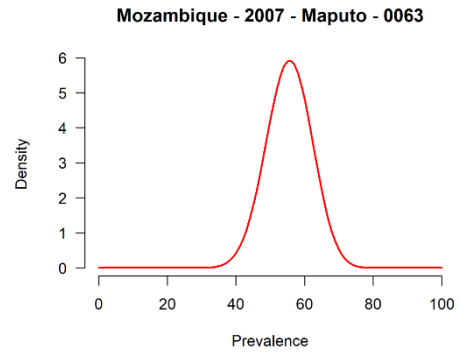
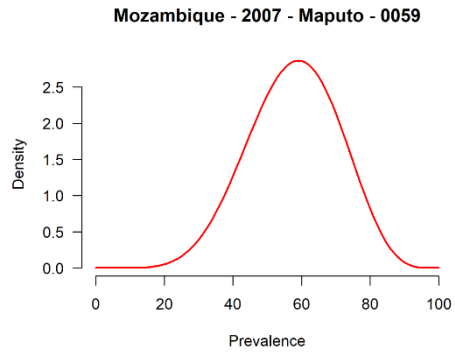
Mozambique - 2006 - Maputo - 0053

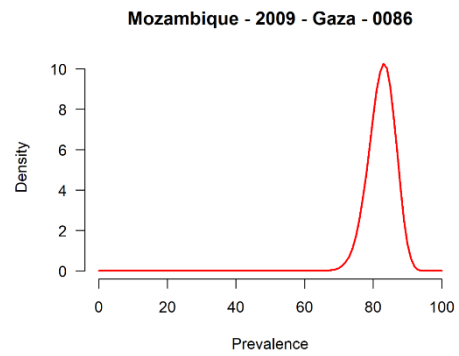
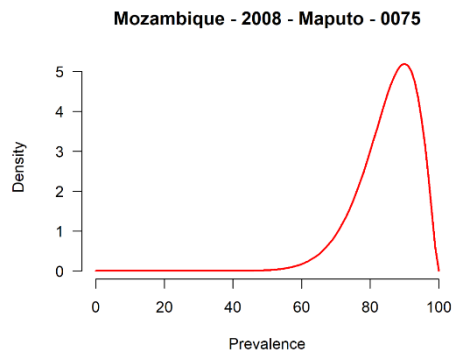
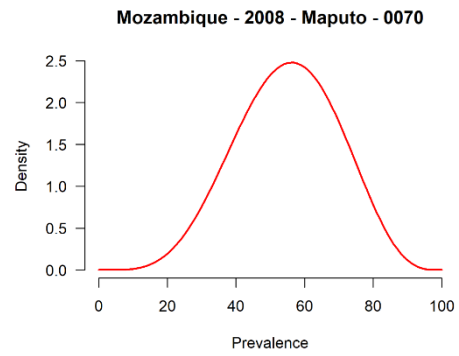
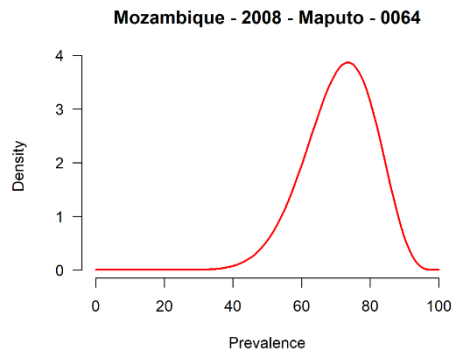
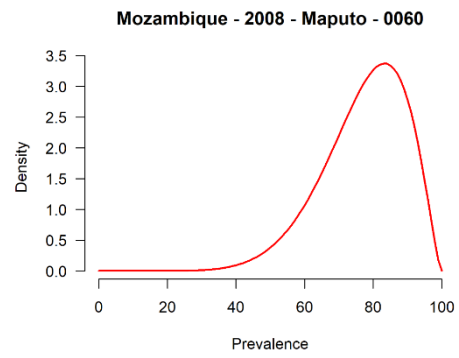
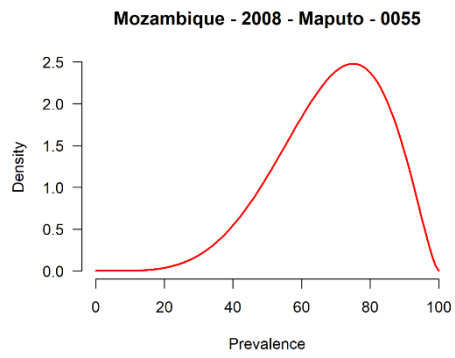
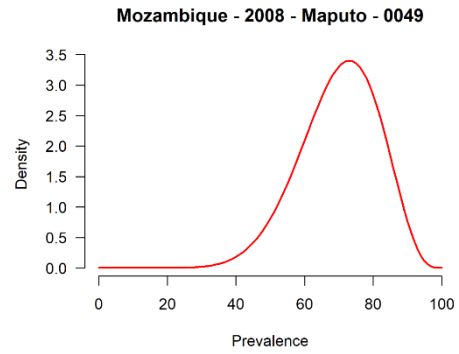
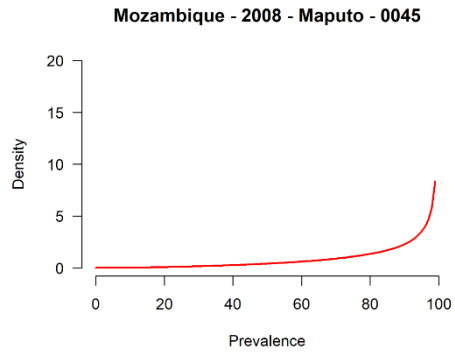


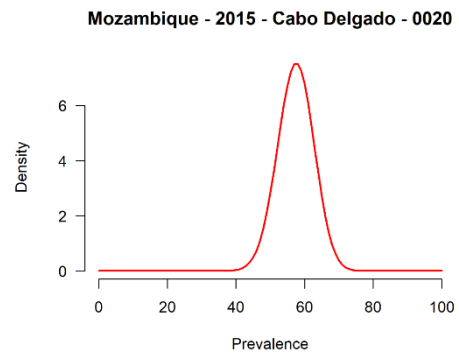
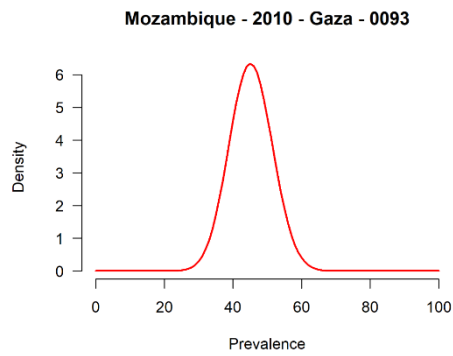
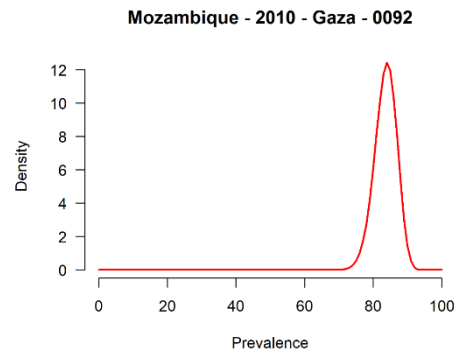
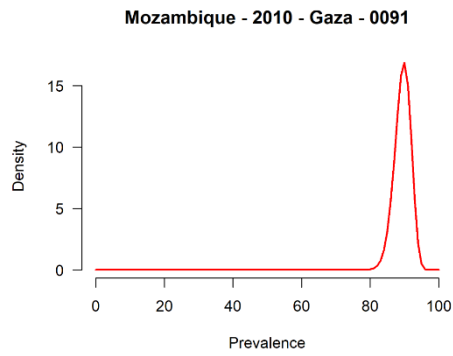
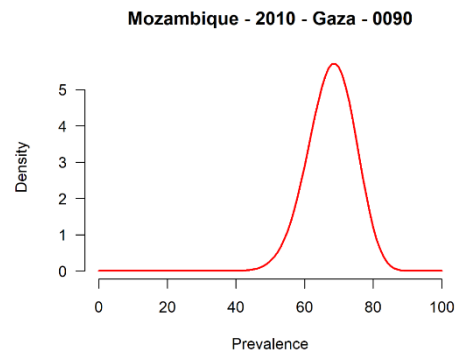
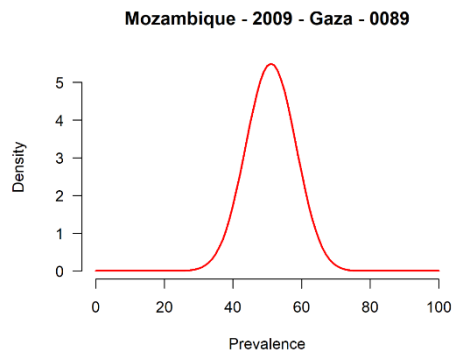
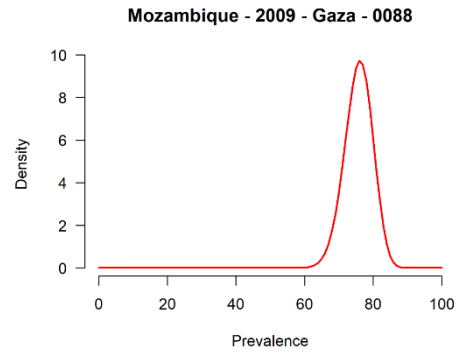
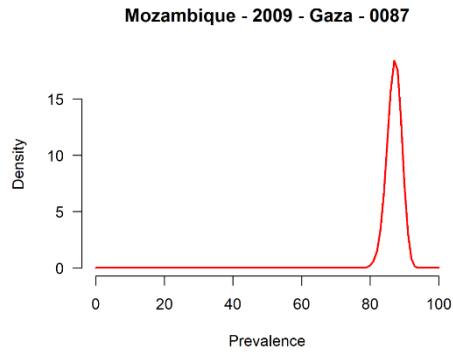
Mozambique - 2006 - Maputo - 0058

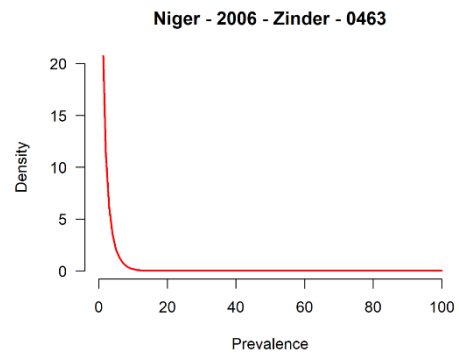
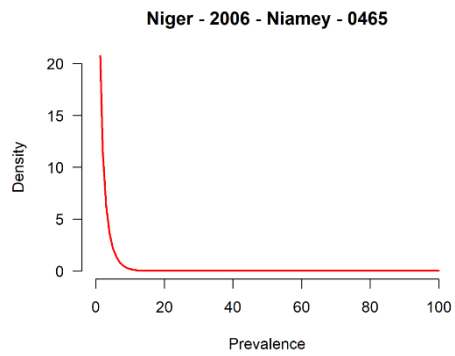
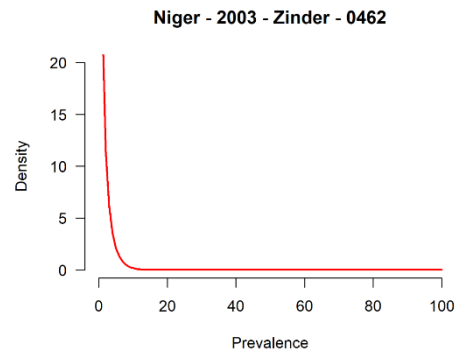
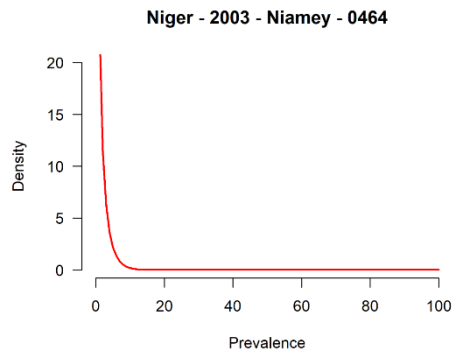
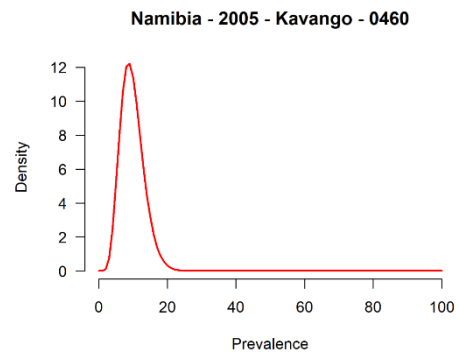
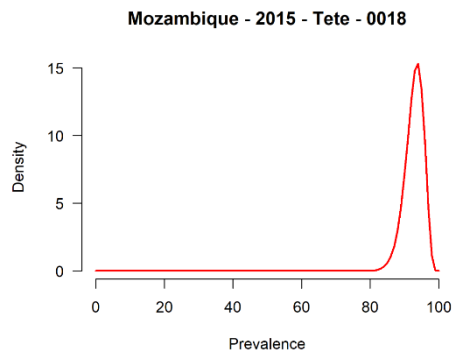
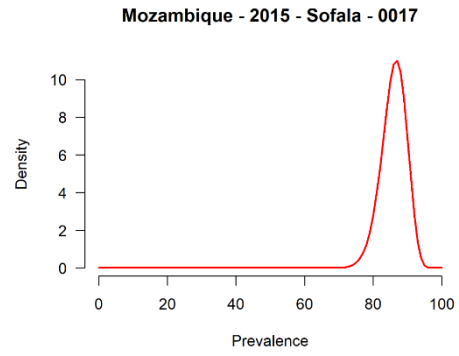
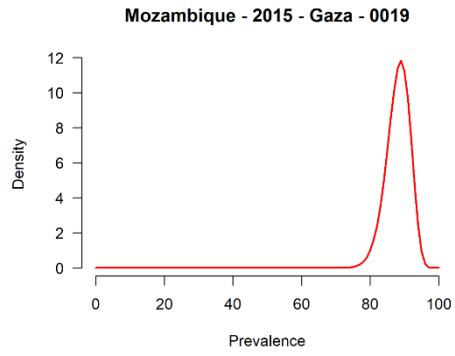




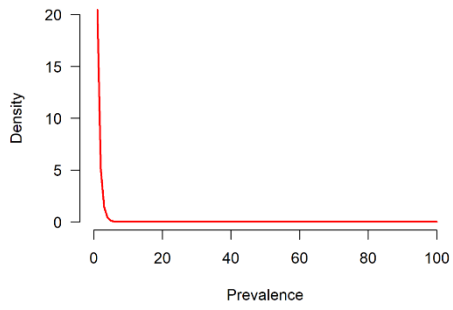




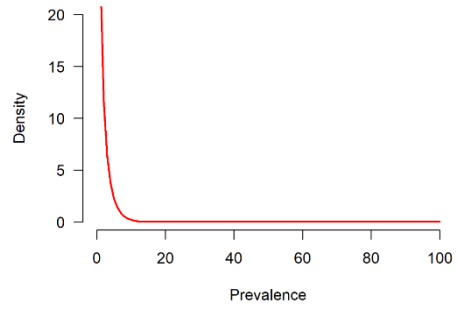




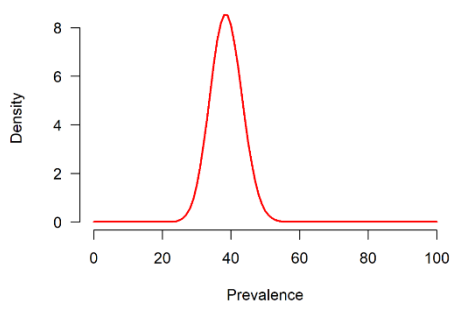
Niger - 2012 - Maradi - 0466



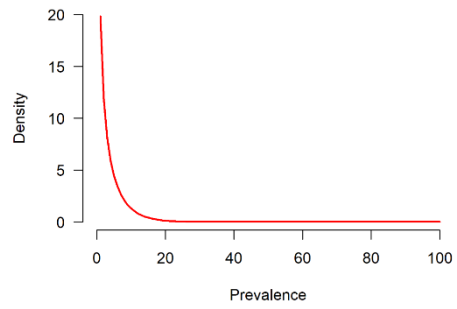
Nigeria - 2003 - Oyo - 0468



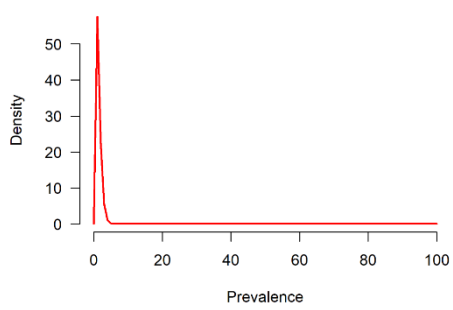
Nigeria - 2004 - Oyo - 0476



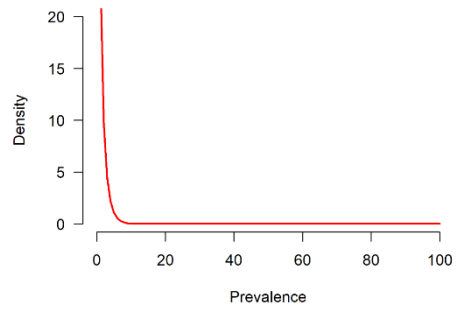
Nigeria - 2005 - FCT - Abuja - 0477



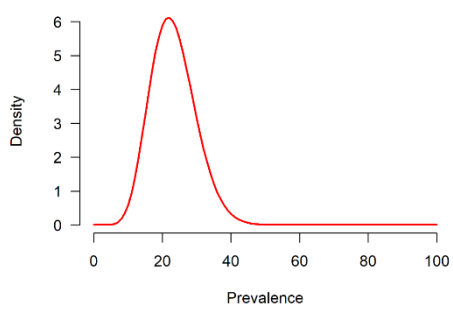
Nigeria - 2008 - Oyo - 0469



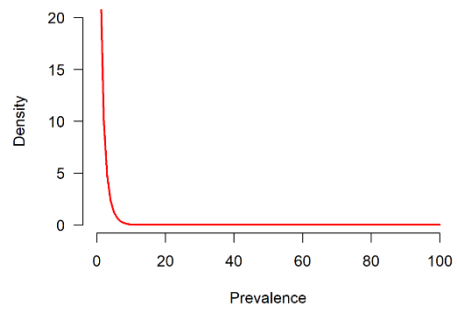
Nigeria - 2010 - Enugu - 0471



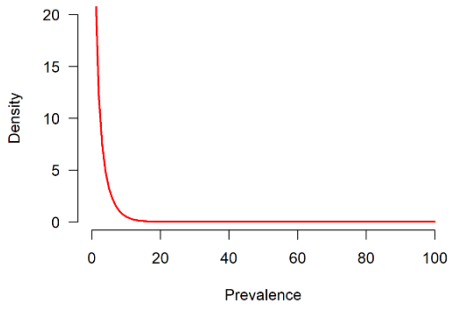
Nigeria - 2011 - Lagos - 0474



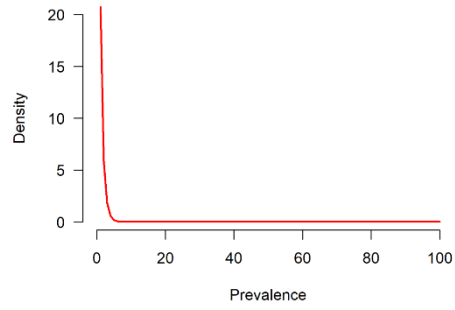
Nigeria - 2012 - Borno - 0472



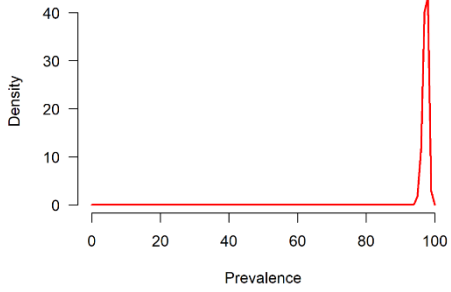
Nigeria - 2014 - Cross River - 0475



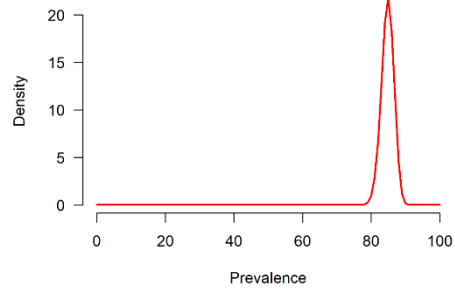
Nigeria - 2015 - Edo - 0470



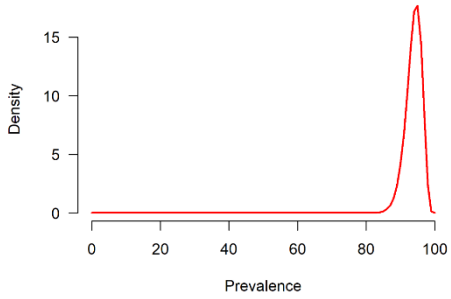
Rwanda - 2006 - Iburasirazuba - 0481



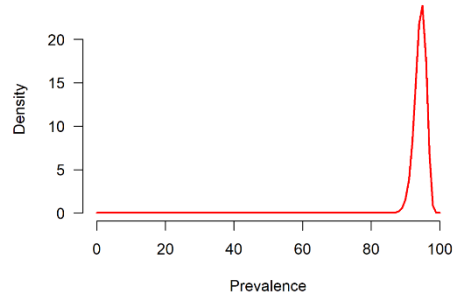
Rwanda - 2006 - Iburengerazuba - 0482



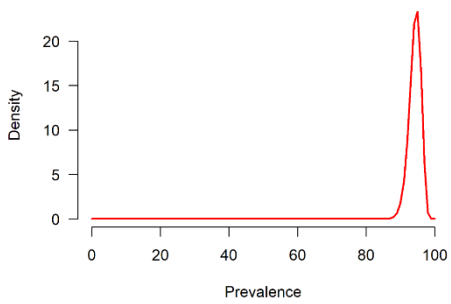
Rwanda - 2010 - Amajyepfo - 0483



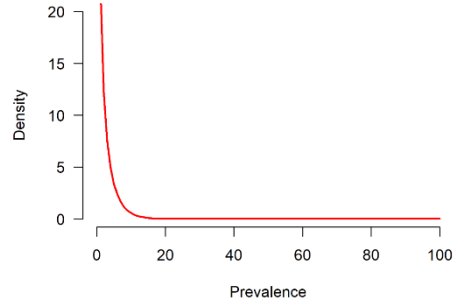
Rwanda - 2015 - Iburasirazuba - 0479

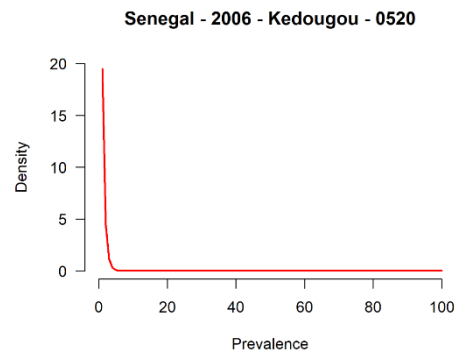
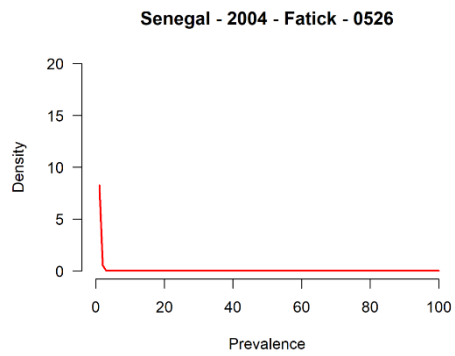
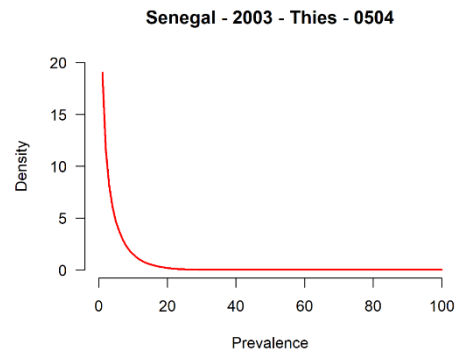
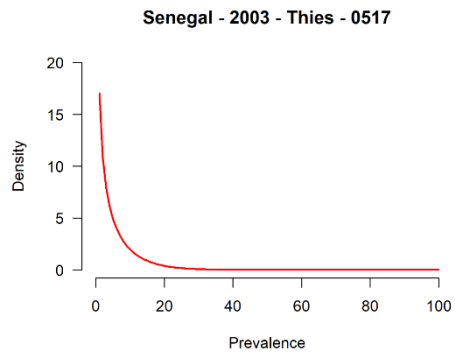
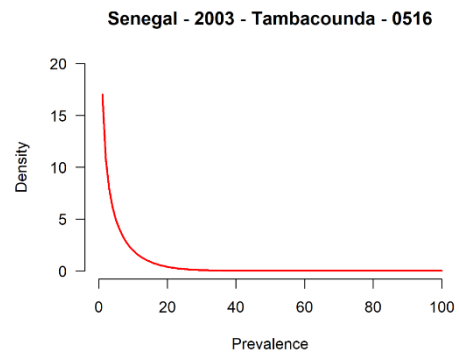
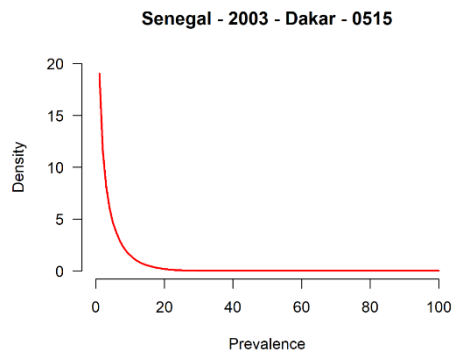
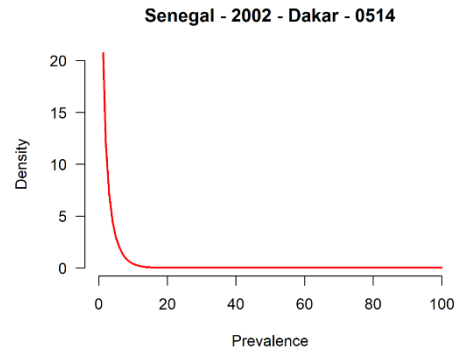
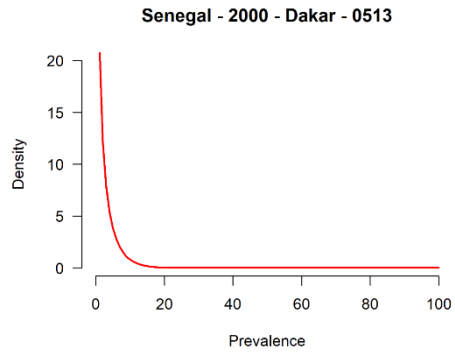


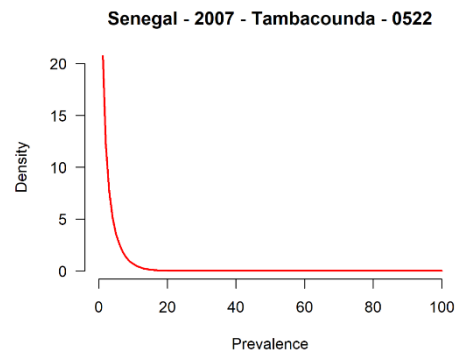
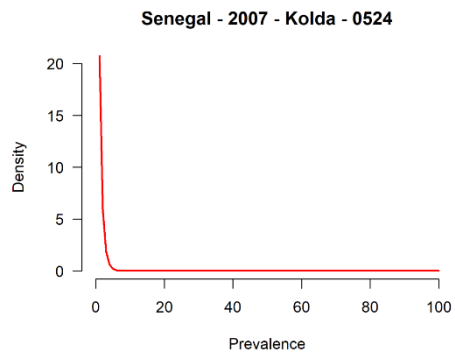
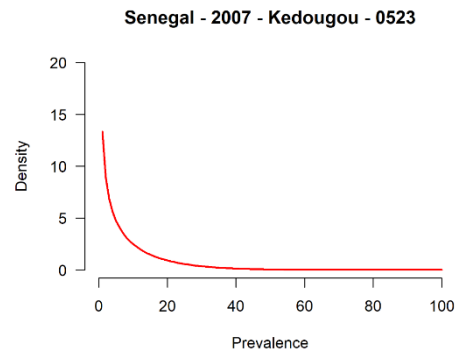
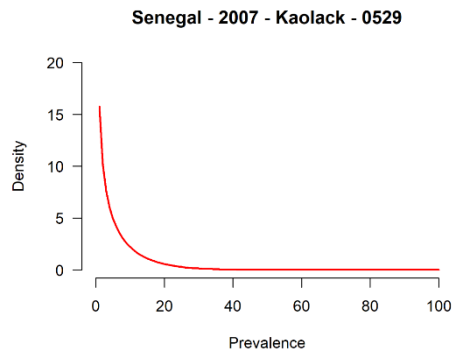
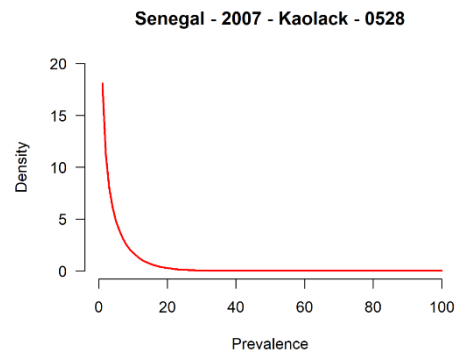
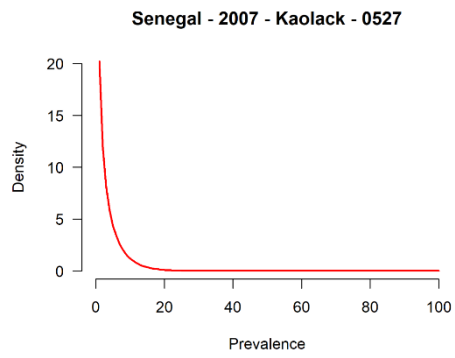
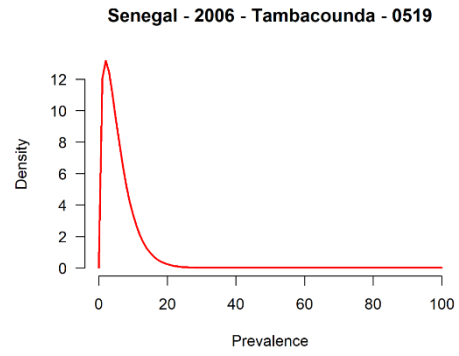
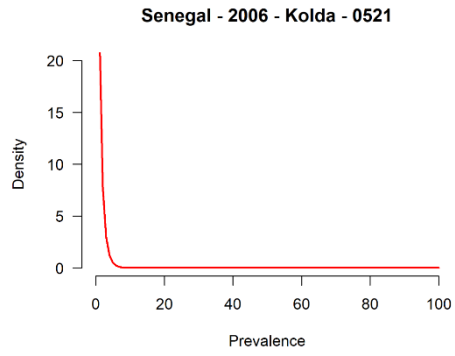
Rwanda - 2015 - Iburengerazuba - 0480



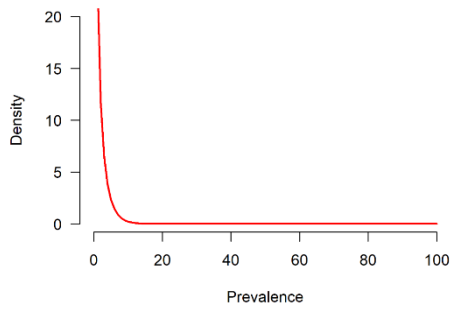
Senegal - 1999 - Fatick - 0512



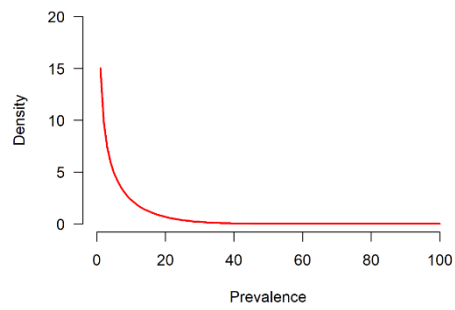




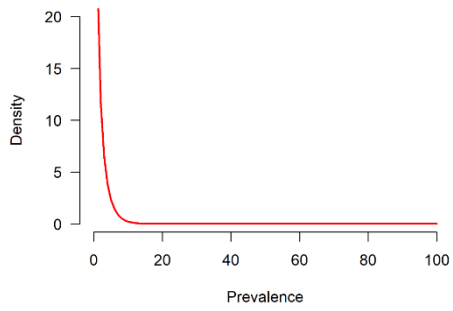
Senegal - 2008 - Diourbel - 0485



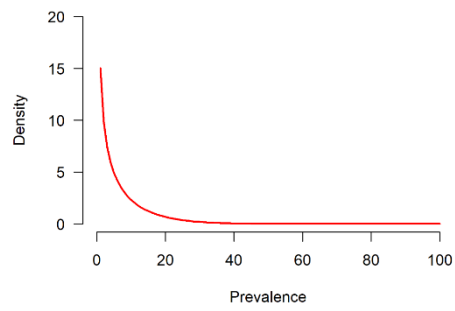
Senegal - 2008 - Diourbel - 0486



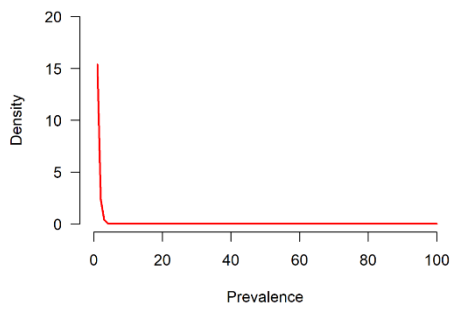
Senegal - 2008 - Fatick - 0491



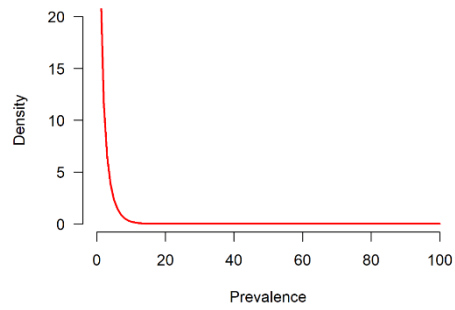
Senegal - 2008 - Fatick - 0492



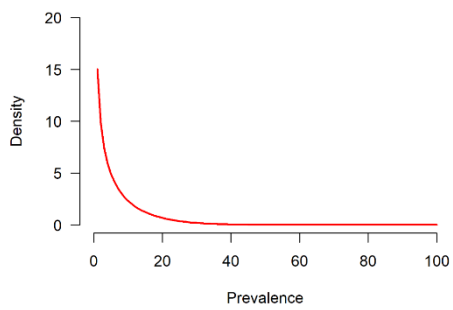
Senegal - 2008 - Tambacounda - 0525



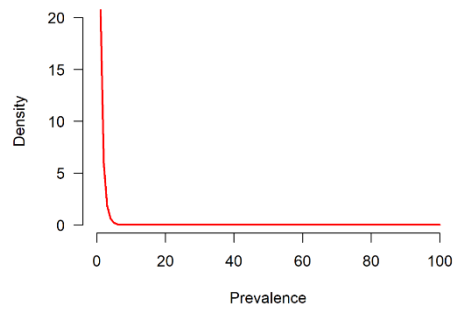
Senegal - 2008 - Thies - 0497



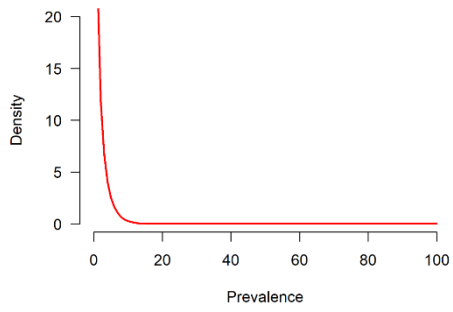
Senegal - 2008 - Thies - 0498



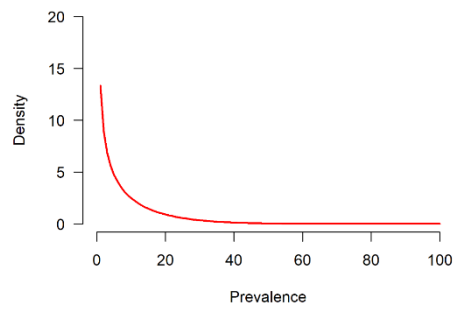
Senegal - 2008 - Thies - 0505



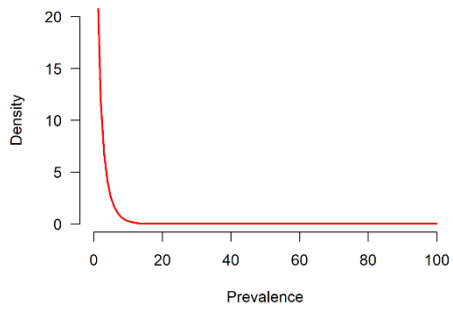
Senegal - 2009 - Diourbel - 0487



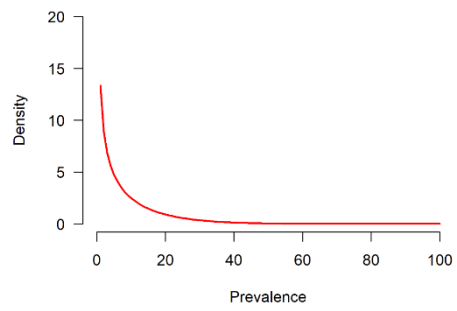
Senegal - 2009 - Diourbel - 0488



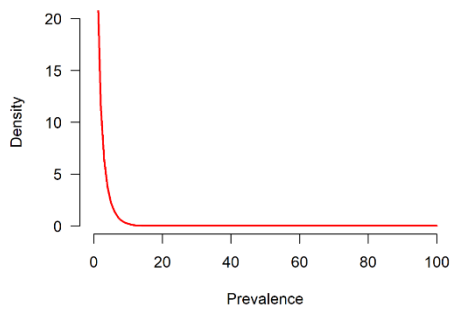
Senegal - 2009 - Fatick - 0493



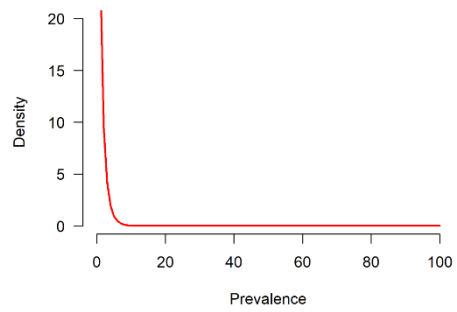
Senegal - 2009 - Fatick - 0494



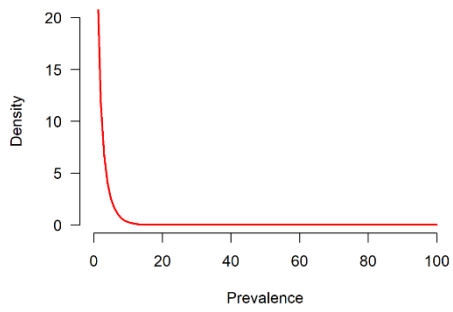
Senegal - 2009 - Tambacounda - 0531



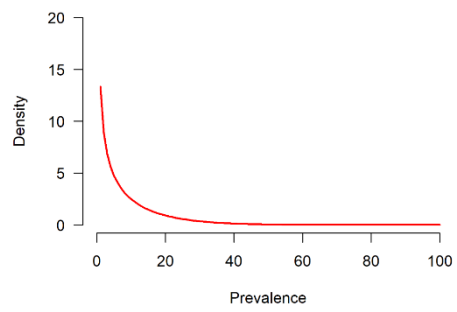
Senegal - 2009 - Tambacounda - 0533

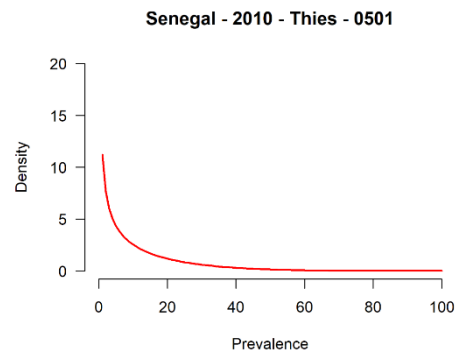
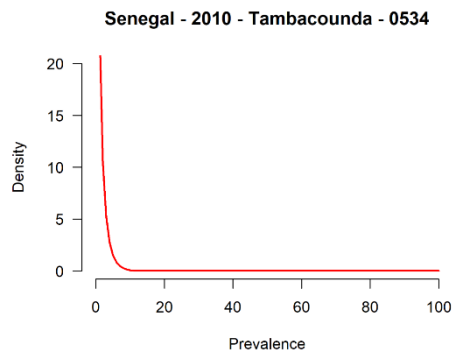
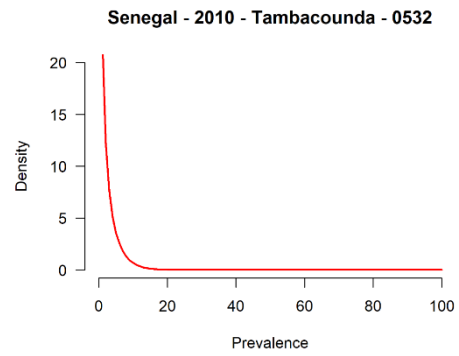
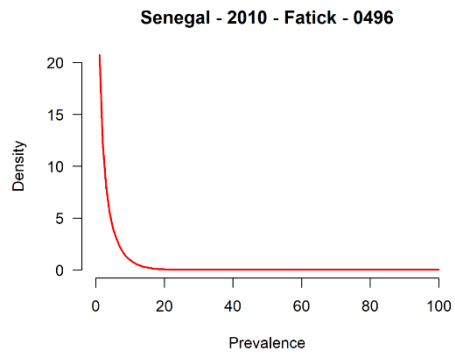
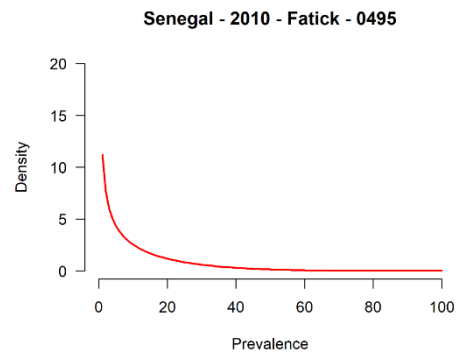
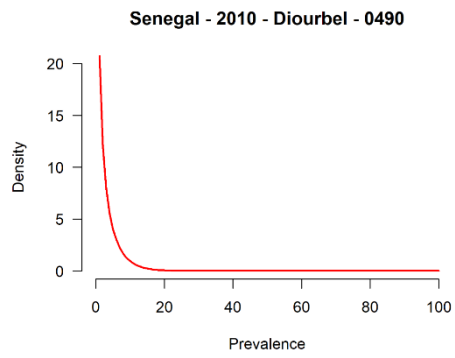
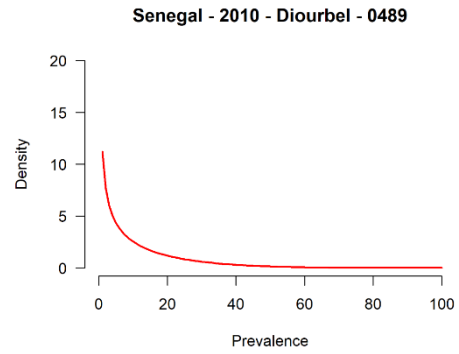
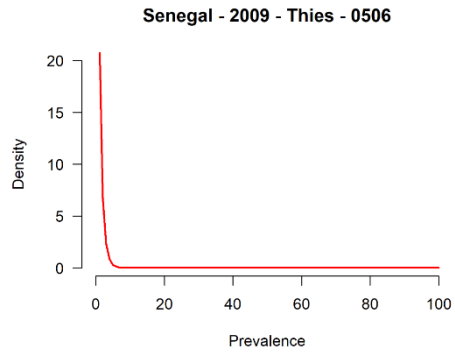


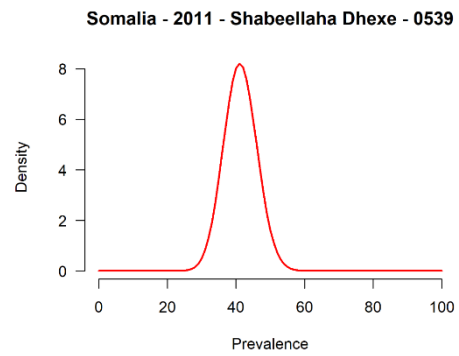
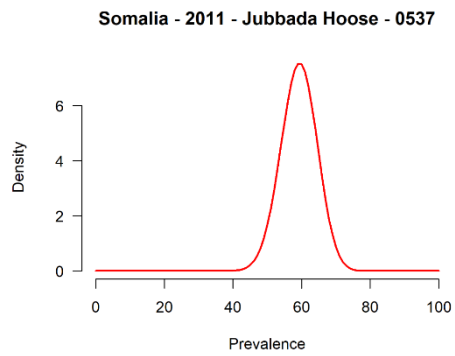
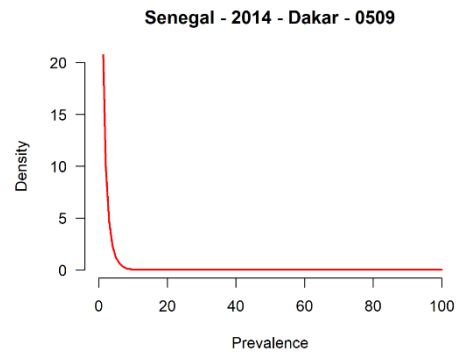
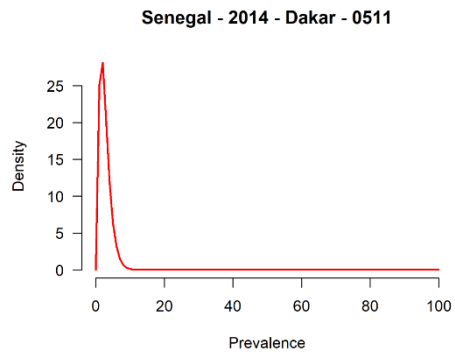
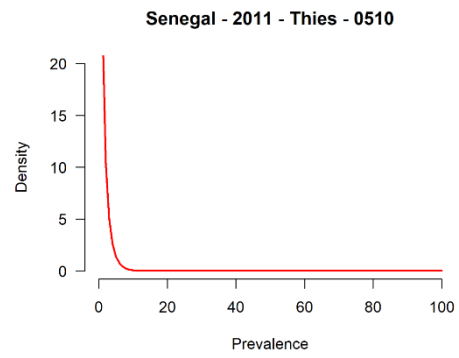
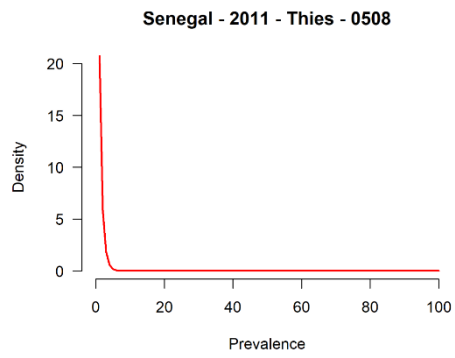
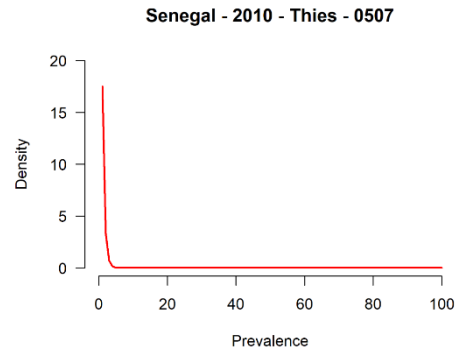
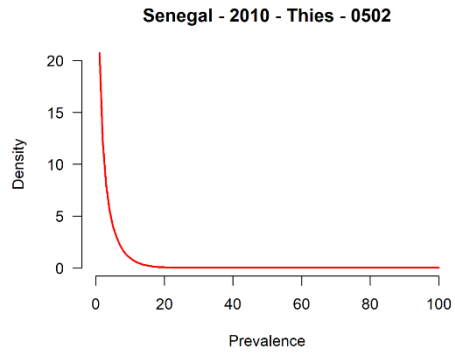
Senegal - 2009 - Thies - 0499



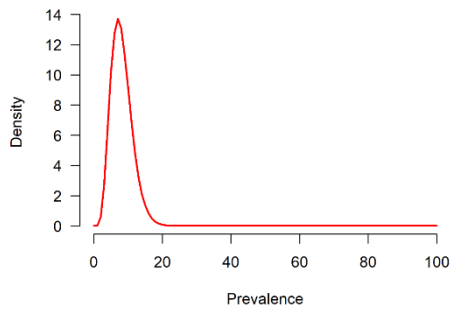
Senegal - 2009 - Thies - 0500



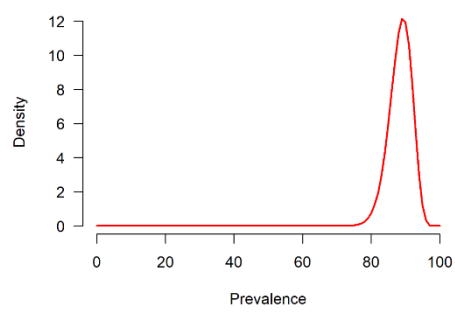




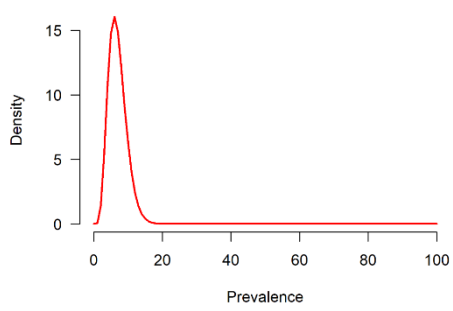
Somalia - 2011 - Shabeellaha Hoose - 0538



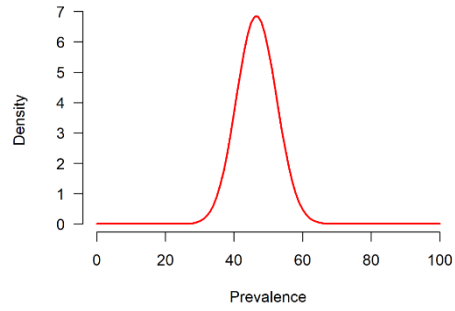
Somalia - 2015 - Bari - 0540



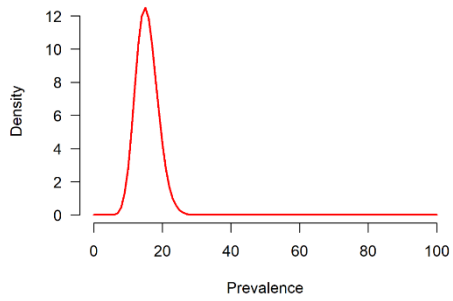
South Africa - 1998 - Mpumalanga - 0583



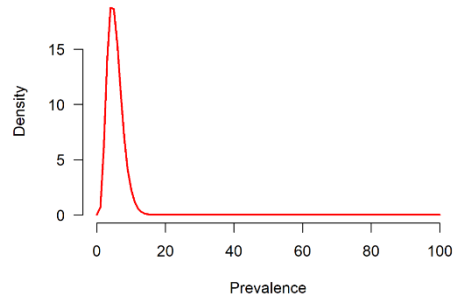
South Africa - 1999 - Kwazulu-Natal - 0580



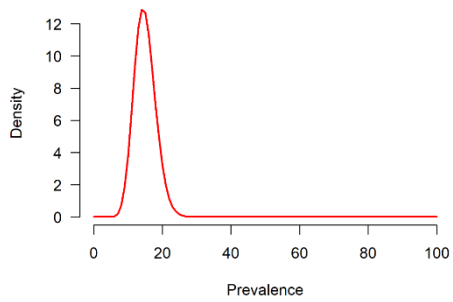
South Africa - 1999 - Kwazulu-Natal - 0581



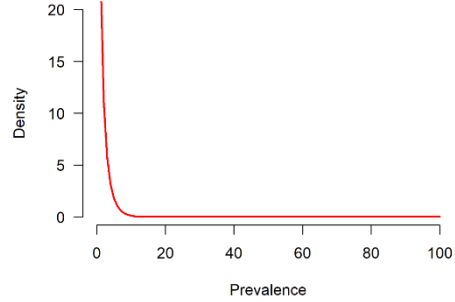
South Africa - 2000 - Mpumalanga - 0584



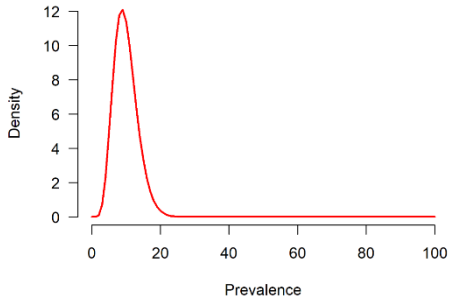
South Africa - 2002 - Mpumalanga - 0582



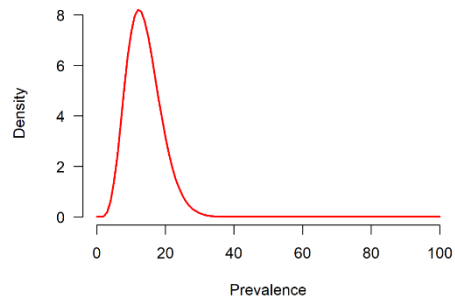
South Sudan - 2001 - Jonglei - 0588



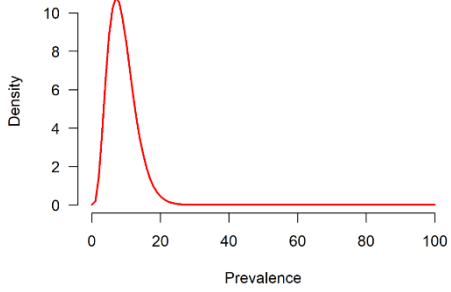
South Sudan - 2002 - Northern Bahr El Ghazal - 0587



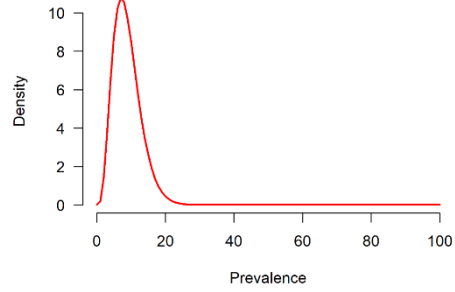
Sudan - 1998 - Gadaref - 0554



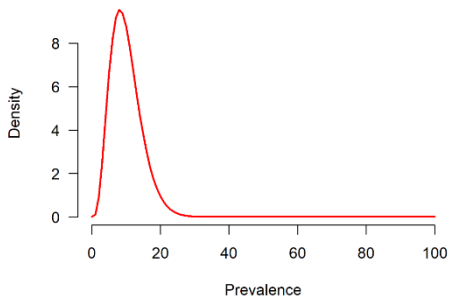
Sudan - 1998 - Gadaref - 0555



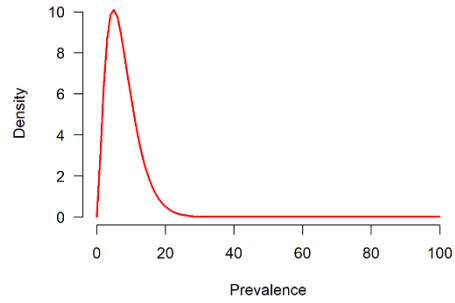
Sudan - 1998 - Gadaref - 0549



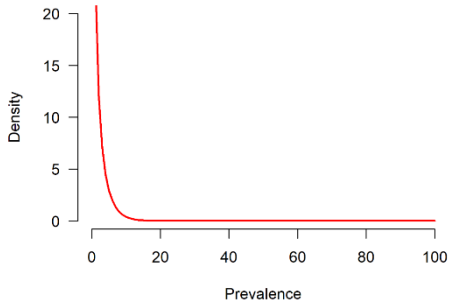
Sudan - 1998 - Khartoum - 0556



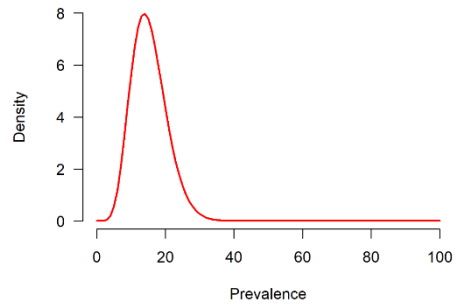
Sudan - 1999 - Gadaref - 0557

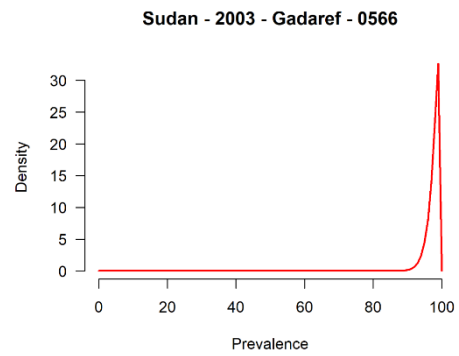
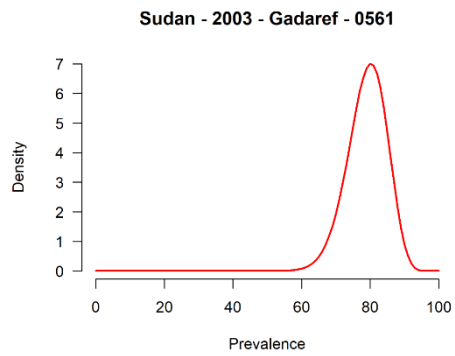
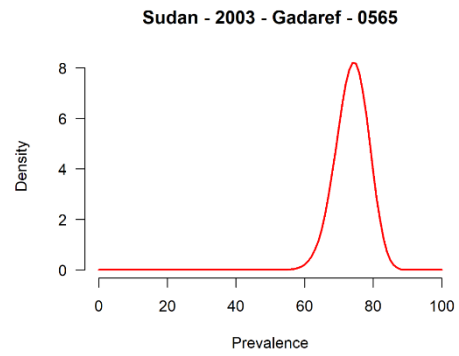
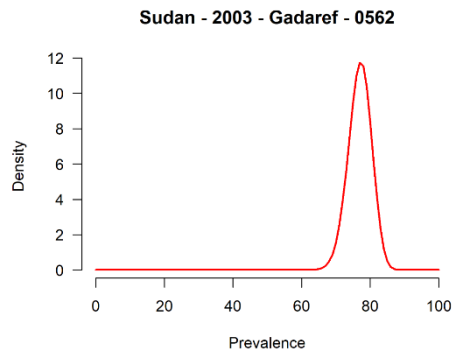
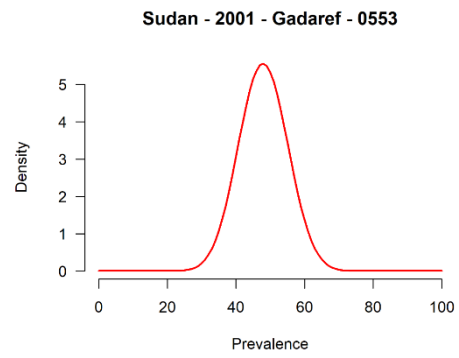
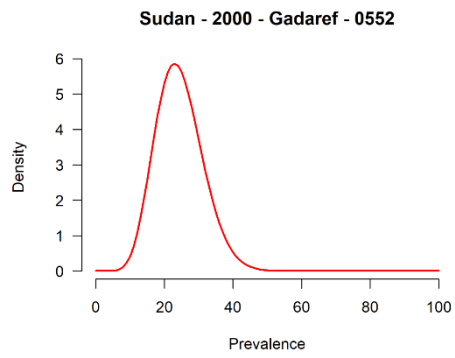
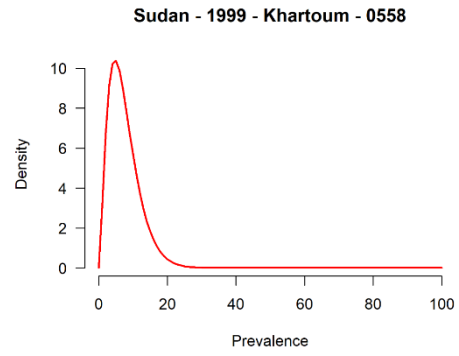
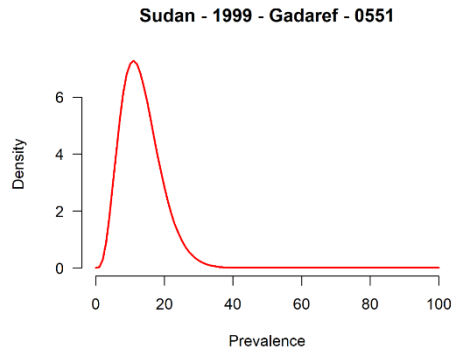


Sudan - 1999 - Gadaref - 0559

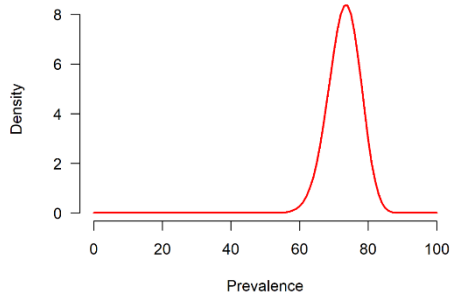


Sudan - 1999 - Gadaref - 0550

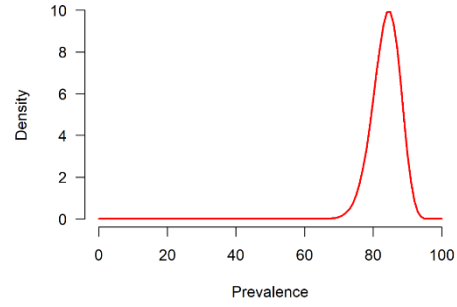




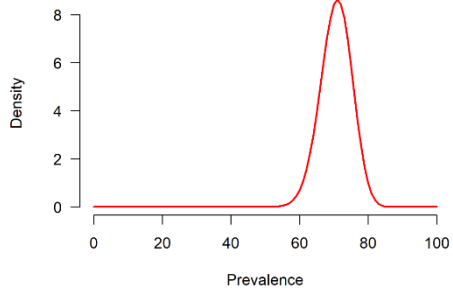
Sudan - 2003 - Northern Kordofan - 0563



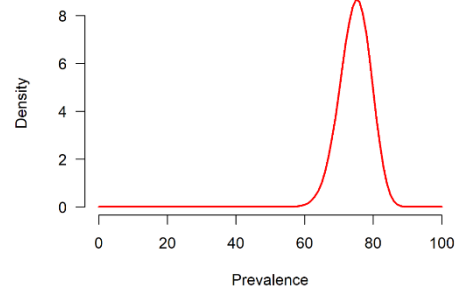
Sudan - 2003 - Northern Kordofan - 0564



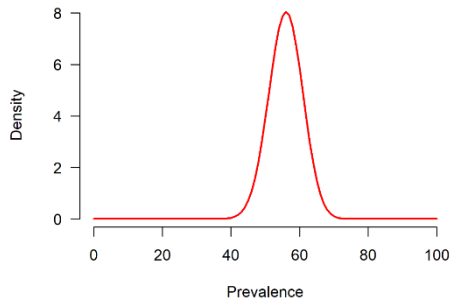
Sudan - 2011 - Gadaref - 0543



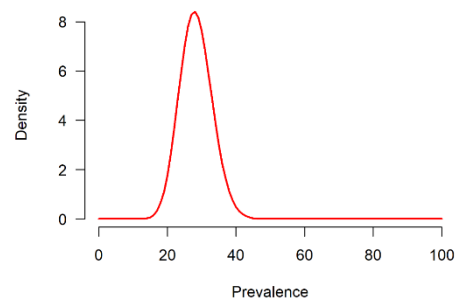
Sudan - 2011 - Kassala - 0545



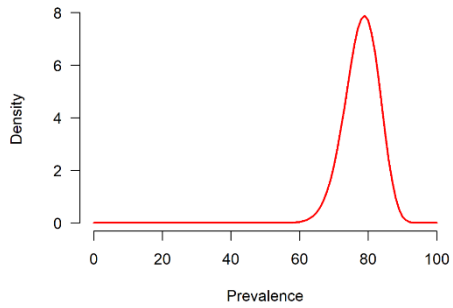
Sudan - 2011 - Sennar - 0542



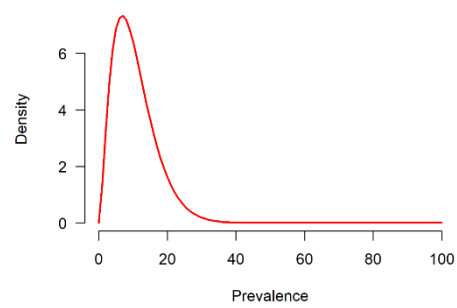
Sudan - 2011 - White Nile - 0544



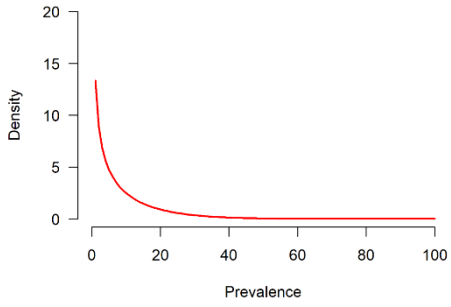
Sudan - 2012 - Kassala - 0546



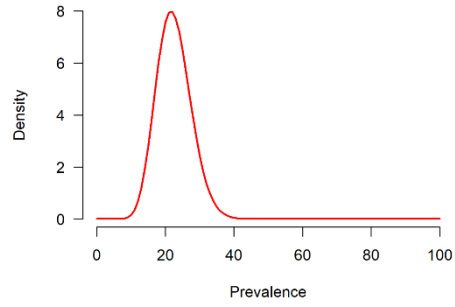
Swaziland - 1999 - Lubombo - 0590



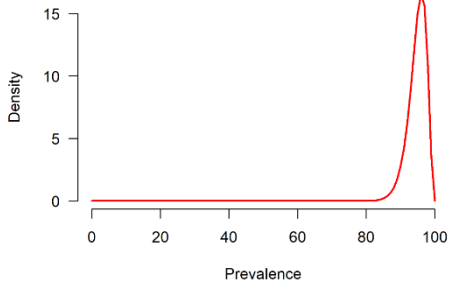
Swaziland - 2007 - Lubombo - 0591



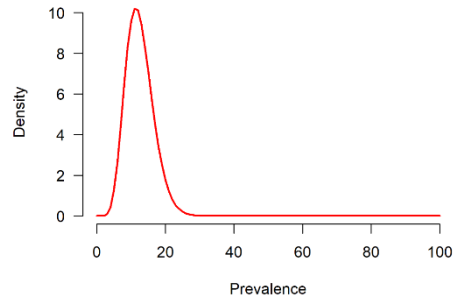
Tanzania - 1998 - Pwani - 0630



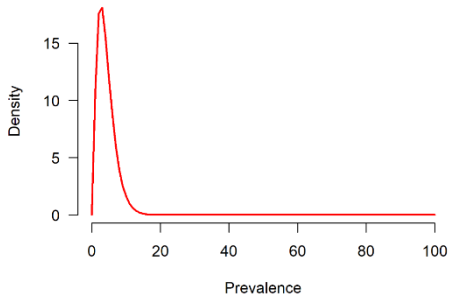
Tanzania - 1998 - Tanga - 0632



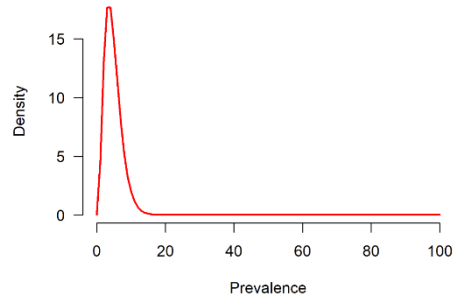
Tanzania - 1999 - Mbeya - 0636



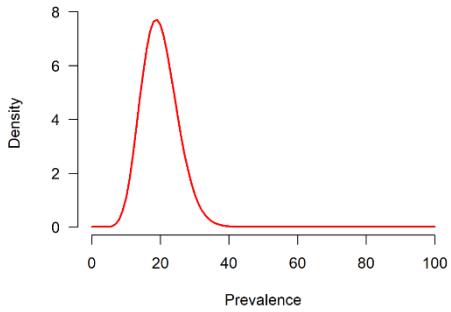
Tanzania - 1999 - Morogoro - 0638



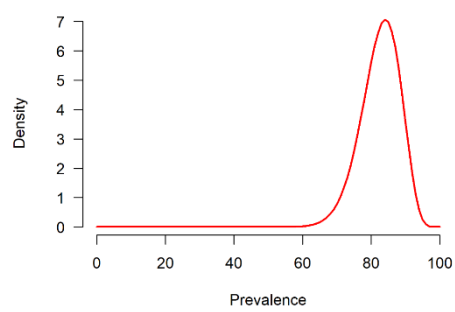
Tanzania - 1999 - Mtwara - 0637

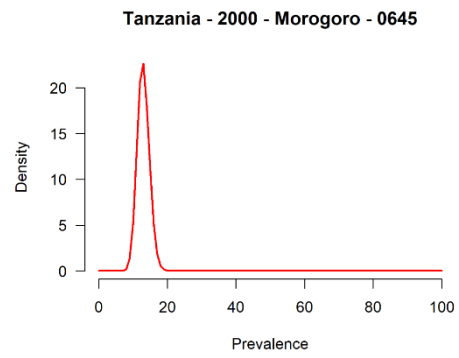
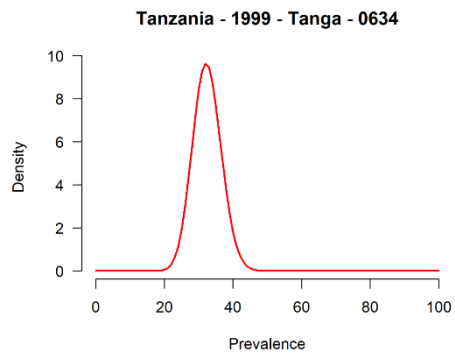
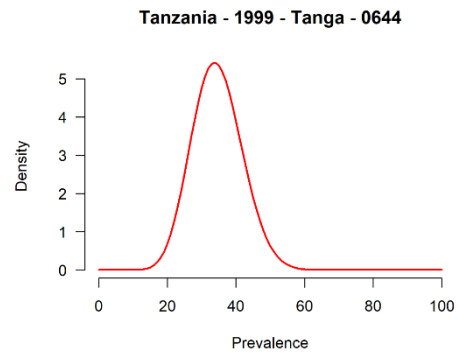
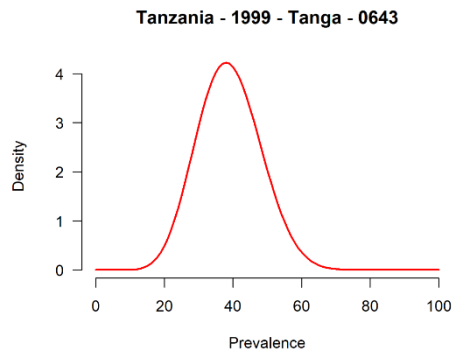
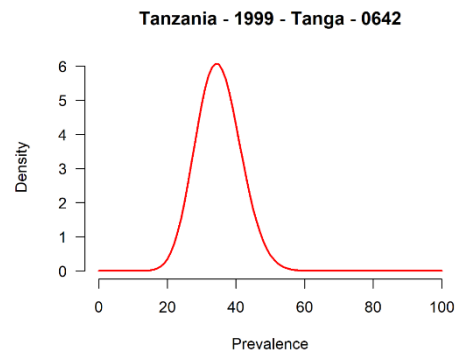
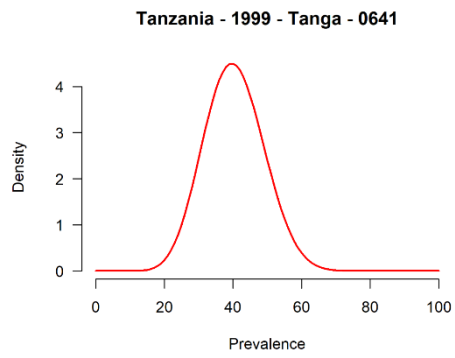
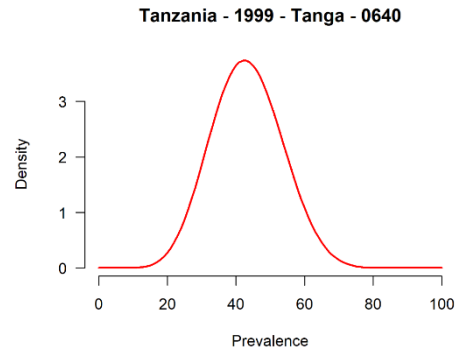
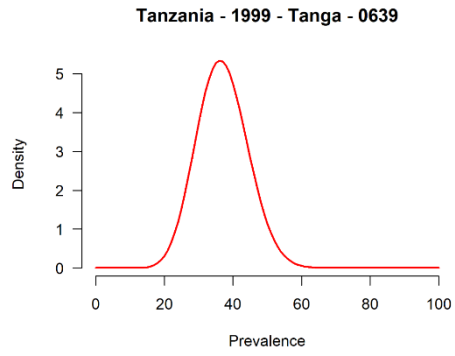


Tanzania - 1999 - Mwanza - 0635

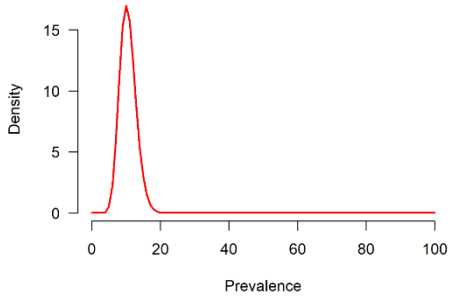


Tanzania - 1999 - Tanga - 0633

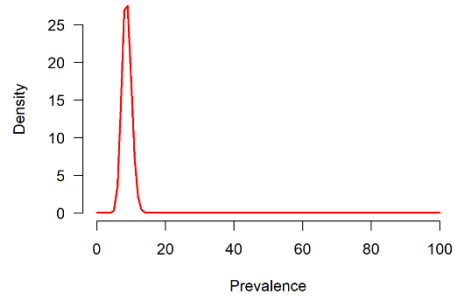




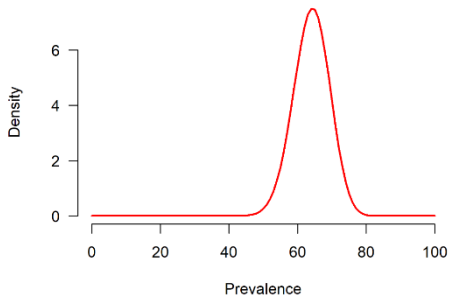
Tanzania - 2000 - Morogoro - 0674



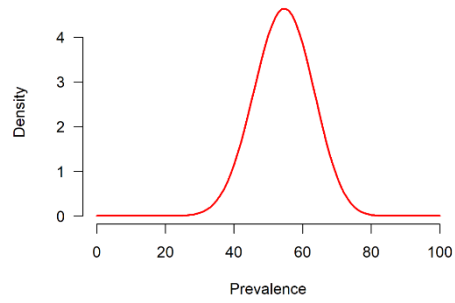
Tanzania - 2000 - Pwani - 0648



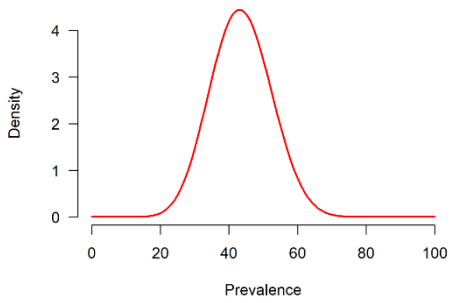
Tanzania - 2001 - Kilimanjaro - 0651



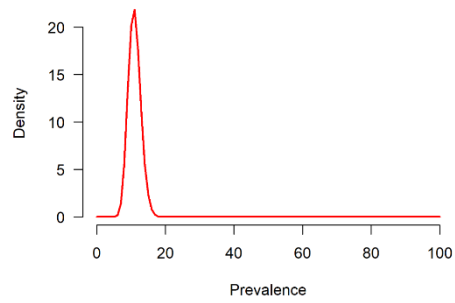
Tanzania - 2001 - Kilimanjaro - 0652



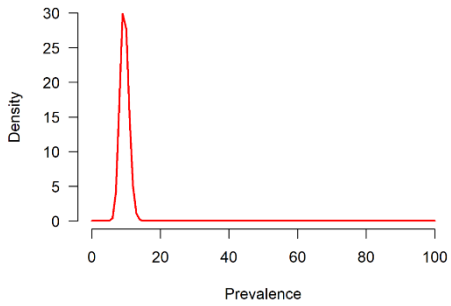
Tanzania - 2001 - Kilimanjaro - 0653



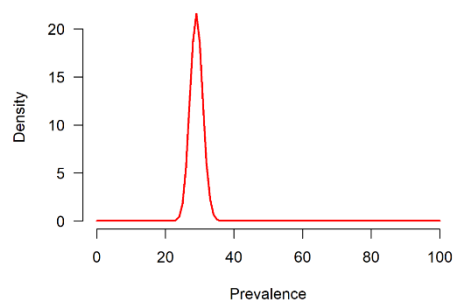
Tanzania - 2001 - Morogoro - 0646



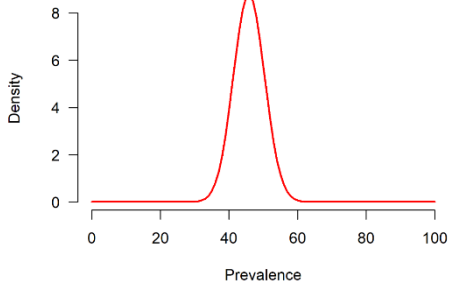
Tanzania - 2001 - Pwani - 0649



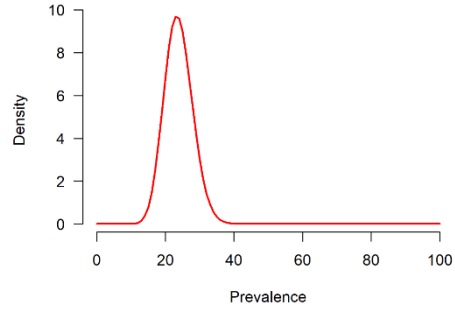
Tanzania - 2002 - Morogoro - 0647



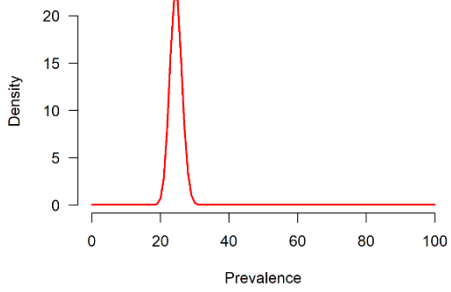
Tanzania - 2002 - Morogoro - 0681



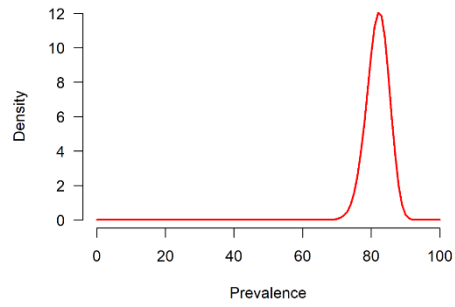
Tanzania - 2002 - Pwani - 0680



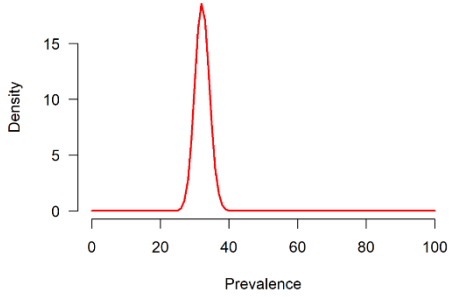
Tanzania - 2002 - Pwani - 0650



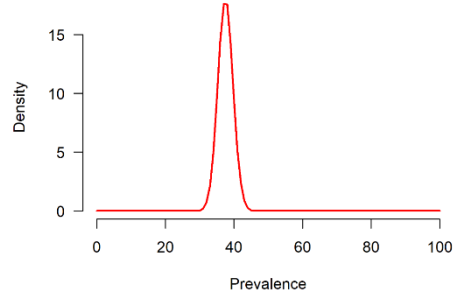
Tanzania - 2003 - Tanga - 0654



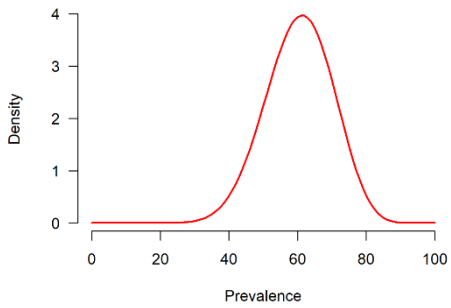
Tanzania - 2004 - Lindi - 0662



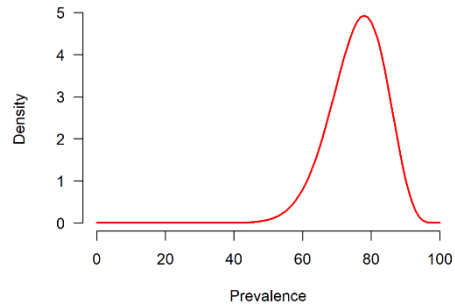
Tanzania - 2004 - Lindi - 0663



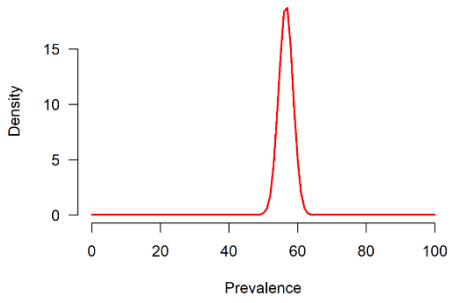
Tanzania - 2004 - Lindi - 0664



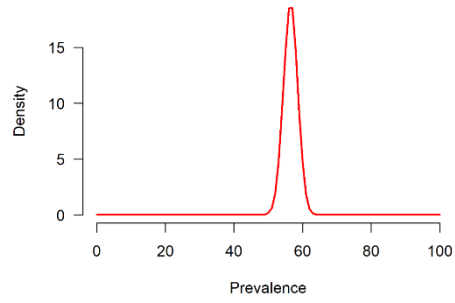
Tanzania - 2004 - Lindi - 0665



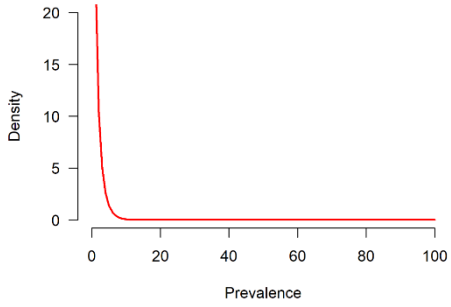
Tanzania - 2004 - Morogoro - 0676



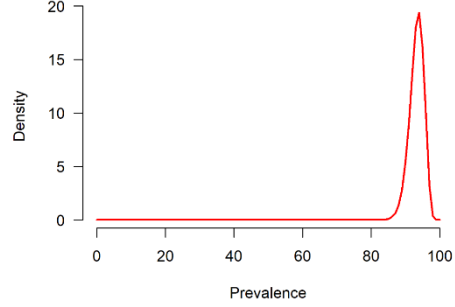
Tanzania - 2004 - Morogoro - 0683



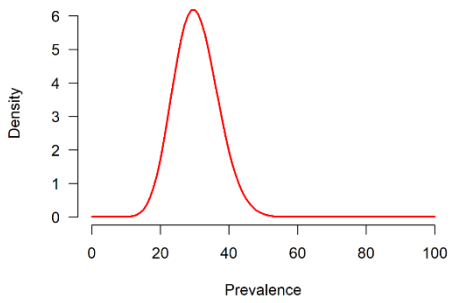
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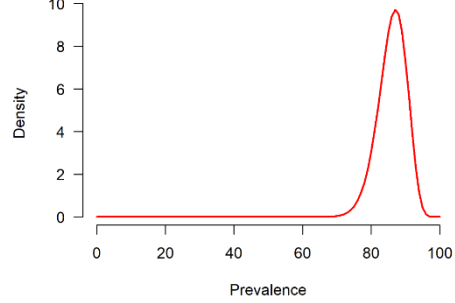
Tanzania - 2004 - Tanga - 0655



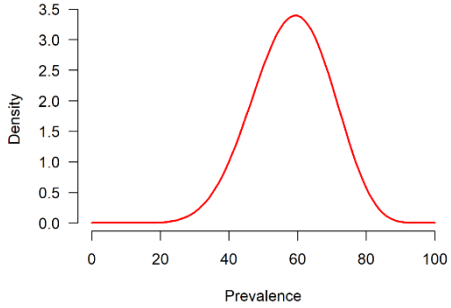
Tanzania - 2005 - Dodoma - 0679



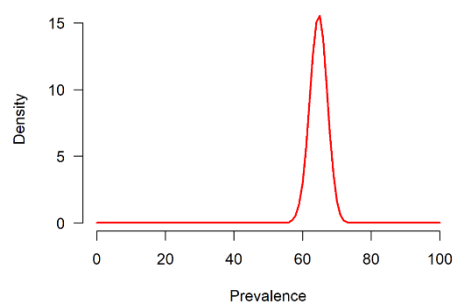
Tanzania - 2005 - Mbeya - 0684

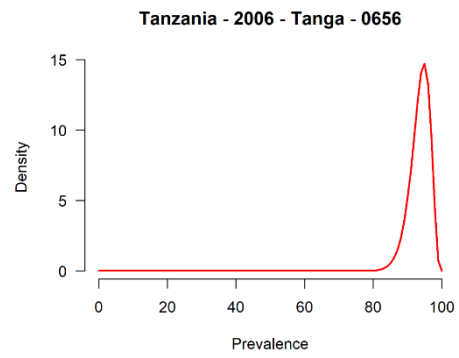
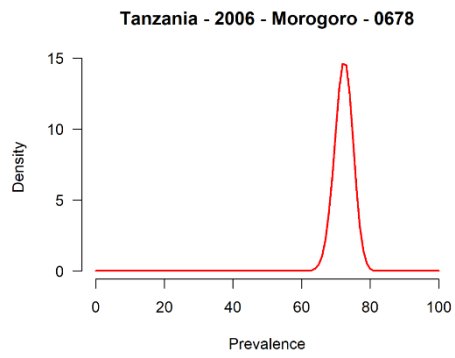
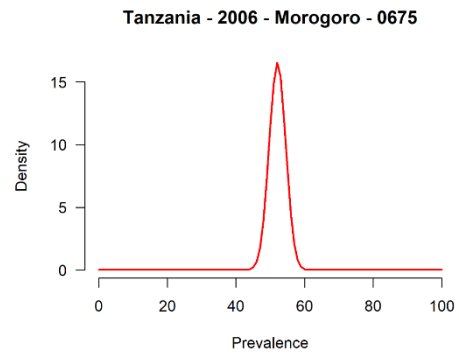
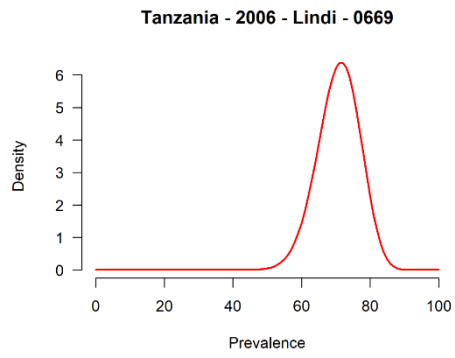
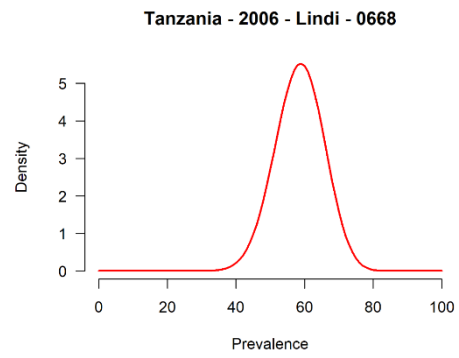
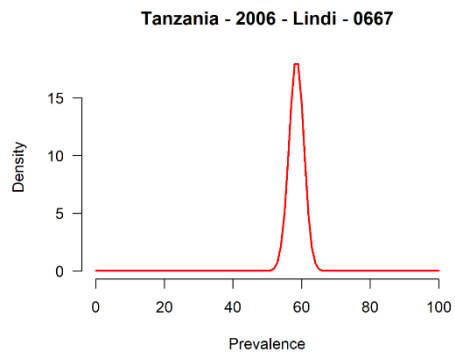
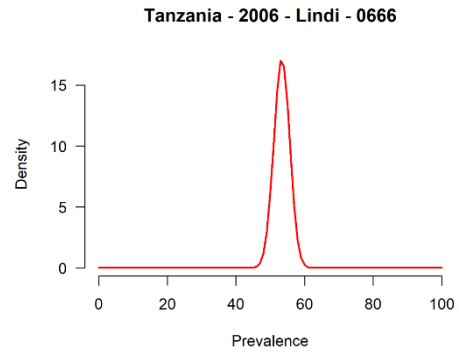
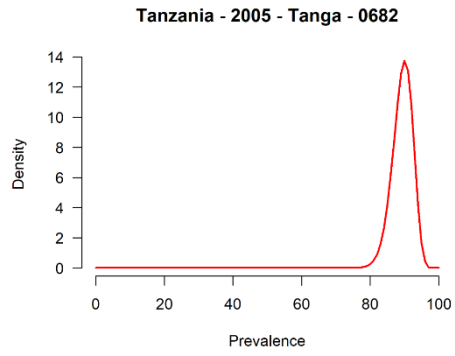


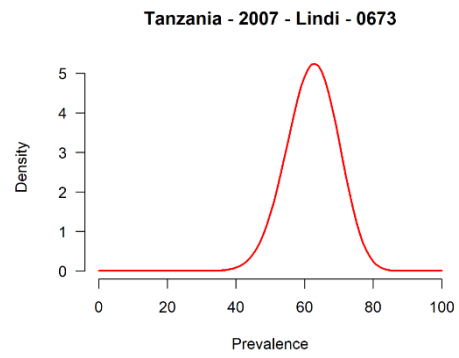
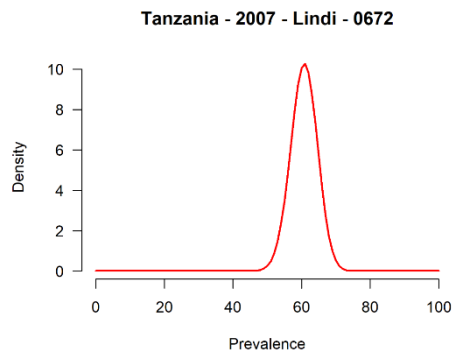
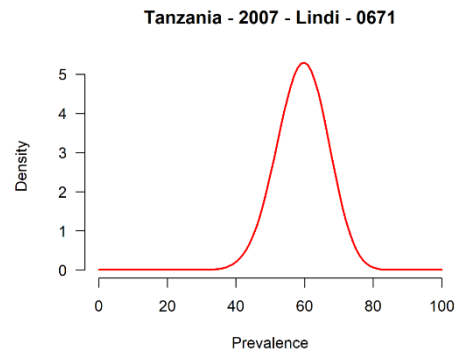
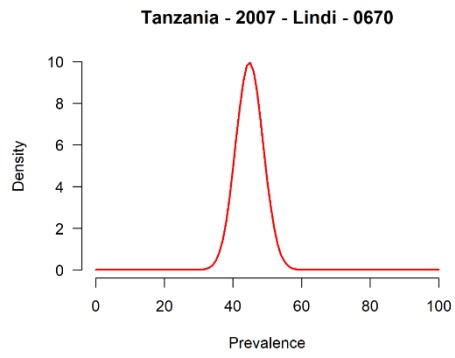
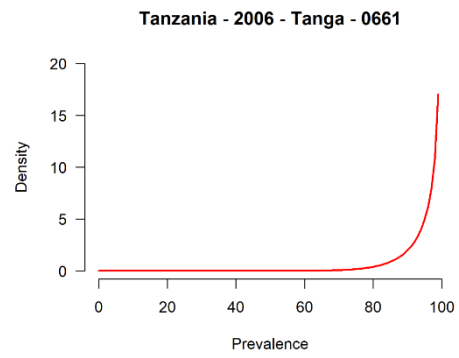
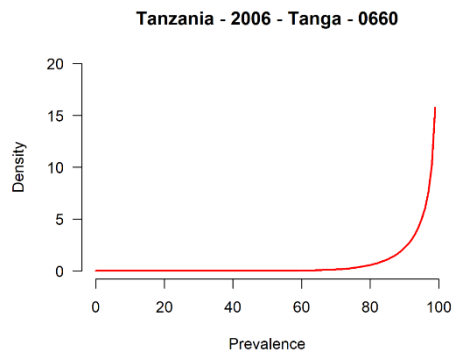
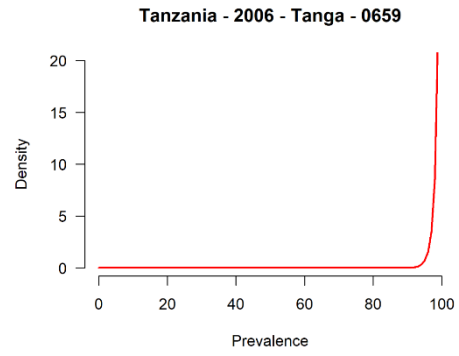
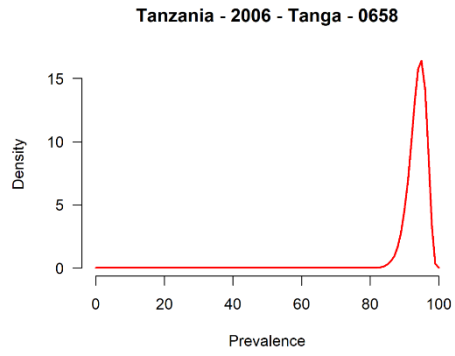
Tanzania - 2005 - Mbeya - 0685



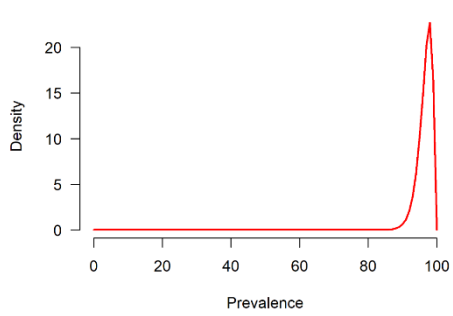
Tanzania - 2005 - Morogoro - 0677



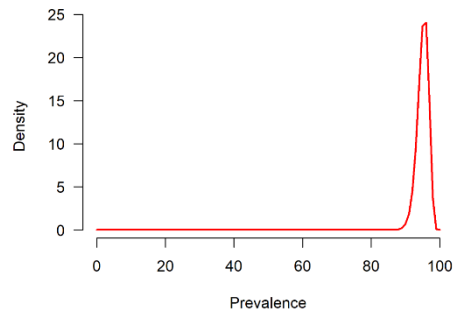




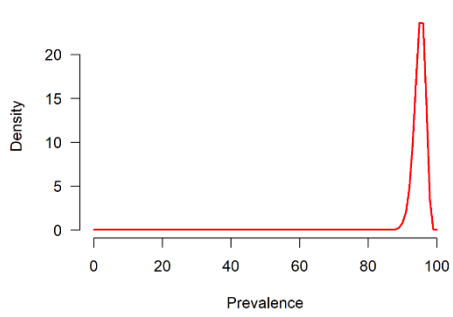
Tanzania - 2007 - Tanga - 0657



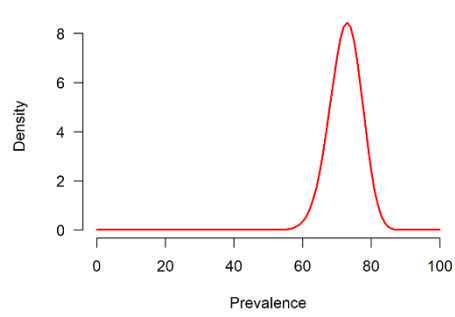
Tanzania - 2011 - Kagera - 0596



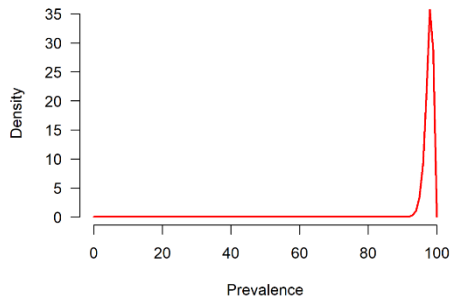
Tanzania - 2011 - Kagera - 0604



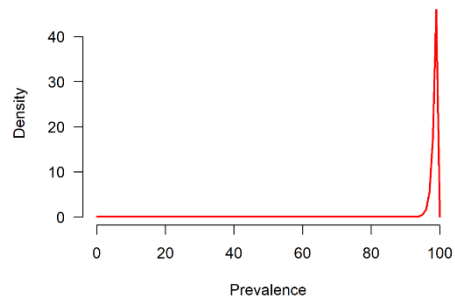
Tanzania - 2011 - Lindi - 0597



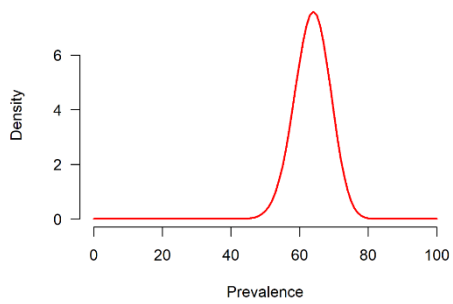
Tanzania - 2011 - Mbeya - 0598



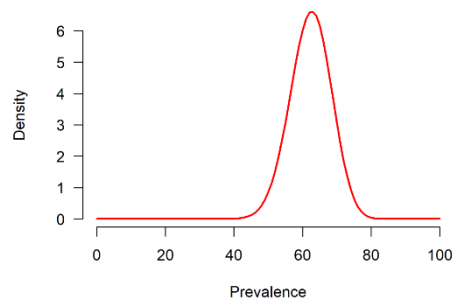
Tanzania - 2011 - Mbeya - 0605



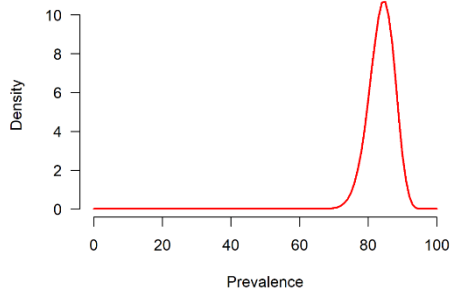
Tanzania - 2011 - Mtwara - 0599



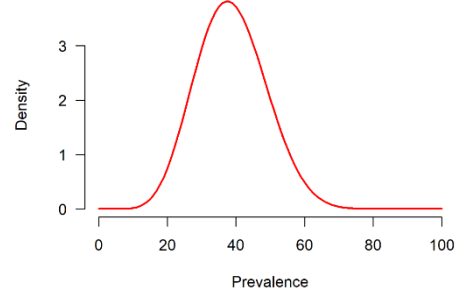
Tanzania - 2011 - Mtwara - 0606



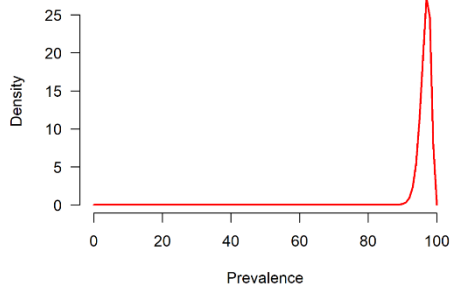
Tanzania - 2011 - Mwanza - 0686



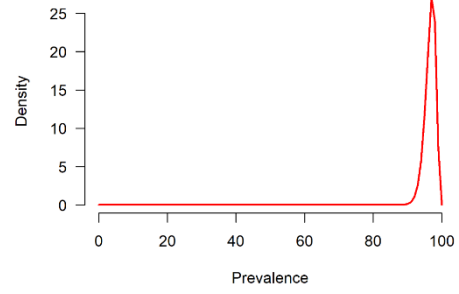
Tanzania - 2011 - Mwanza - 0687



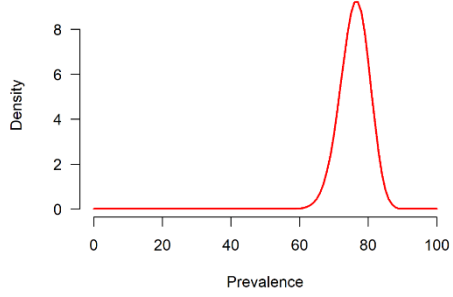
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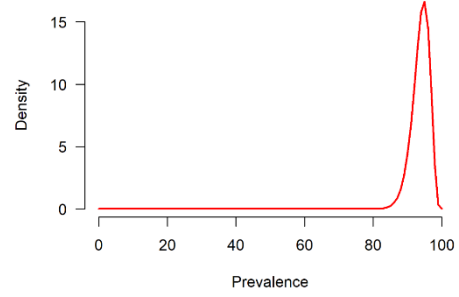
Tanzania - 2011 - Mwanza - 0607



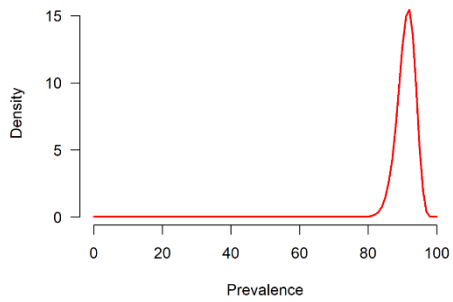
Tanzania - 2011 - Pwani - 0601



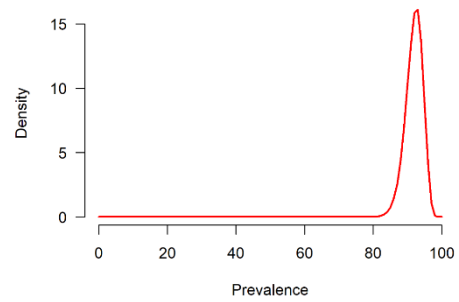
Tanzania - 2011 - Tanga - 0602

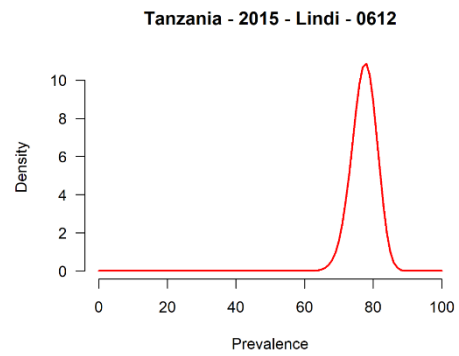
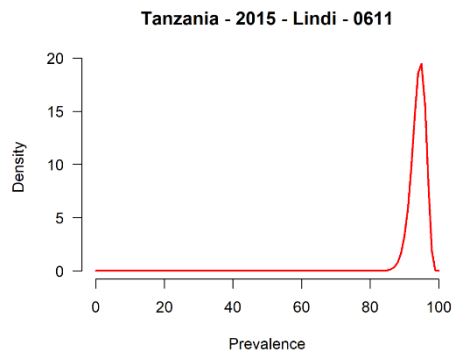
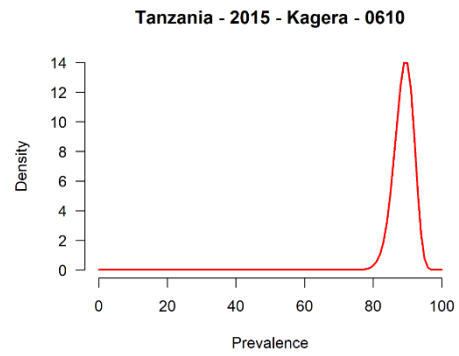
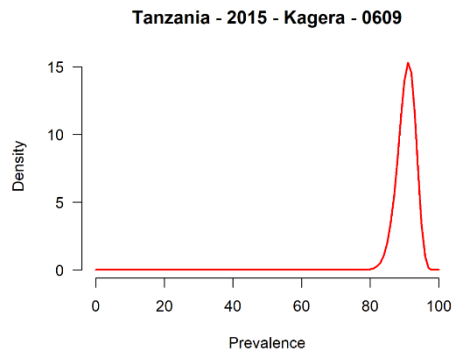
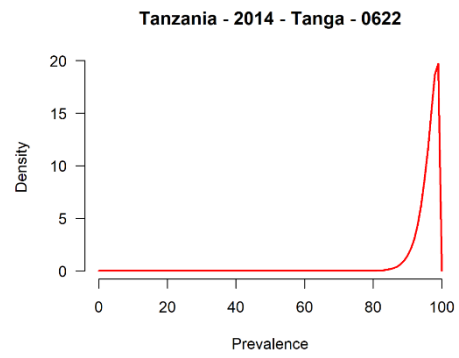
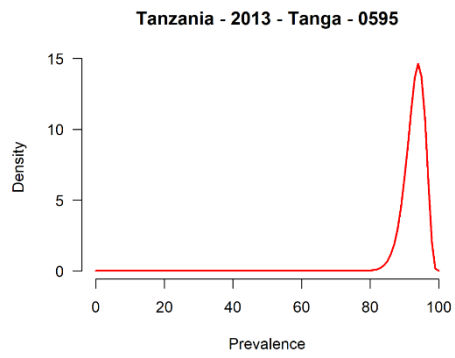
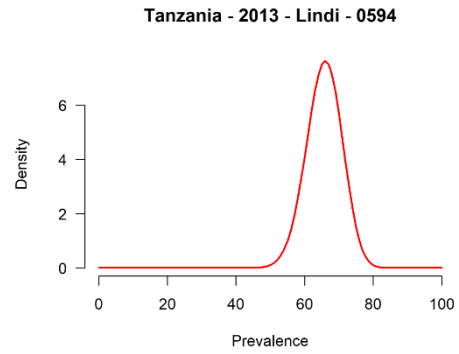
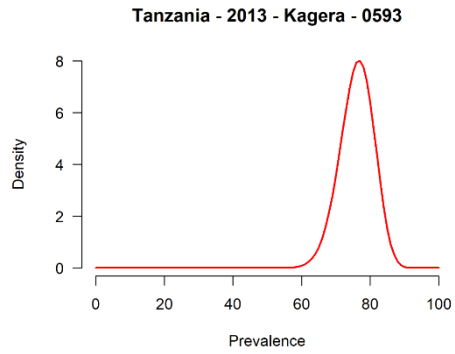


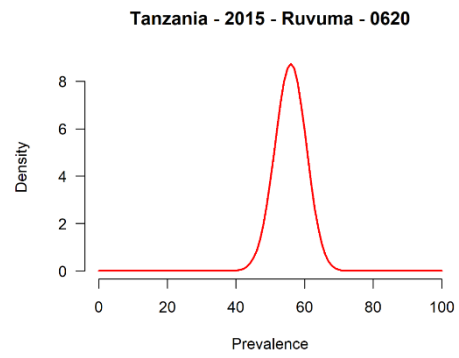
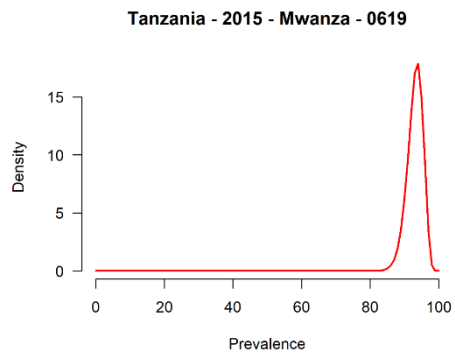
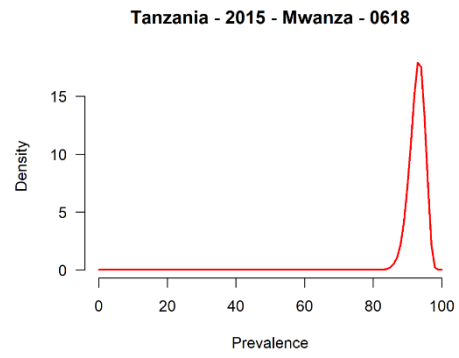
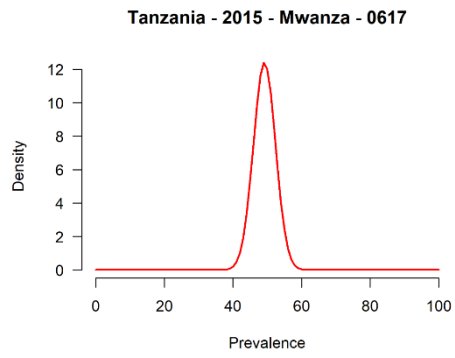
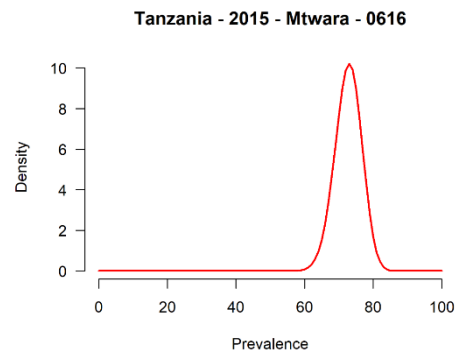
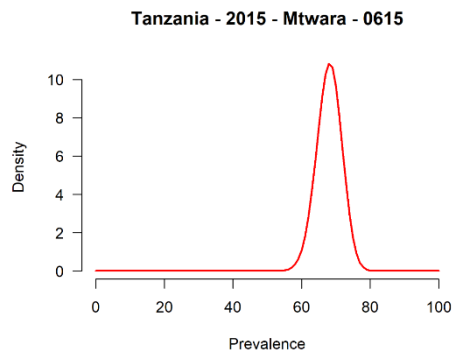
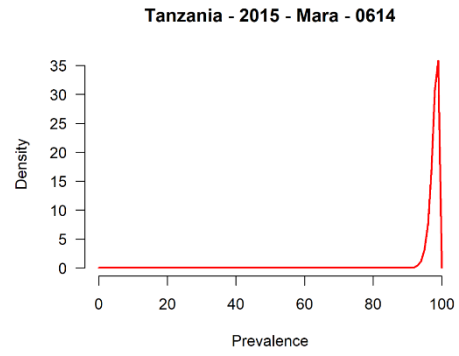
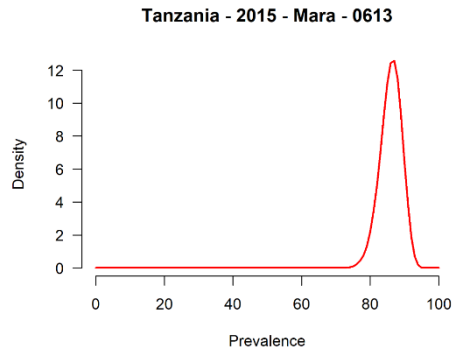
Tanzania - 2011 - Tanga - 0603



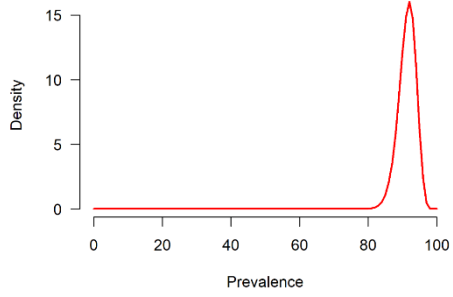
Tanzania - 2011 - Tanga - 0608



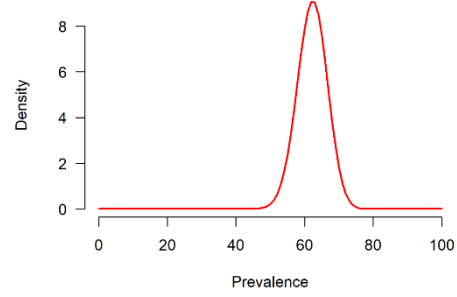




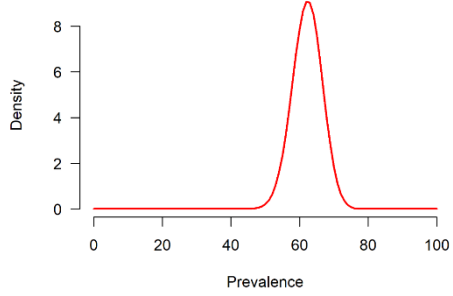
Tanzania - 2015 - Ruvuma - 0621



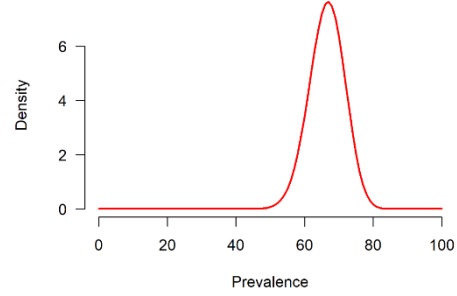
Uganda - 1999 - Bundibugyo - 0752



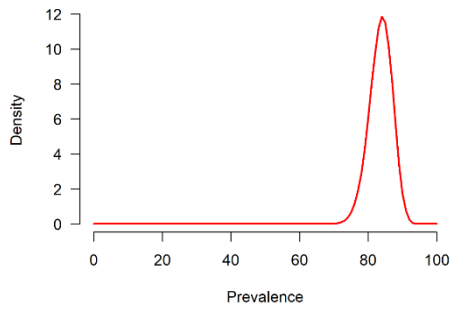
Uganda - 1999 - Kabarole - 0751



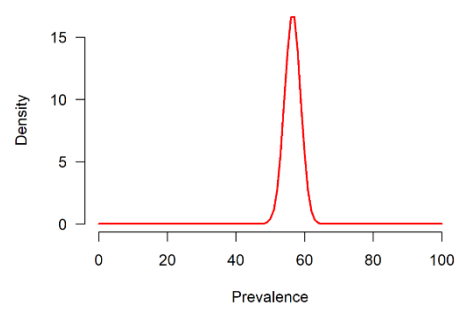
Uganda - 1999 - Kampala - 0742



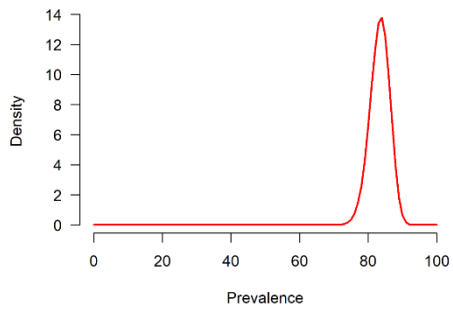
Uganda - 2000 - Kampala - 0743



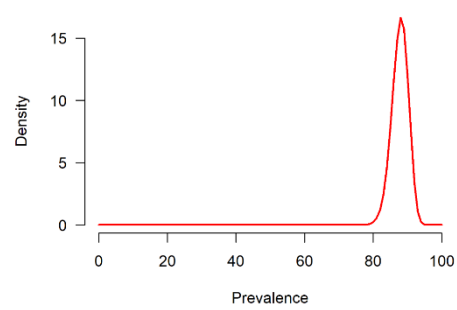
Uganda - 2001 - Kampala - 0744

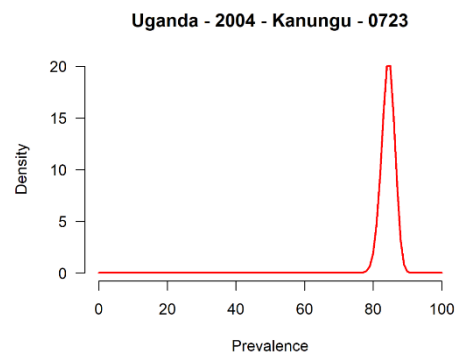
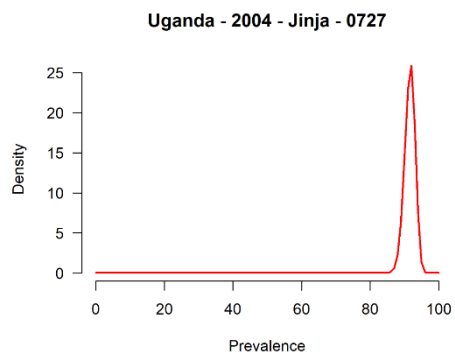
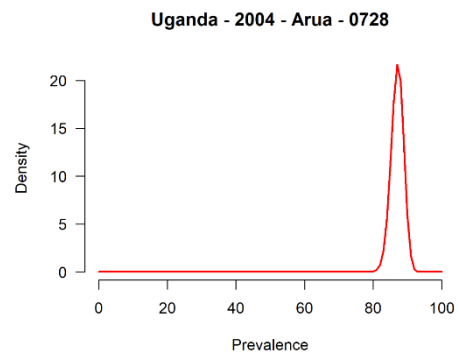
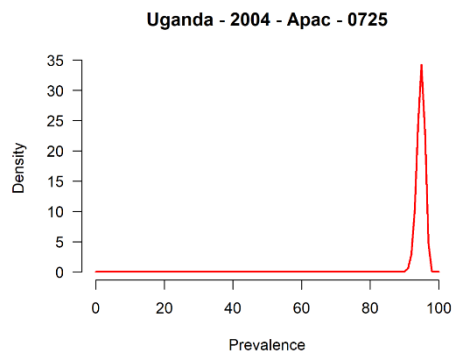
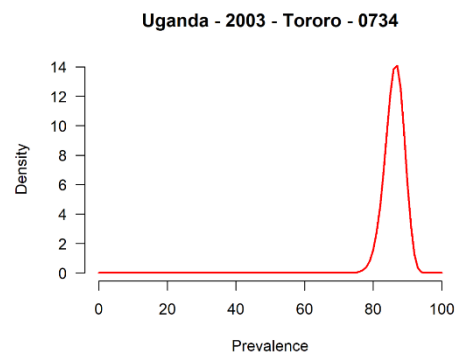
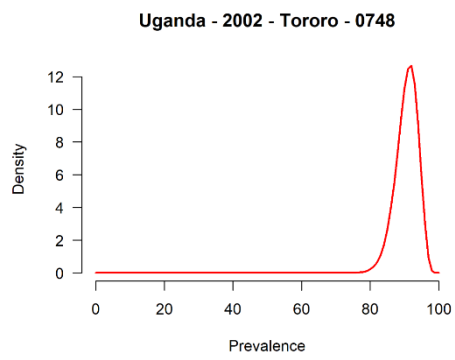
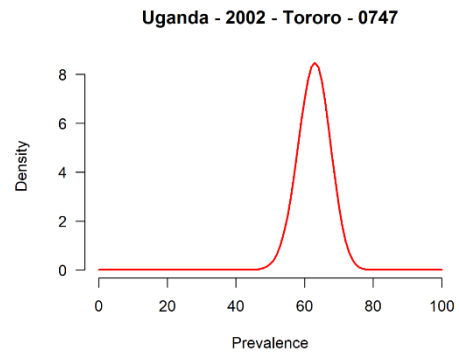
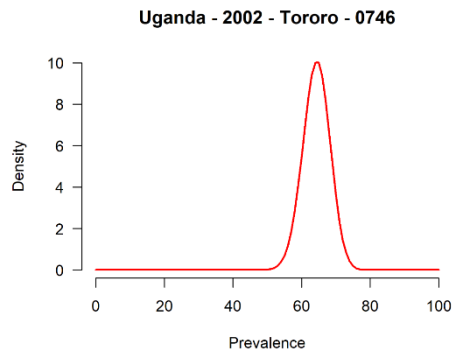


Uganda - 2001 - Kampala - 0745

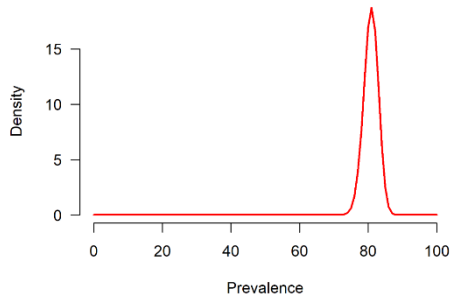


Uganda - 2002 - Kampala - 0749

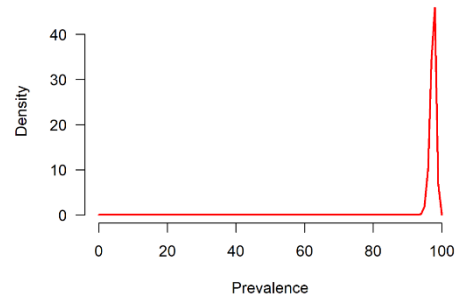




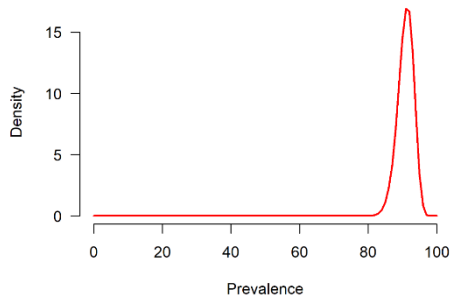
Uganda - 2004 - Mubende - 0724



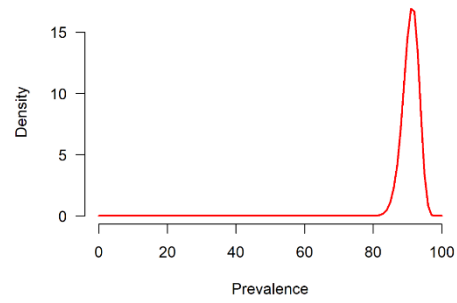
Uganda - 2004 - Tororo - 0726



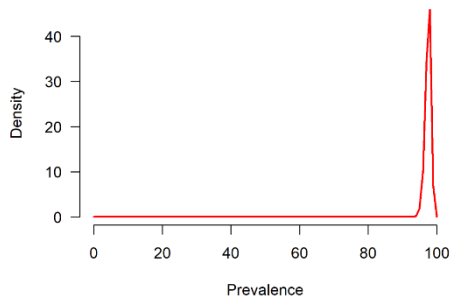
Uganda - 2004 - Tororo - 0735



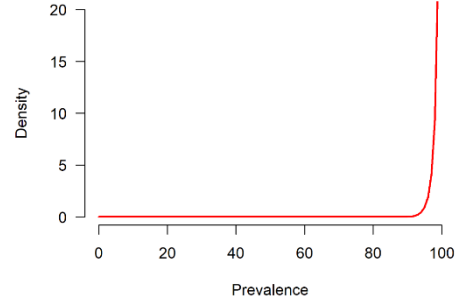
Uganda - 2004 - Tororo - 0736



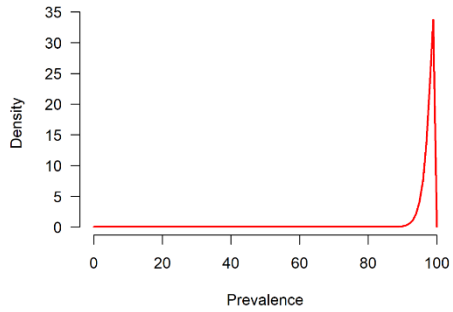
Uganda - 2004 - Tororo - 0711



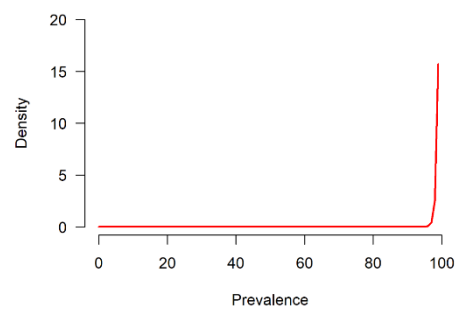
Uganda - 2005 - Kabale - 0741



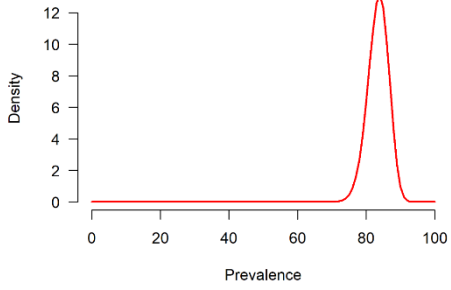
Uganda - 2005 - Rukungiri - 0740



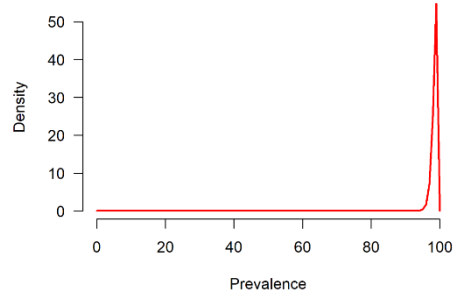
Uganda - 2005 - Tororo - 0737



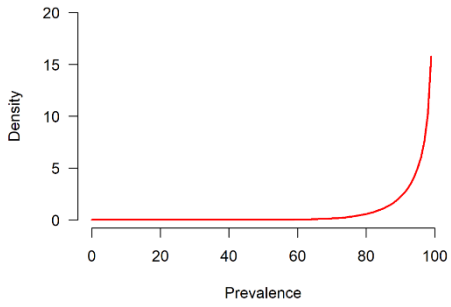
Uganda - 2005 - Tororo - 0738



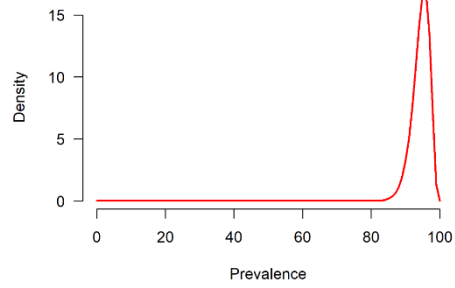
Uganda - 2005 - Tororo - 0712



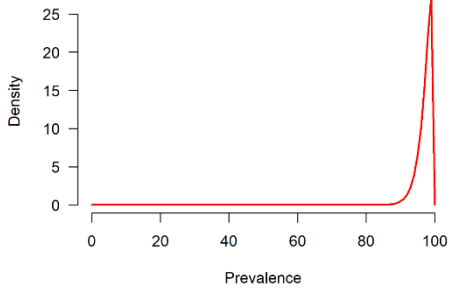
Uganda - 2006 - Kampala - 0753



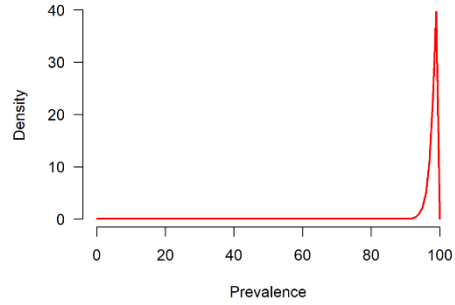
Uganda - 2006 - Kampala - 0754



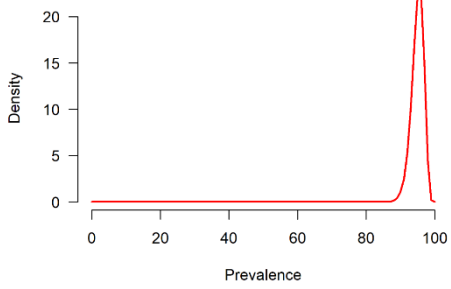
Uganda - 2006 - Tororo - 0732



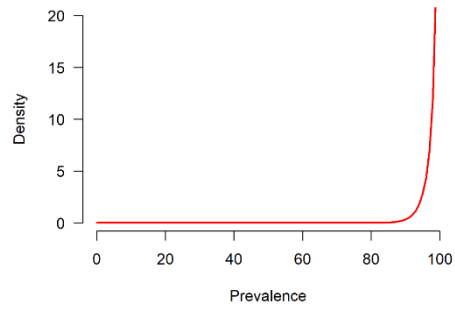
Uganda - 2006 - Tororo - 0733

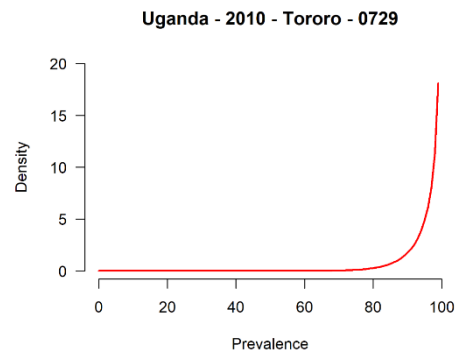
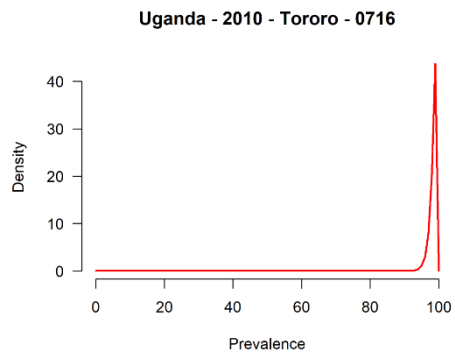
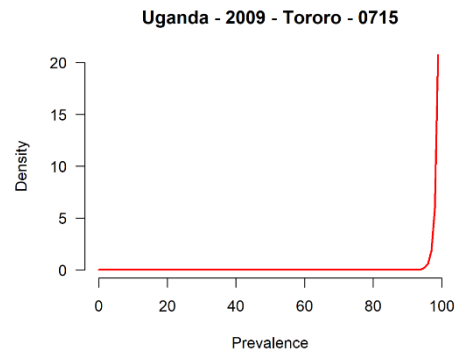
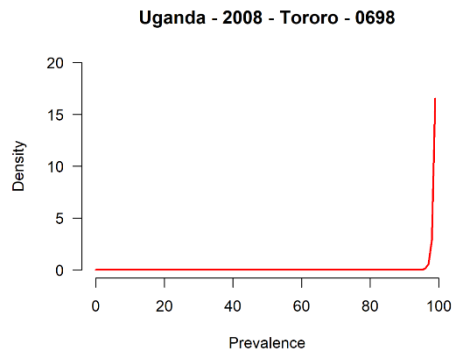
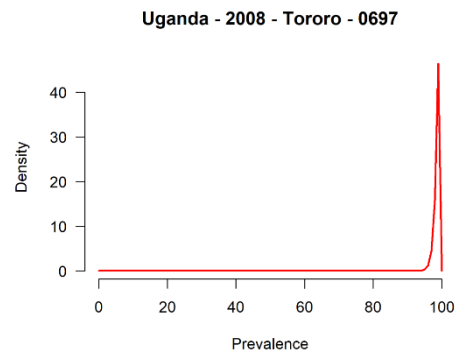
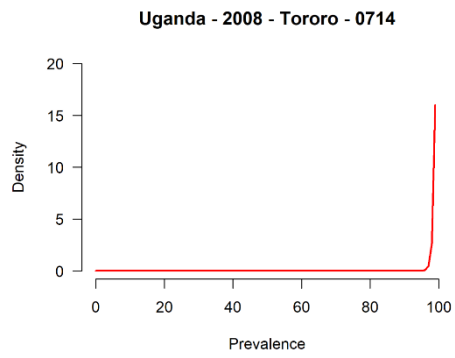
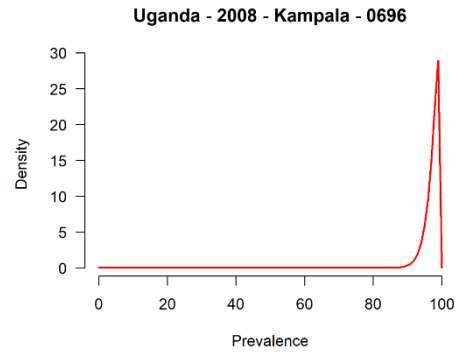
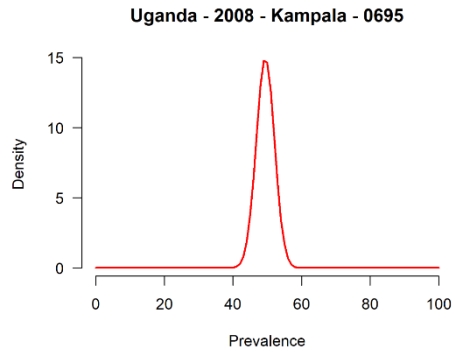


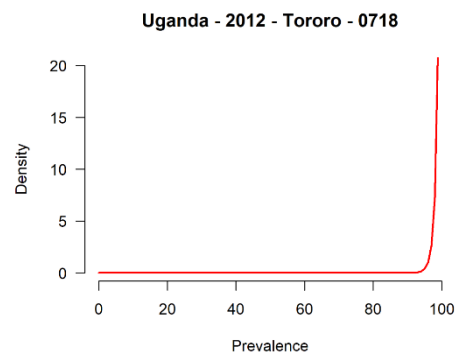
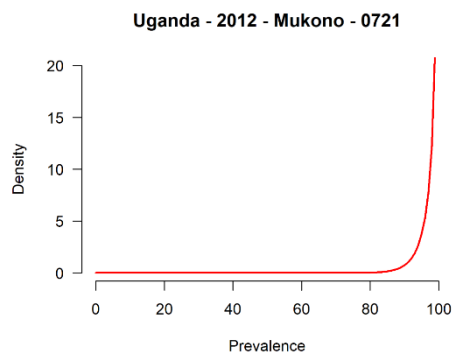
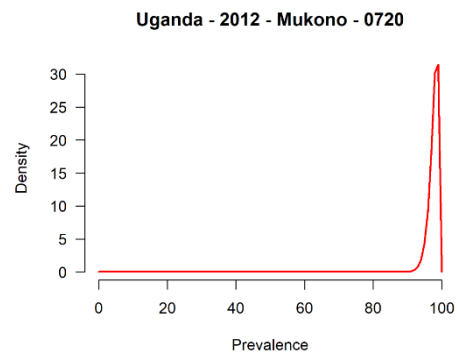
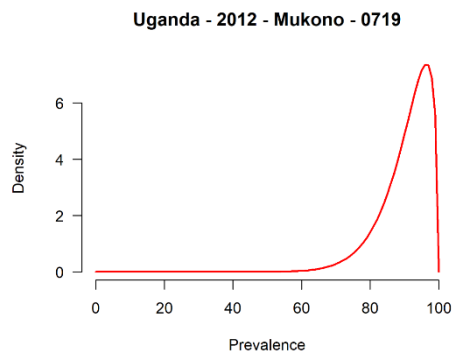
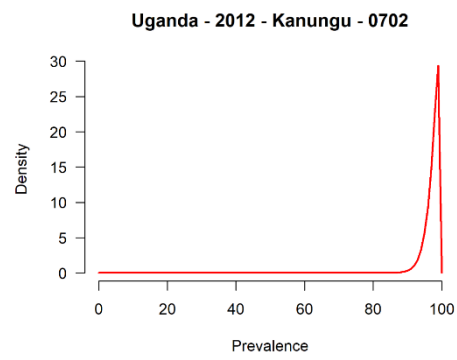
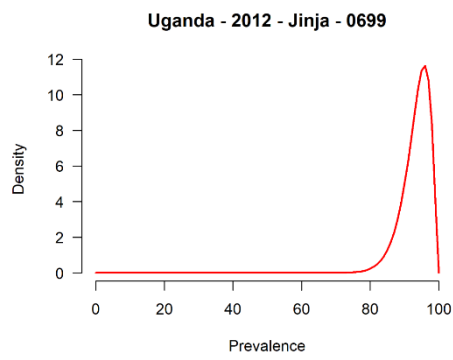
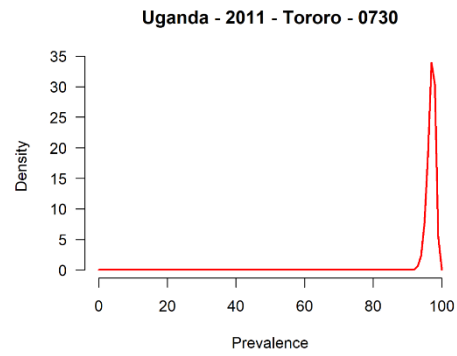
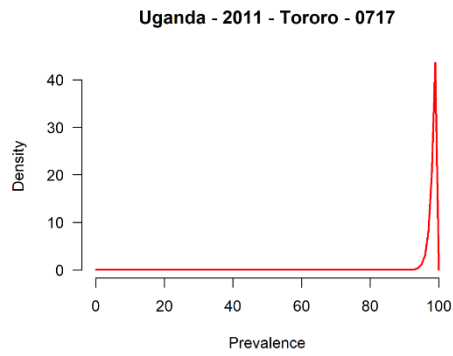
Uganda - 2006 - Tororo - 0739

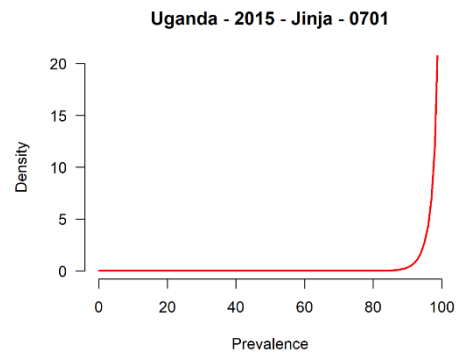
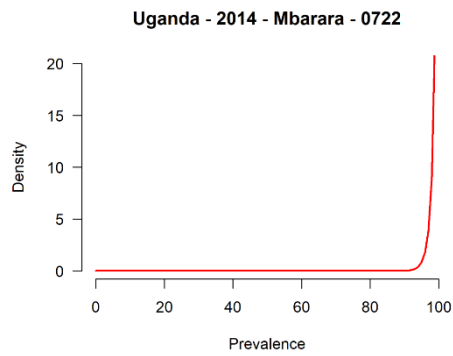
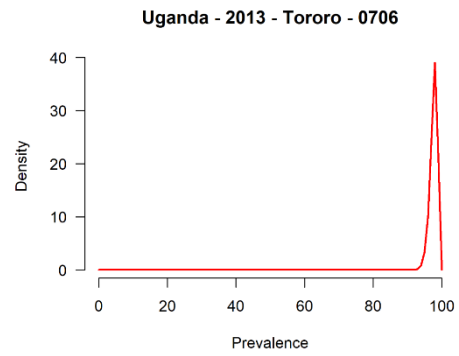
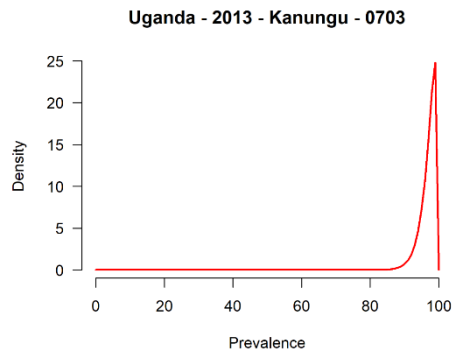
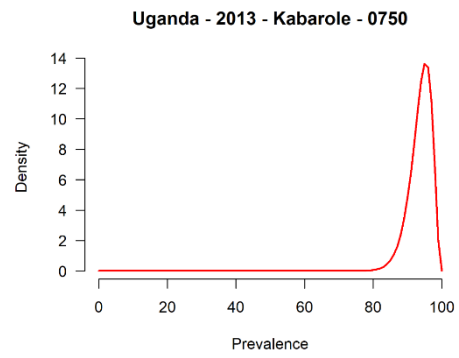
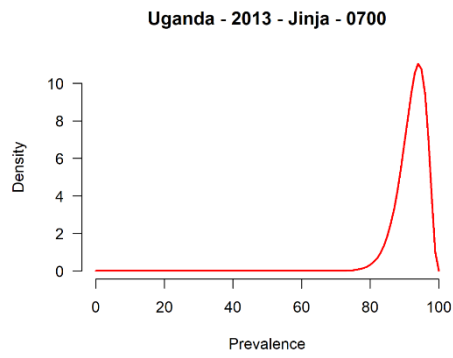
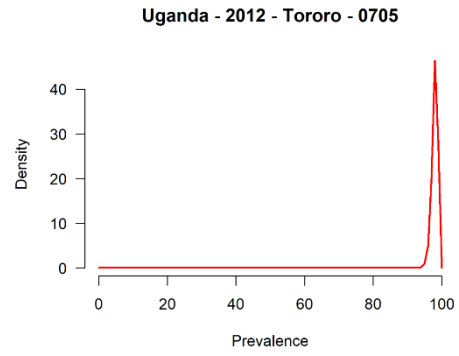
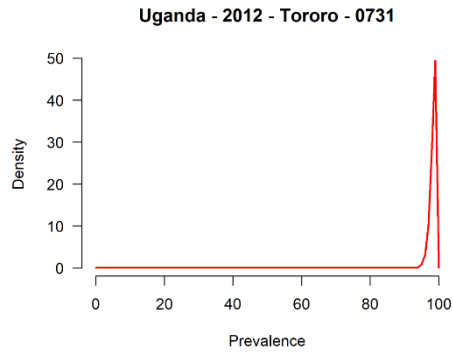


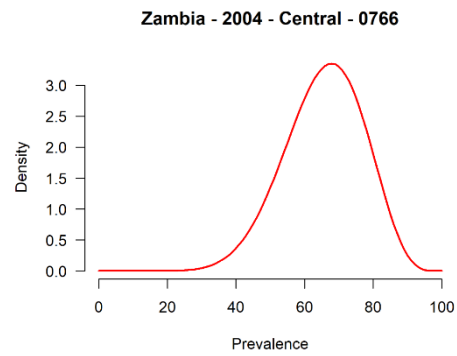
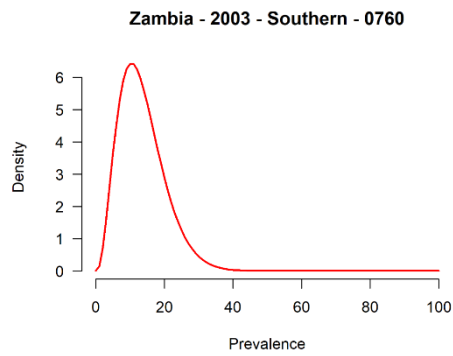
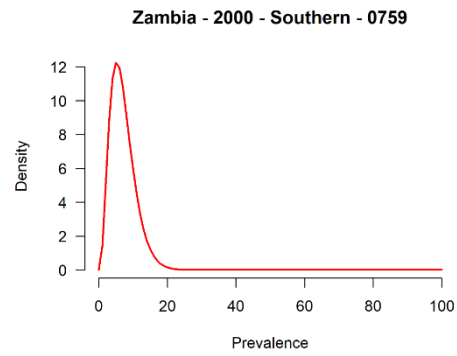
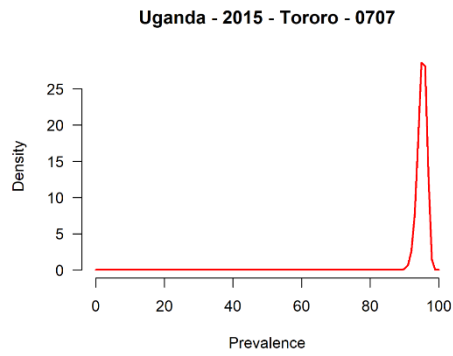
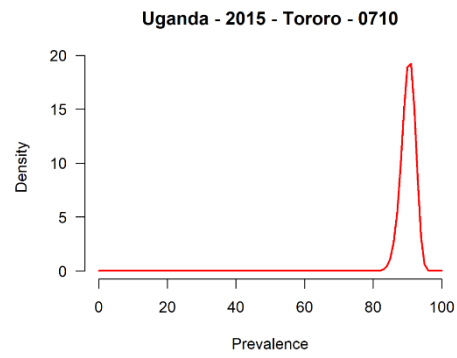
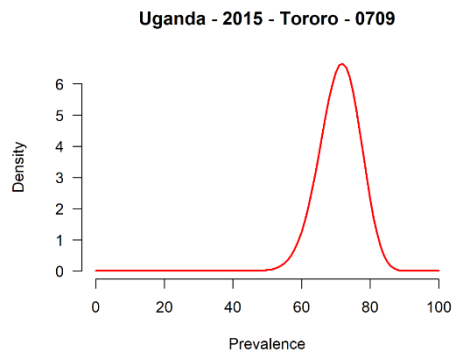
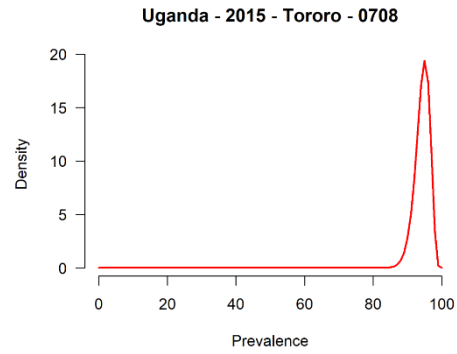
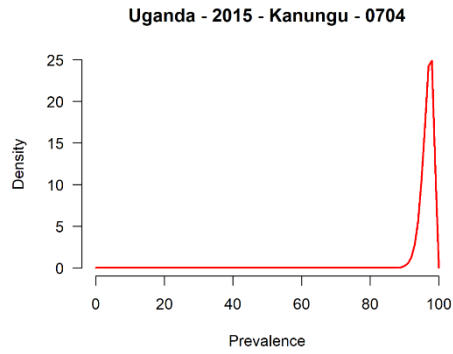
Uganda - 2007 - Tororo - 0713

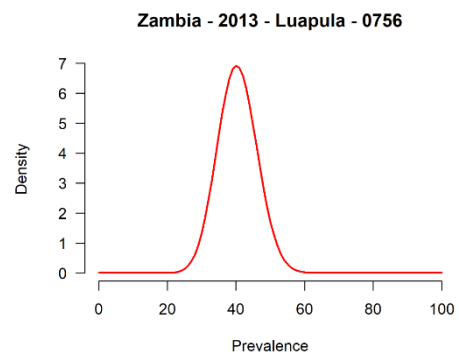
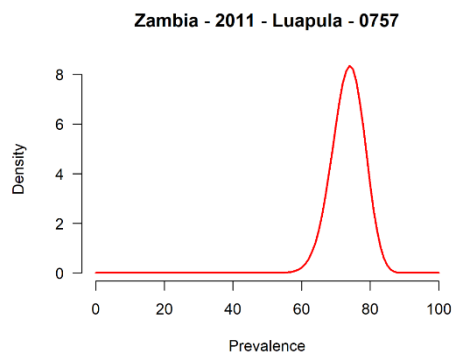
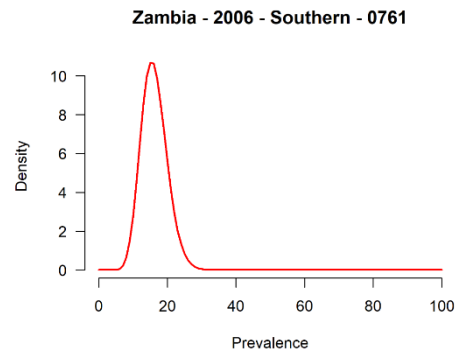
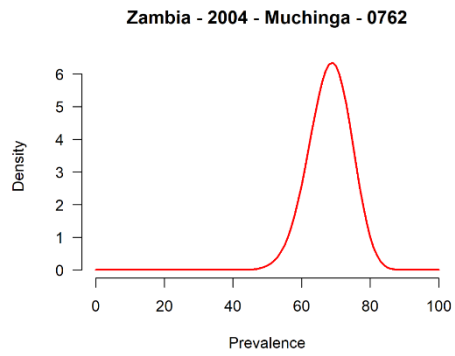
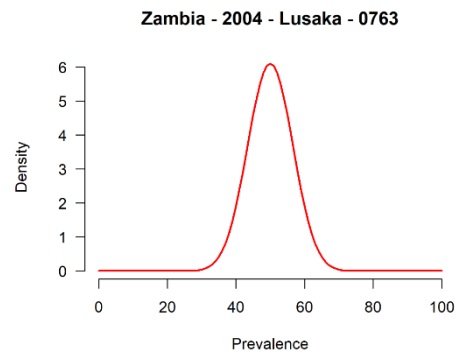
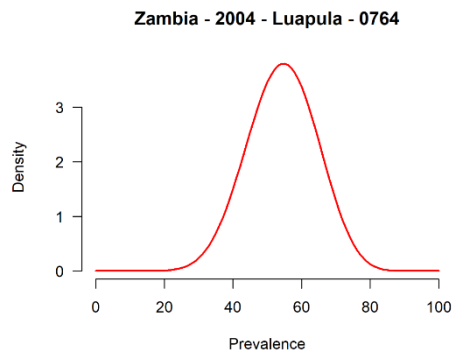
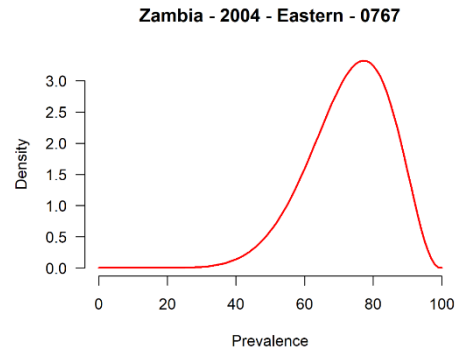
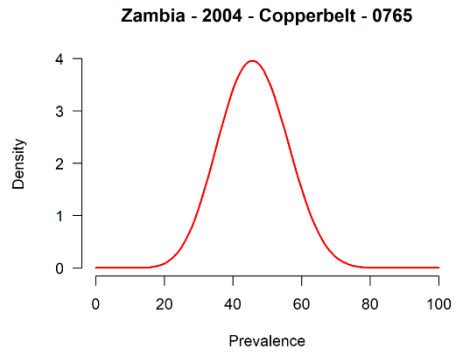




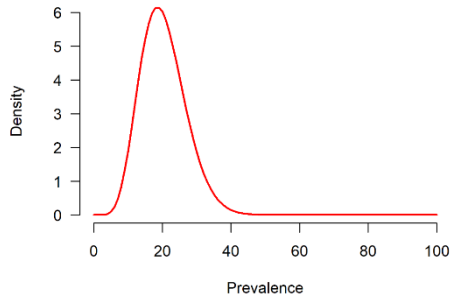




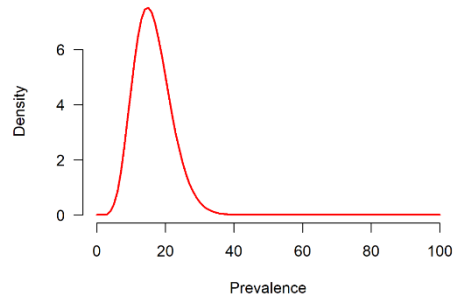




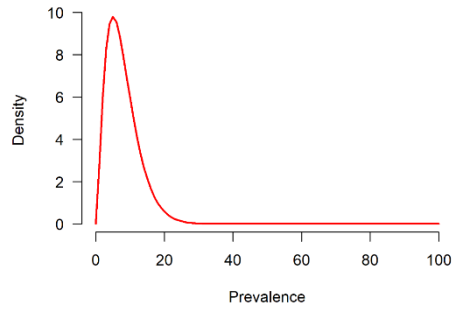
Zimbabwe - 2003 - Mashonaland Central - 0769



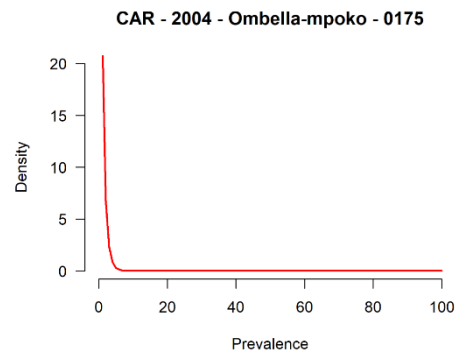
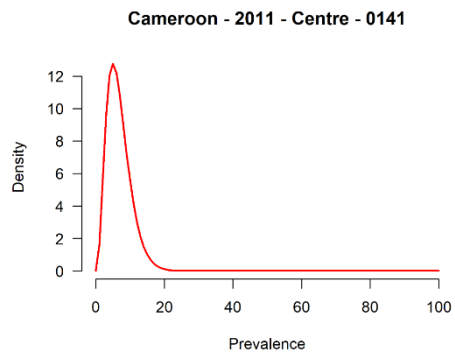
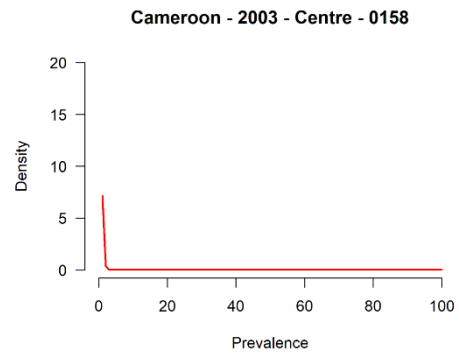
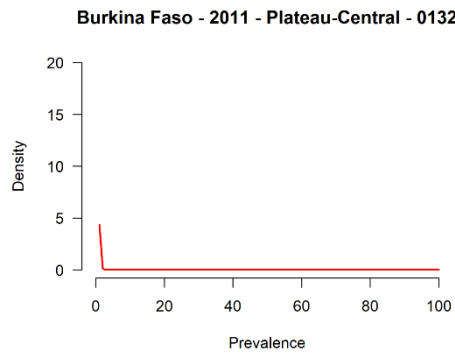
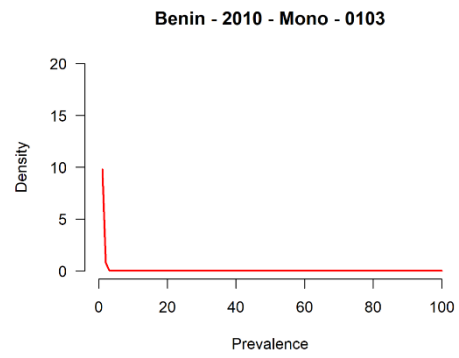
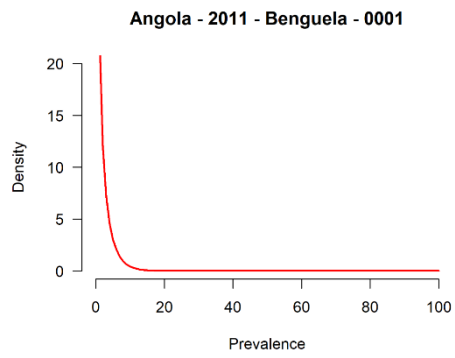
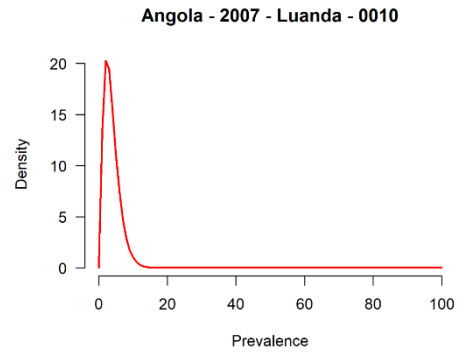
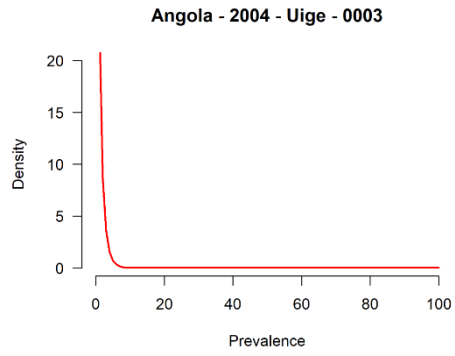
Zimbabwe - 2003 - Mashonaland West - 0770

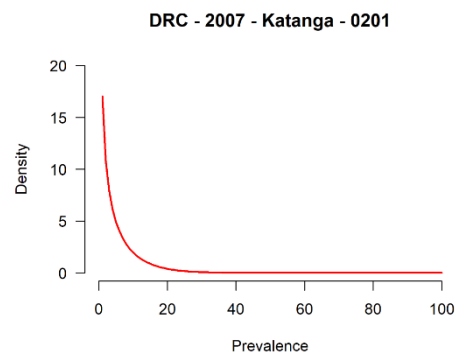
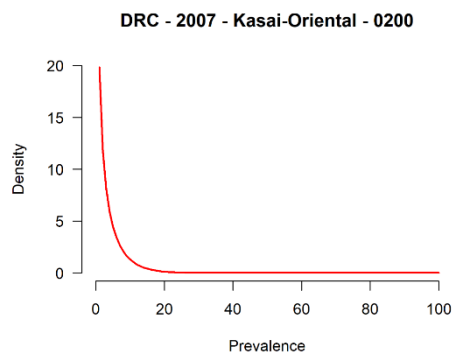
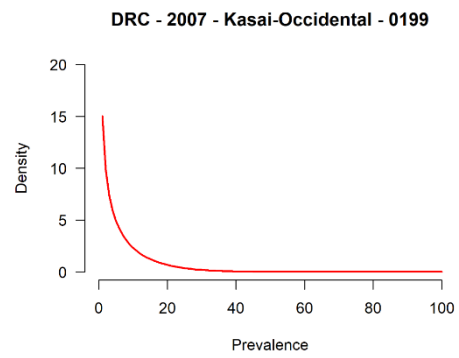
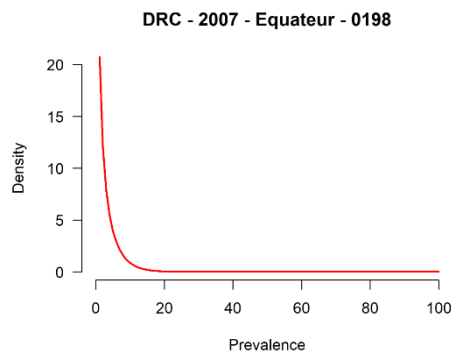
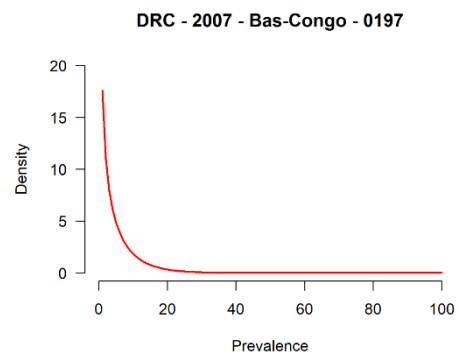
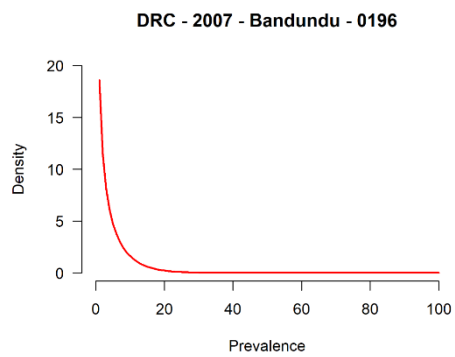
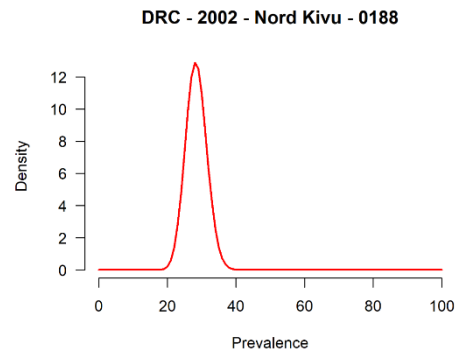
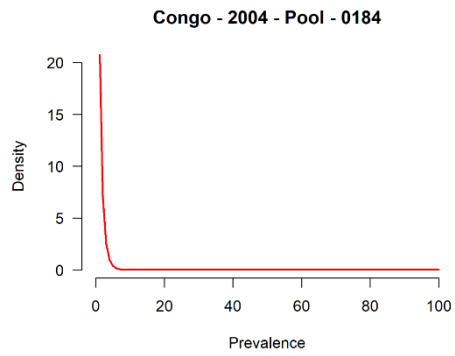


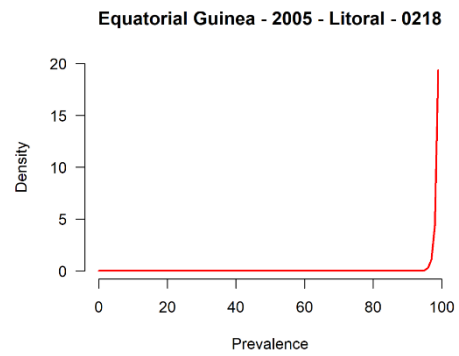
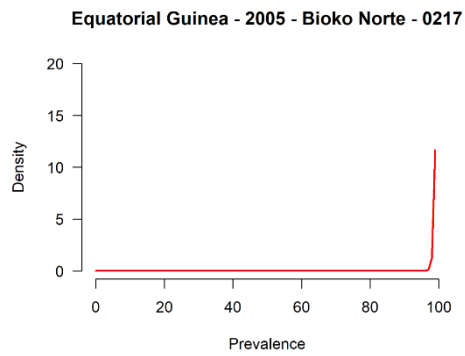
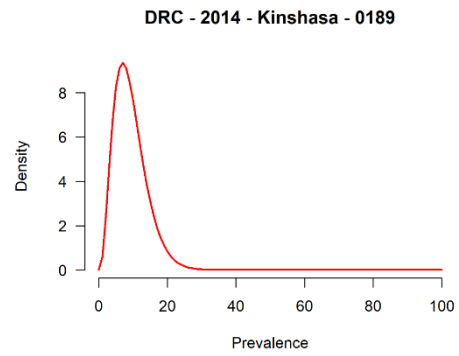
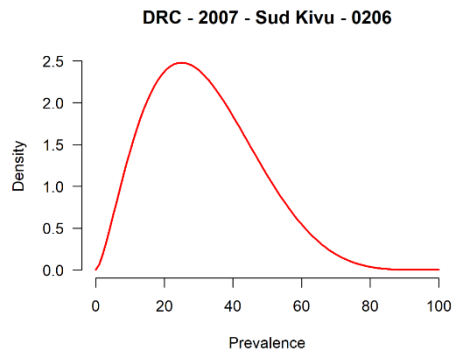
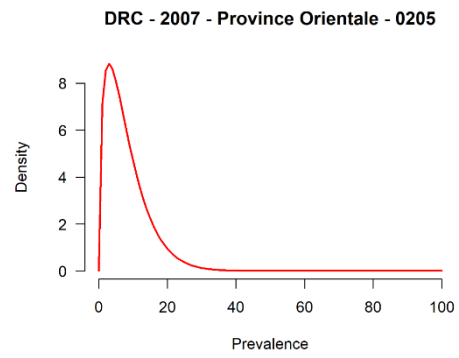
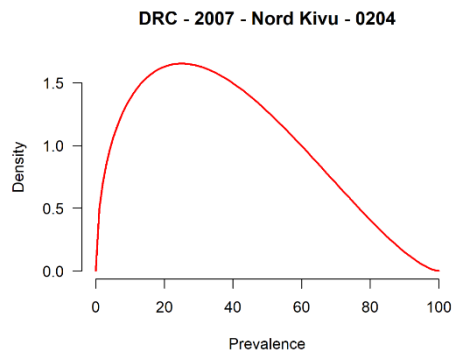
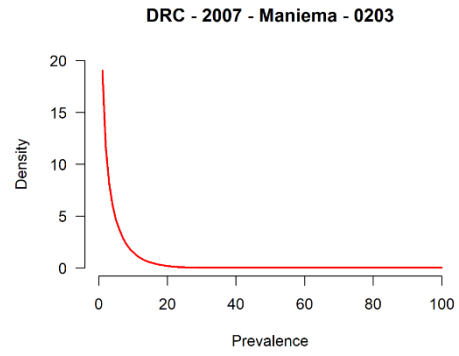
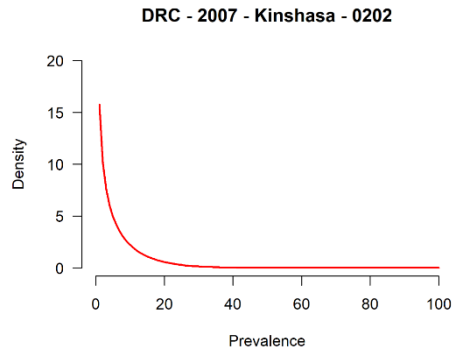
Zimbabwe - 2003 - Masvingo - 0771



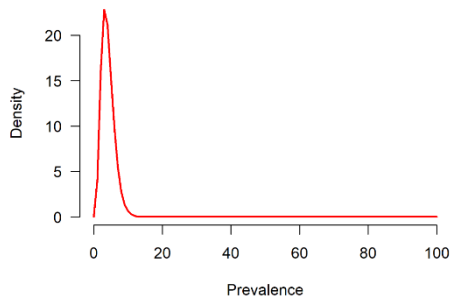
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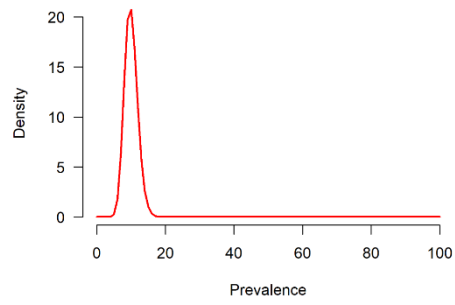




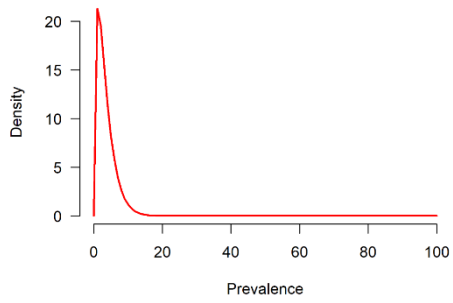
Equatorial Guinea - 2013 - Bioko Norte - 0214



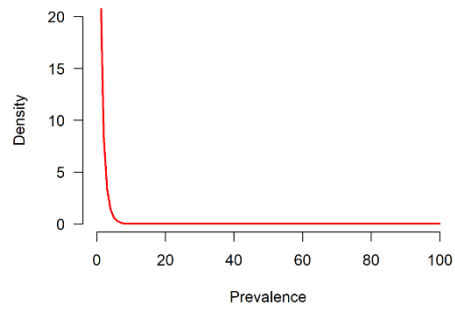
Equatorial Guinea - 2013 - Litoral - 0215



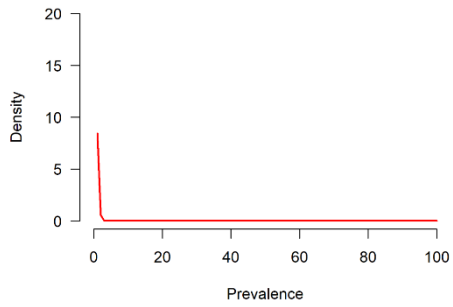
Equatorial Guinea - 2013 - Litoral - 0213



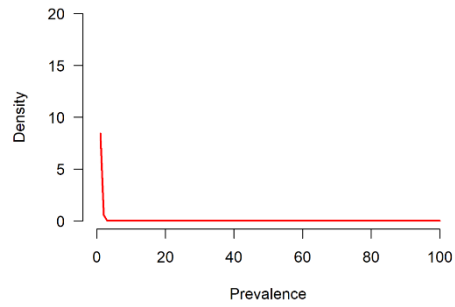
Ethiopia - 2004 - SNNP - 0227



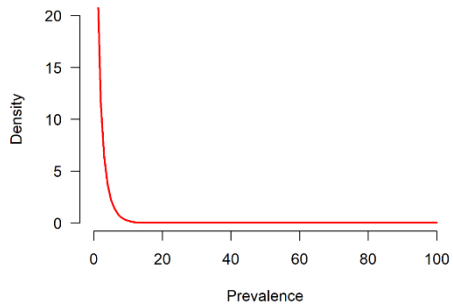
Ethiopia - 2005 - Benishangul Gumuz - 0221



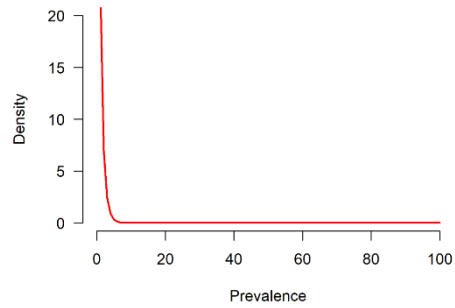
Ethiopia - 2008 - Benishangul Gumuz - 0220



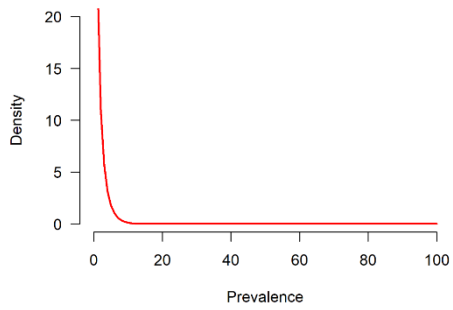
Gabon - 1998 - Haut-Ogooue - 0233



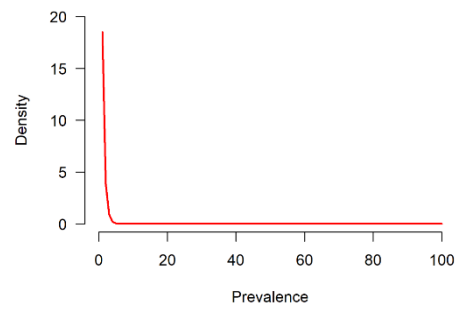
Gabon - 2000 - Haut-Ogooue - 0234



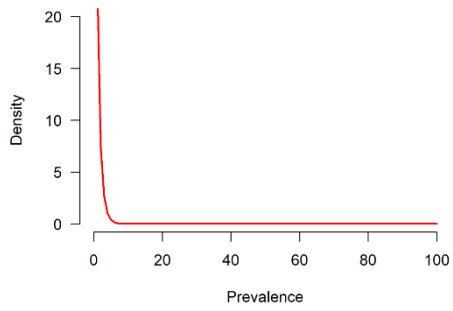
Gabon - 2005 - Estuaire - 0238



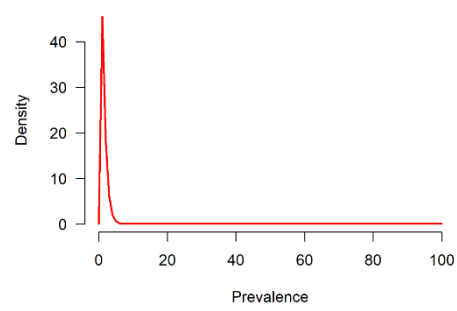
Gabon - 2007 - Moyen-Ogooue - 0242



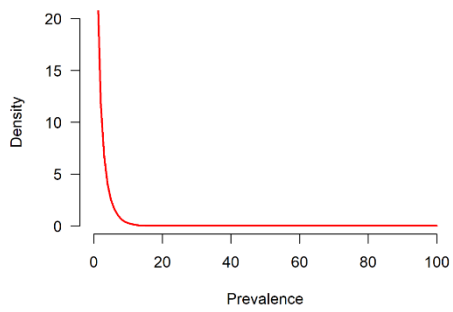
Gabon - 2011 - Estuaire - 0239



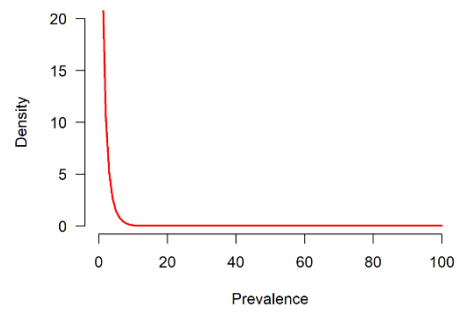
Ghana - 2002 - Northern - 0258



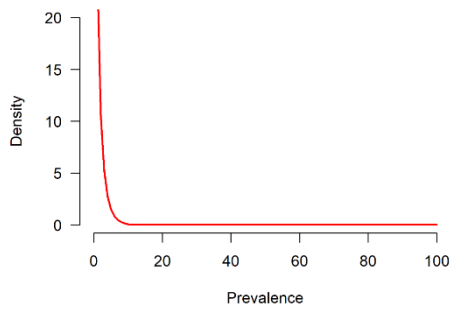
Ghana - 2008 - Ashanti - 0290



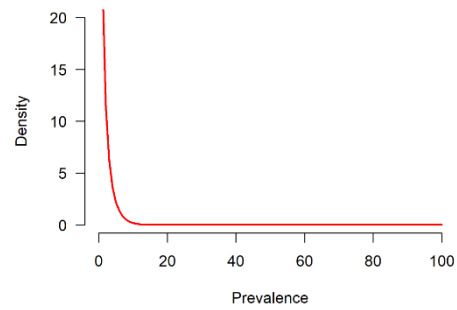
Ghana - 2008 - Brong Ahafo - 0289



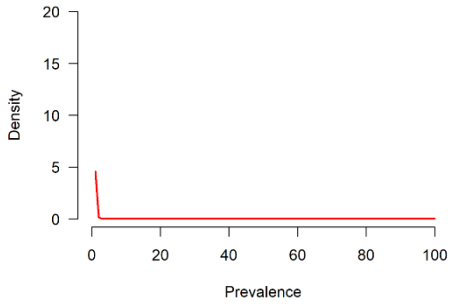
Ghana - 2008 - Central - 0291



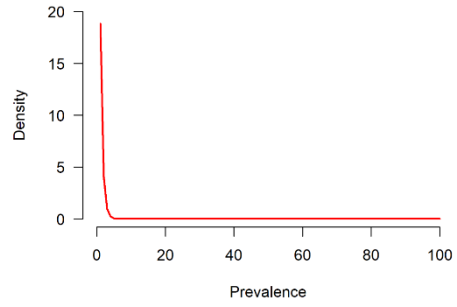
Ghana - 2008 - Upper East - 0288



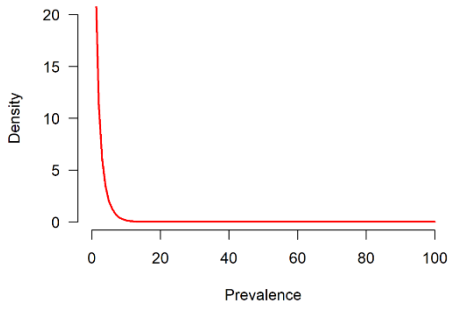
Guinea-Bissau - 2016 - Bissau Autonomous Sector - 0:



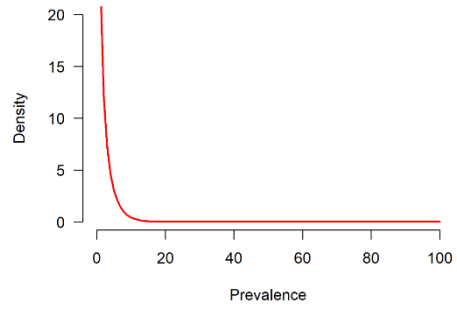
Ivory Coast - 2001 - Abidjan - 0306



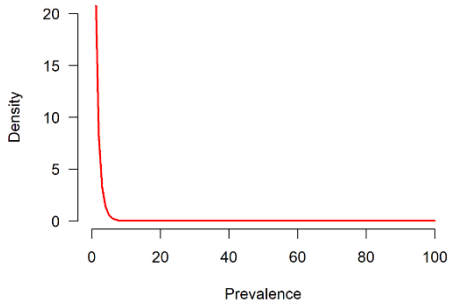
Ivory Coast - 2005 - Comoe - 0307



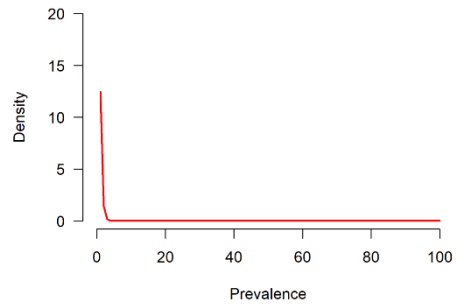
Ivory Coast - 2005 - Lagunes - 0308



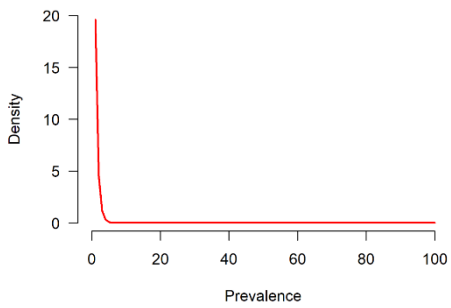
Kenya - 1998 - Coast - 0376



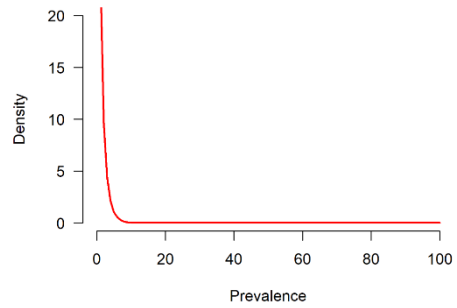
Kenya - 2000 - Nyanza - 0355

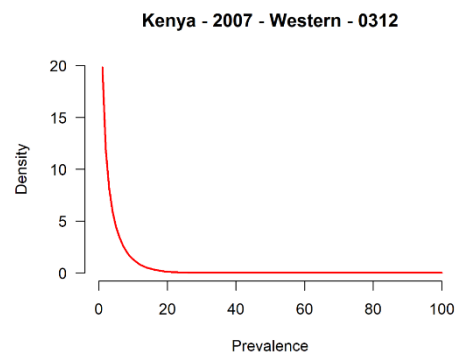
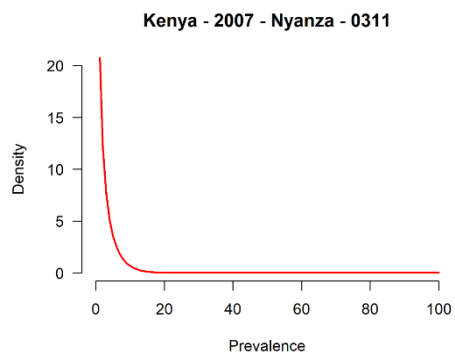
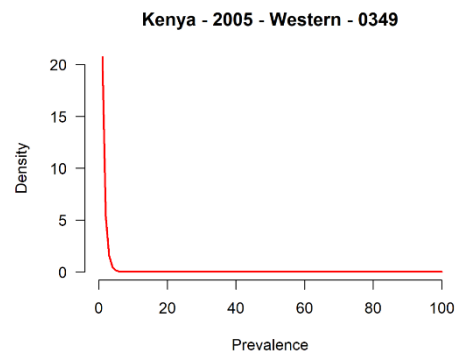
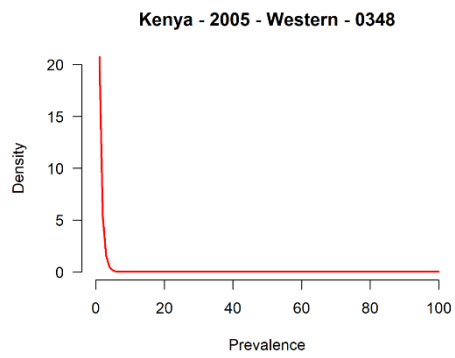
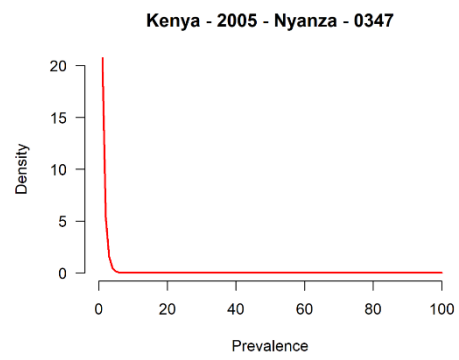
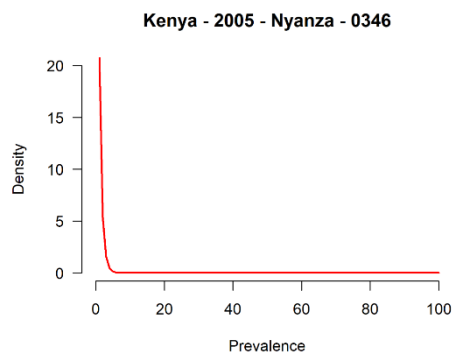
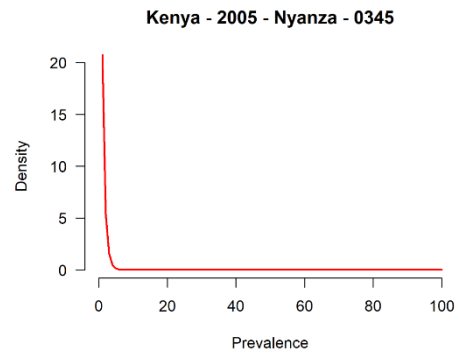
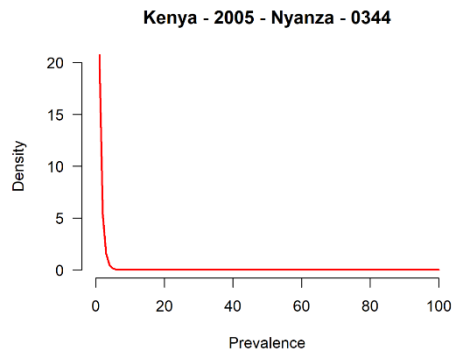


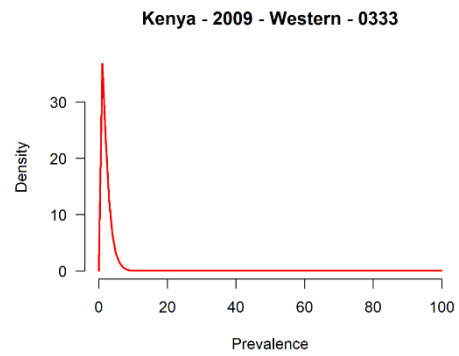
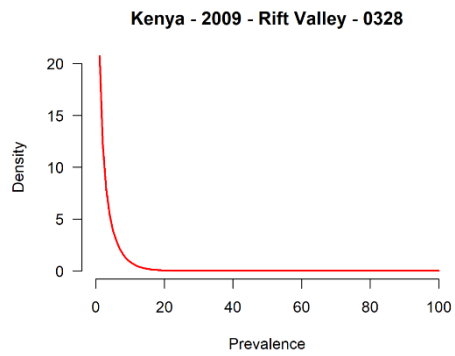
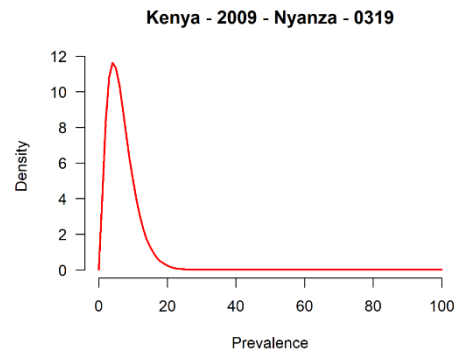
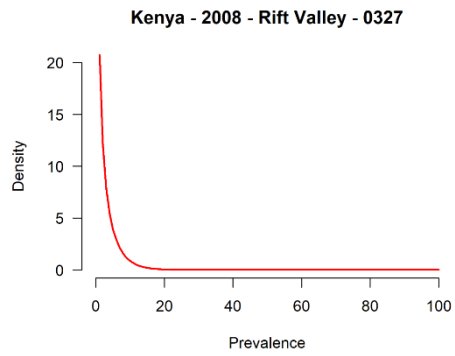
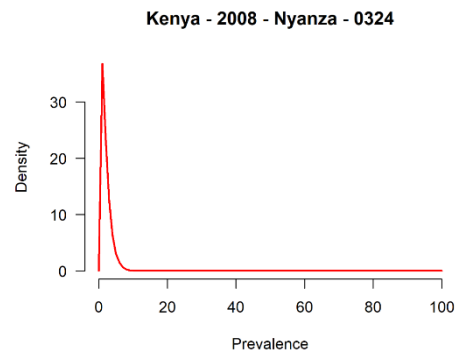
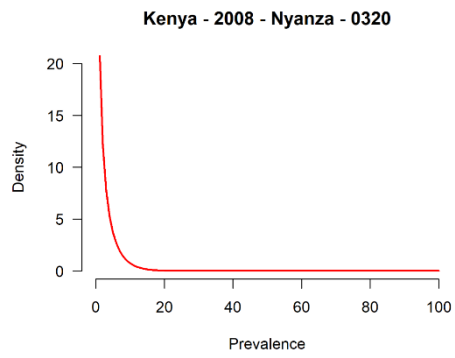
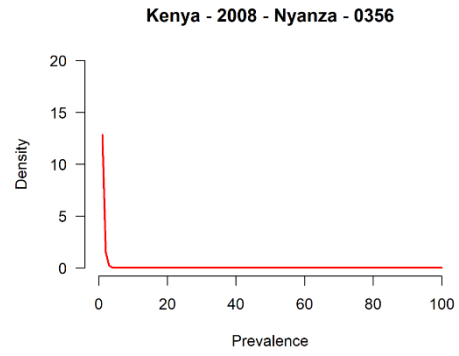
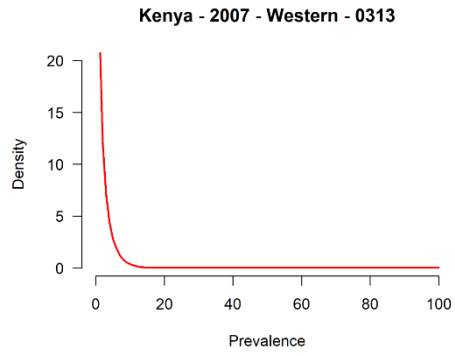
Kenya - 2001 - Western - 0315

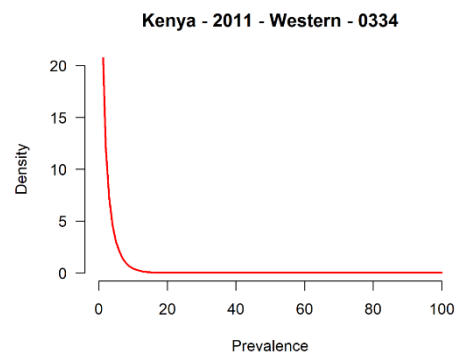
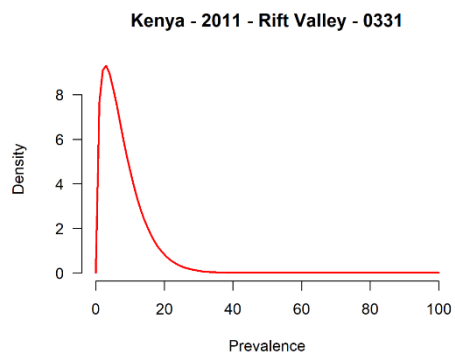
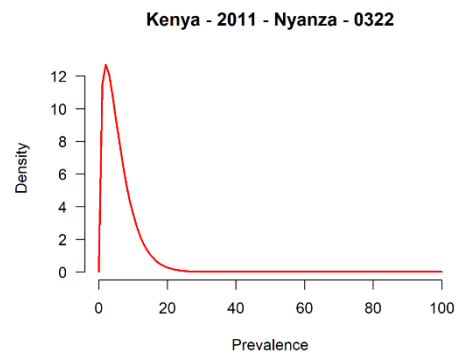
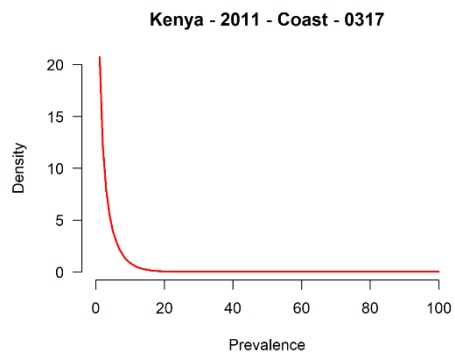
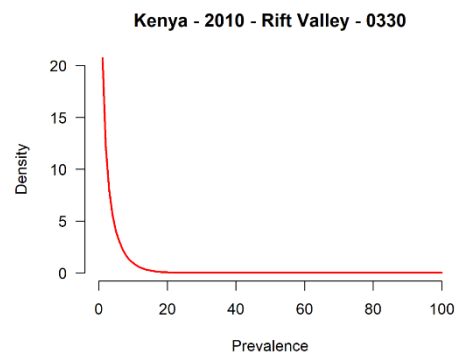
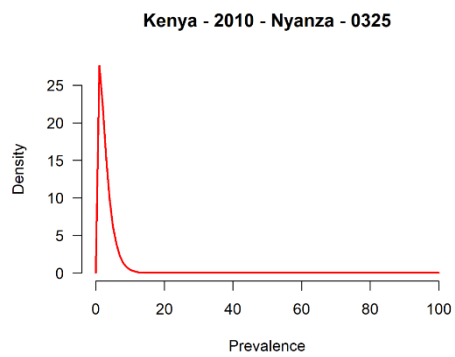
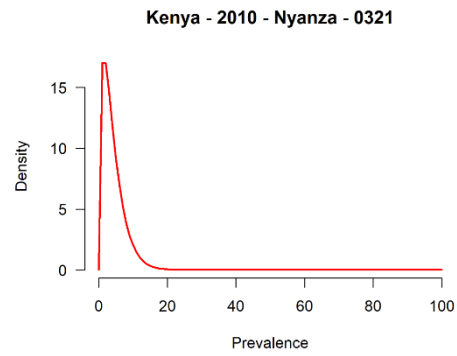
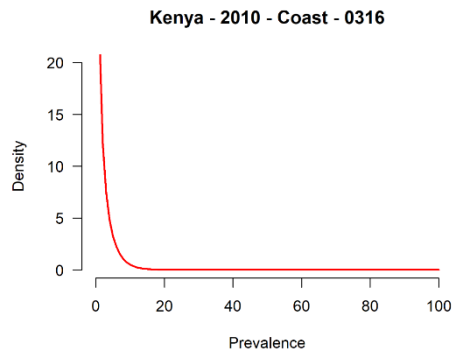


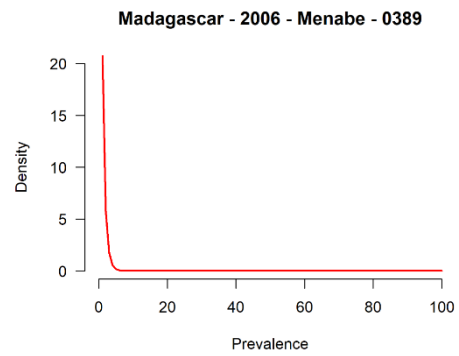
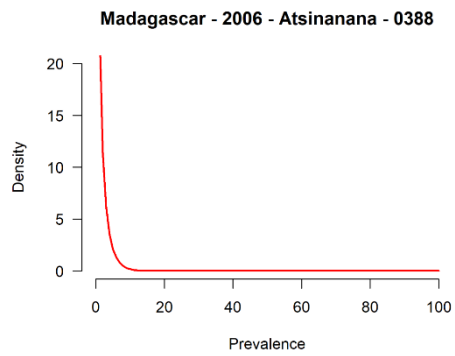
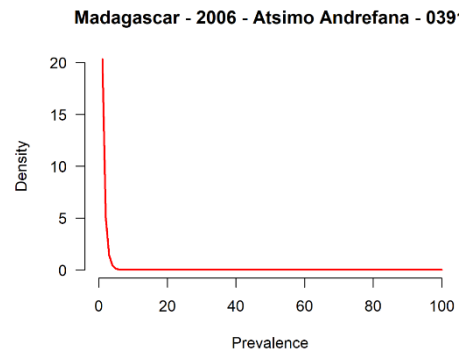
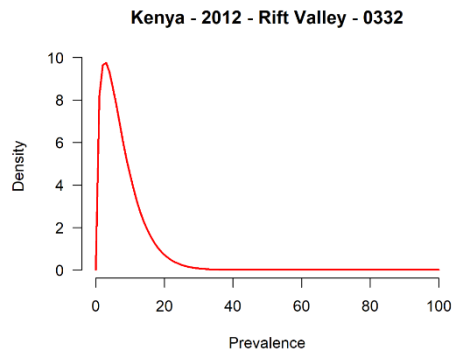
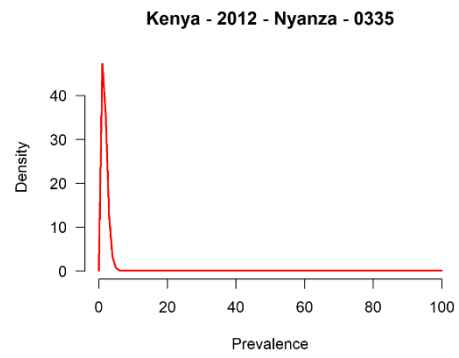
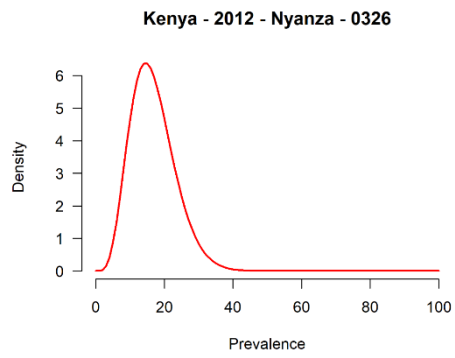
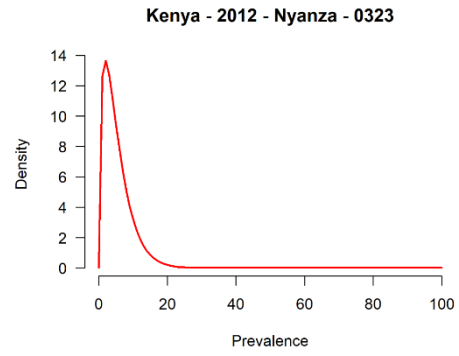
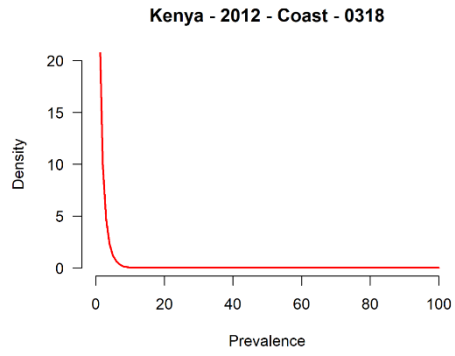
Kenya - 2004 - Nyanza - 0365



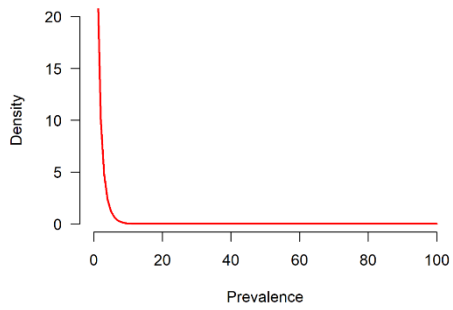




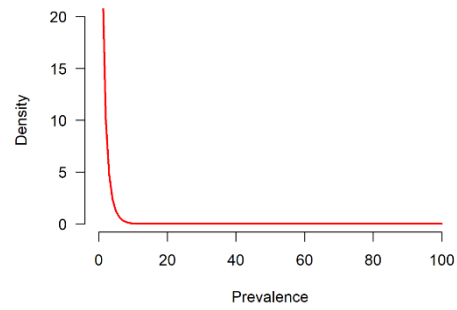




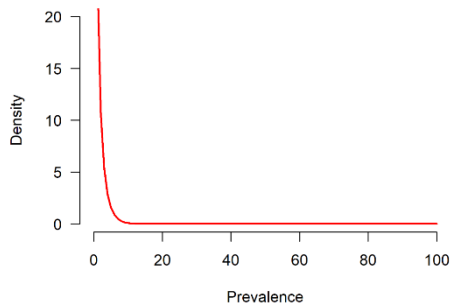
Madagascar - 2006 - Sofia - 0390



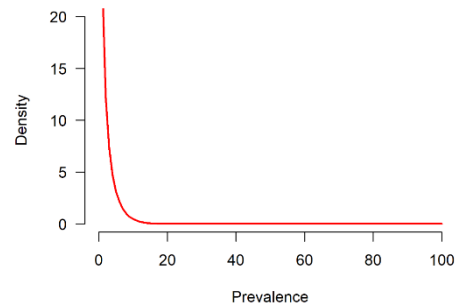
Madagascar - 2007 - Atsimo Andrefana - 0397



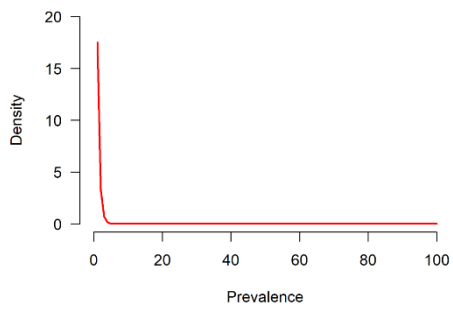
Madagascar - 2007 - Atsimo Atsinanana - 0396



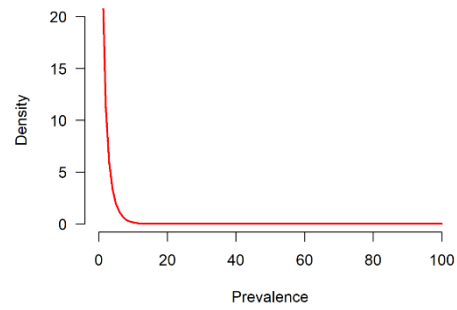
Madagascar - 2007 - Atsinanana - 0392



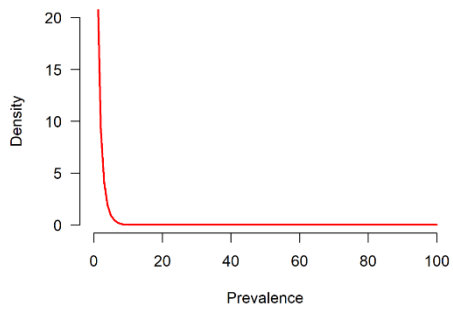
Madagascar - 2007 - Menabe - 0393



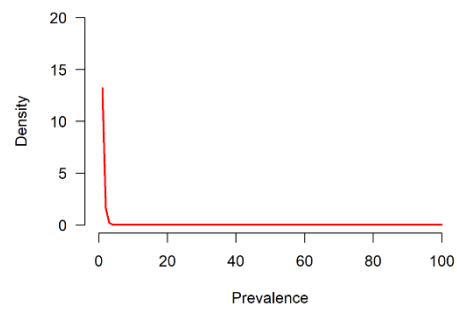
Madagascar - 2007 - Sava - 0394



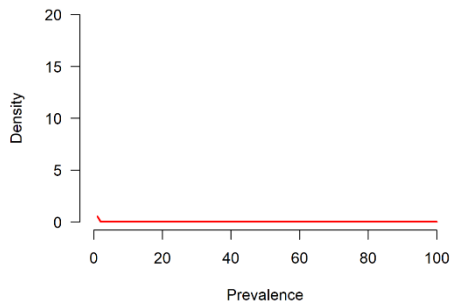
Madagascar - 2007 - Sofia - 0395



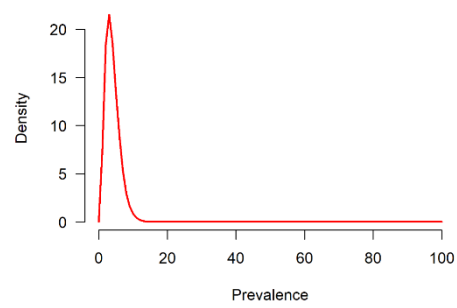
Malawi - 2000 - Central Region - 0415



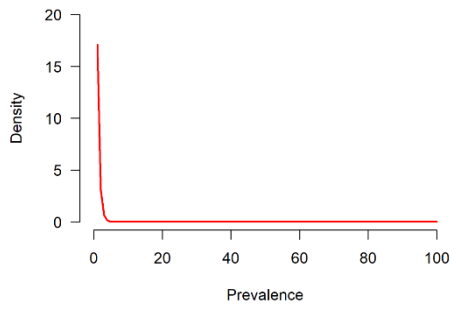
Malawi - 2001 - Southern Region - 0412



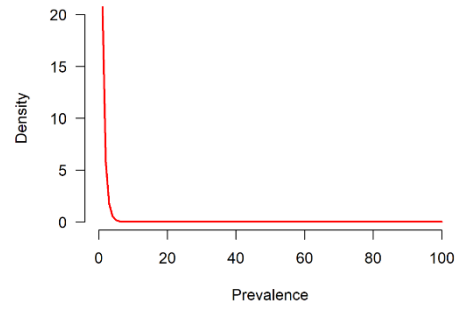
Malawi - 2003 - Southern Region - 0416



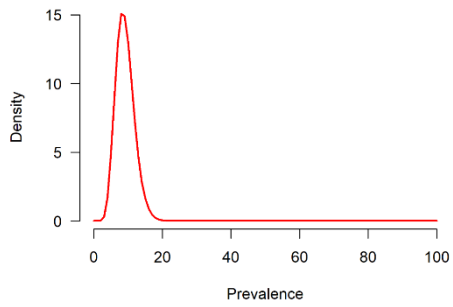
Malawi - 2005 - Southern Region - 0423



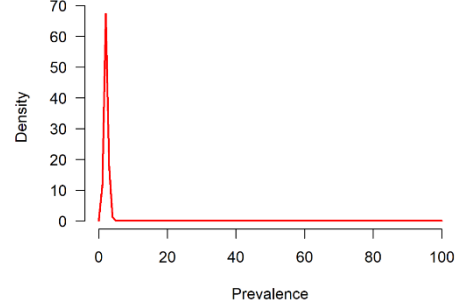
Malawi - 2005 - Southern Region - 0424



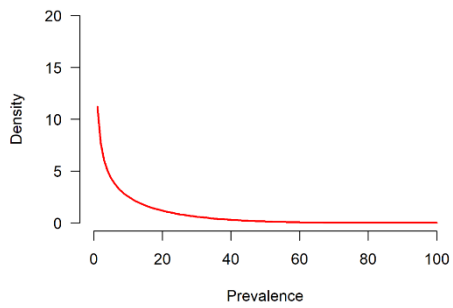
Malawi - 2005 - Southern Region - 0417



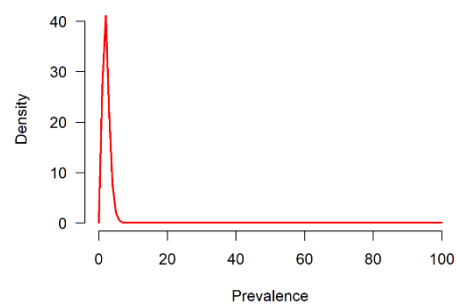
Malawi - 2009 - Southern Region - 0413



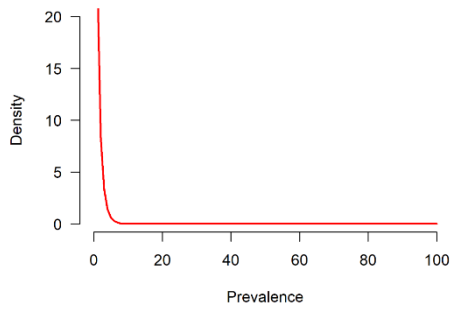
Malawi - 2011 - Southern Region - 0G25



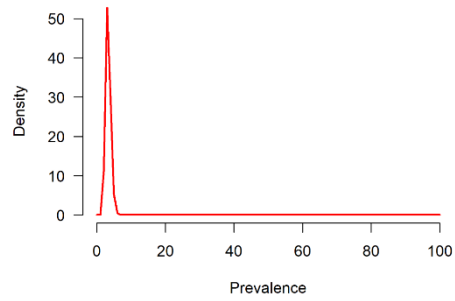
Malawi - 2011 - Southern Region - 0409



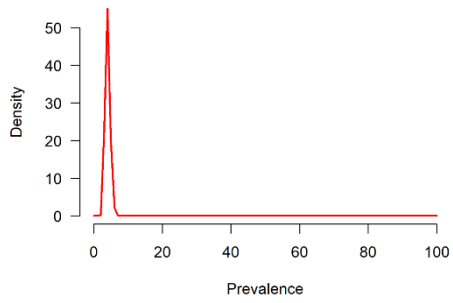
Malawi - 2011 - Southern Region - 0425



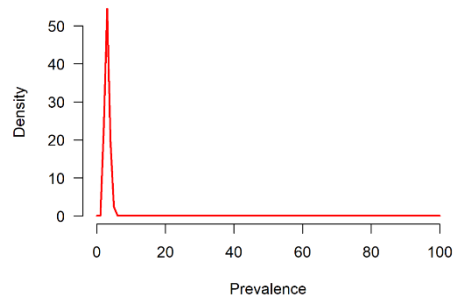
Malawi - 2012 - Southern Region - 0399



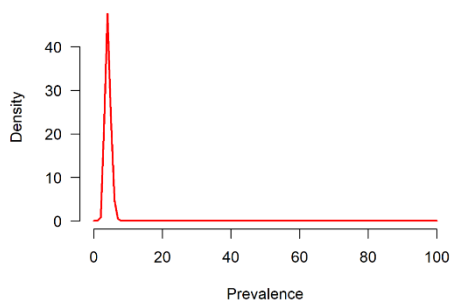
Malawi - 2012 - Southern Region - 0400



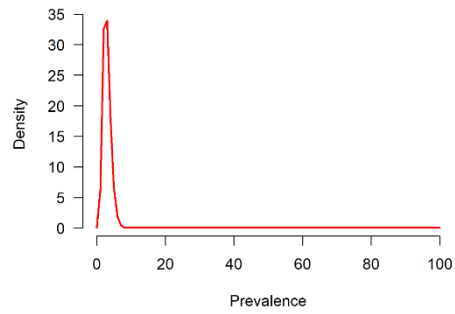
Malawi - 2012 - Southern Region - 0401



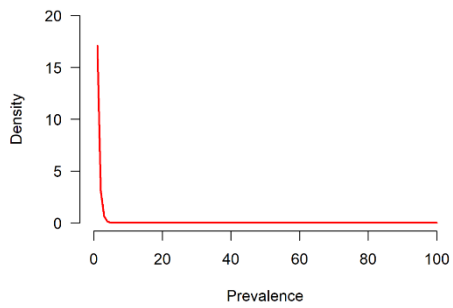
Malawi - 2012 - Southern Region - 0414



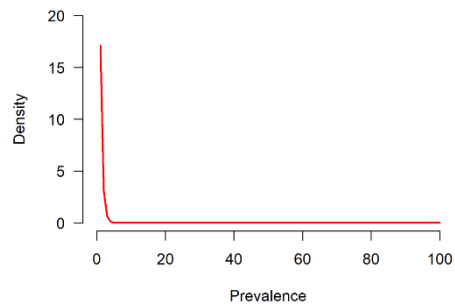
Malawi - 2012 - Southern Region - 0404



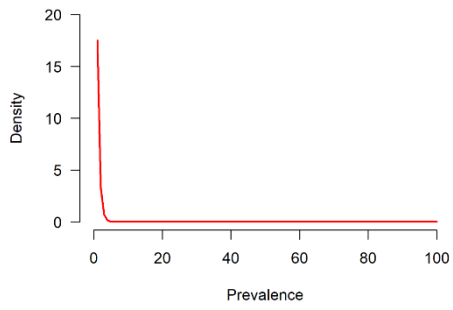
Mali - 2010 - Kayes - 0452



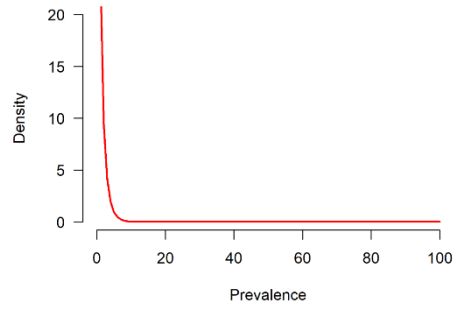
Mali - 2010 - Segou - 0451



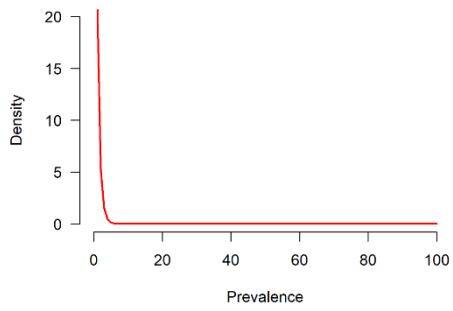
Mali - 2010 - Segou - 0435



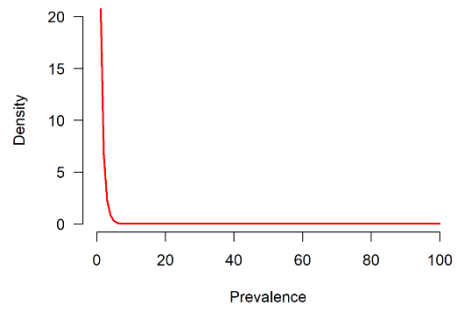
Mauritania - 1998 - Hodh el Gharbi - 0457



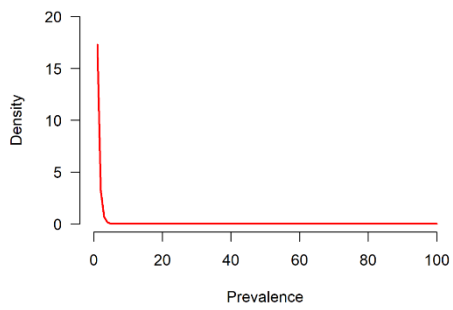
Mauritania - 1998 - Hodh el Gharbi - 0458



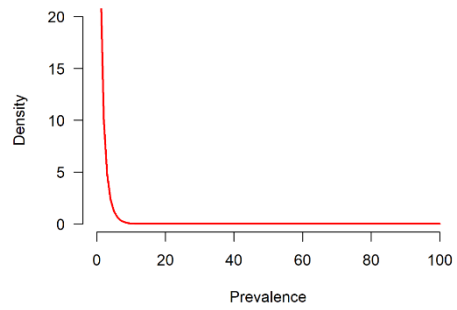
Mauritania - 2010 - Hodh el Gharbi - 0454



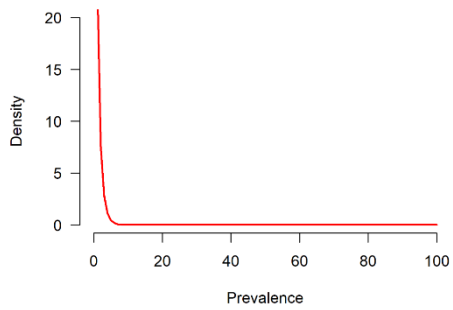
Mauritania - 2010 - Hodh el Gharbi - 0455



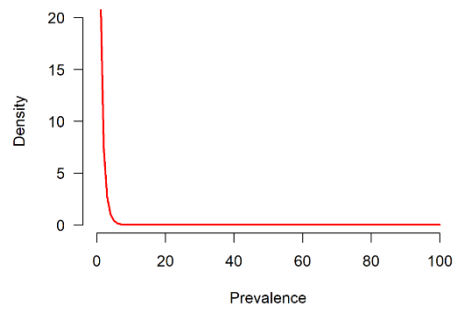
Mauritania - 2010 - Hodh el Gharbi - 0456

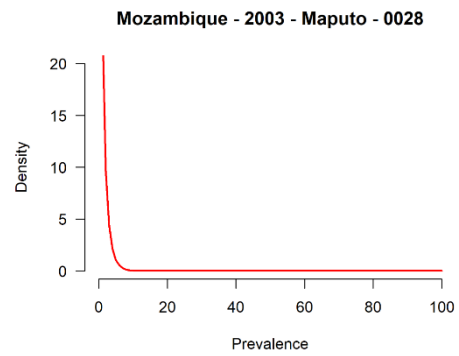
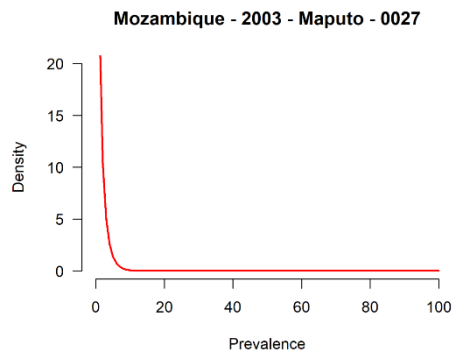
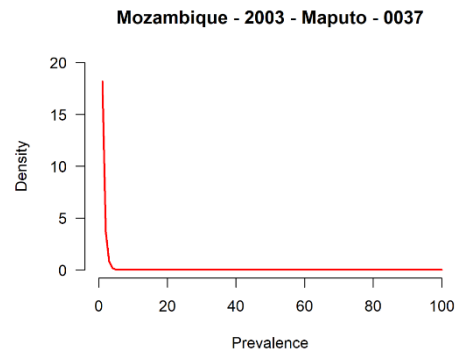
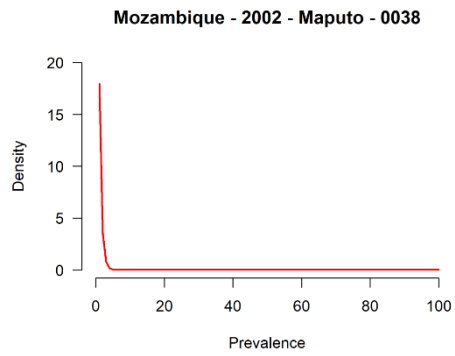
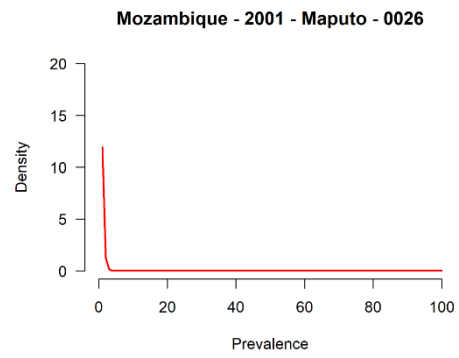
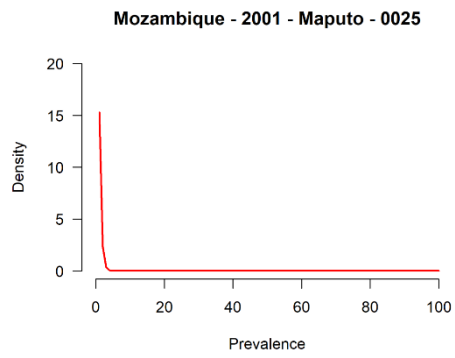
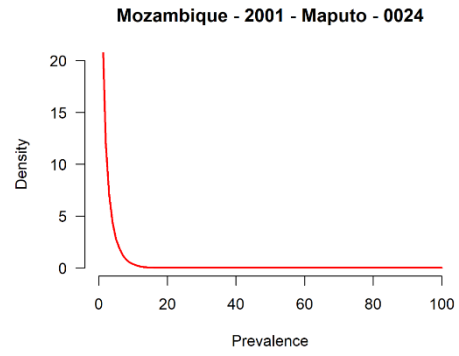
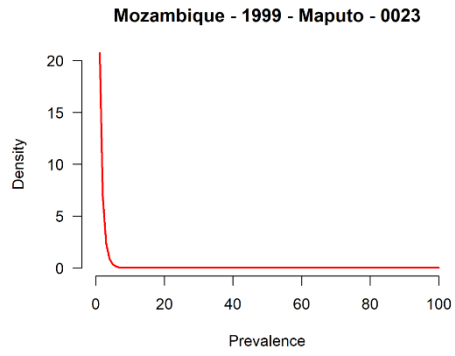


Mozambique - 1999 - Maputo - 0021

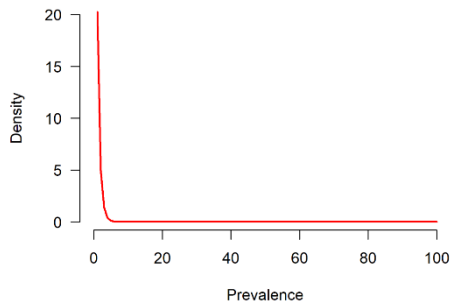


Mozambique - 1999 - Maputo - 0022

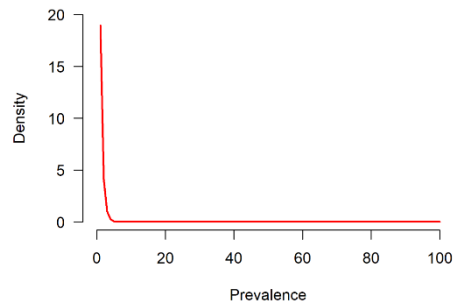




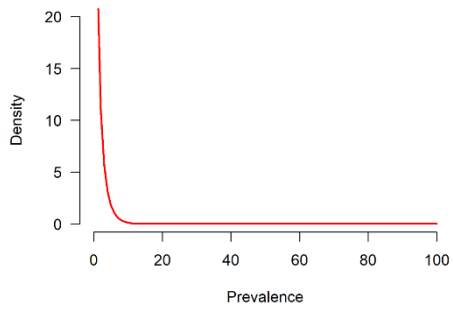
Mozambique - 2003 - Maputo - 0029



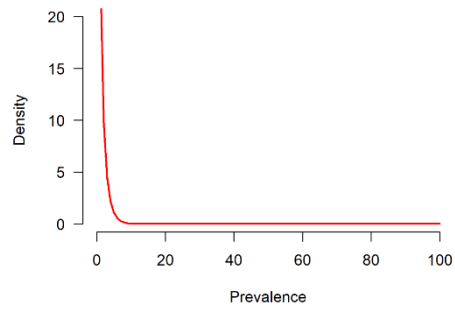
Mozambique - 2004 - Maputo - 0030



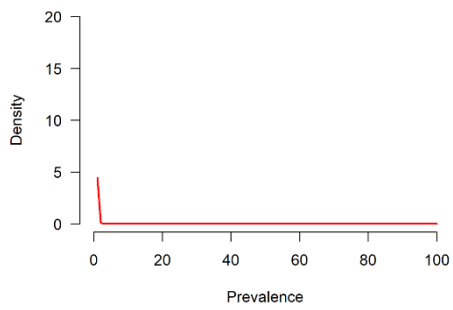
Mozambique - 2004 - Maputo - 0031



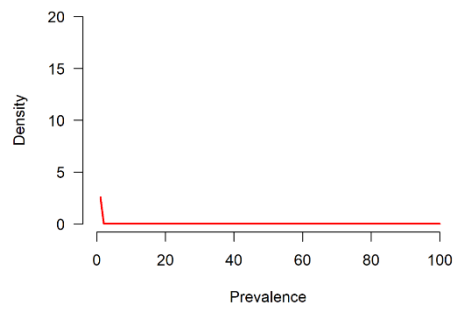
Mozambique - 2004 - Maputo - 0032



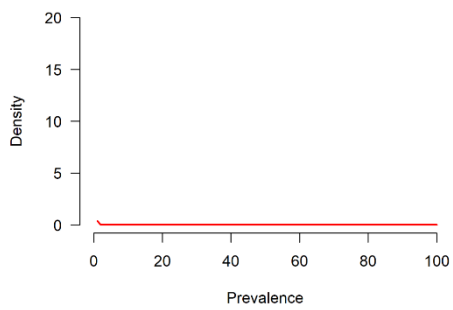
Mozambique - 2006 - Gaza - 0076



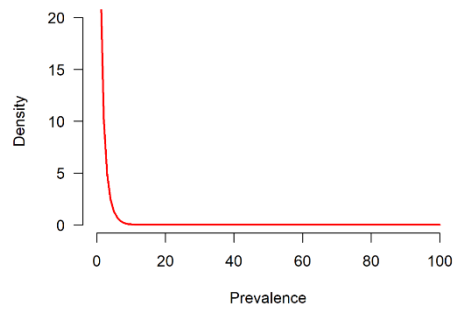
Mozambique - 2006 - Gaza - 0077



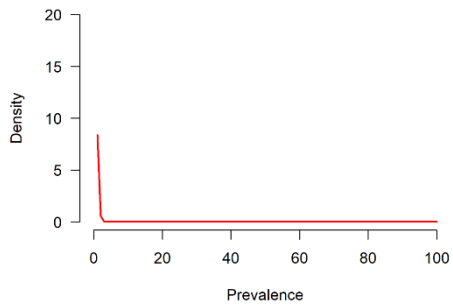
Mozambique - 2006 - Gaza - 0078



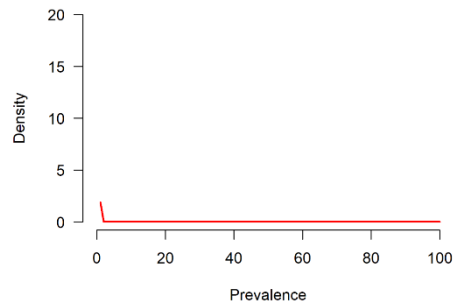
Mozambique - 2007 - Gaza - 0079



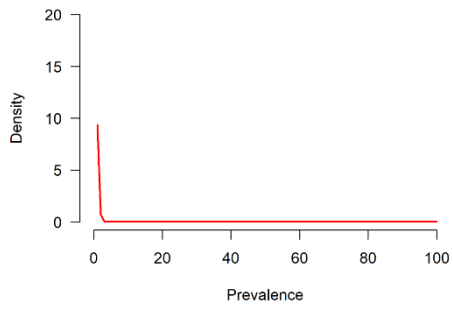
Mozambique - 2007 - Gaza - 0080



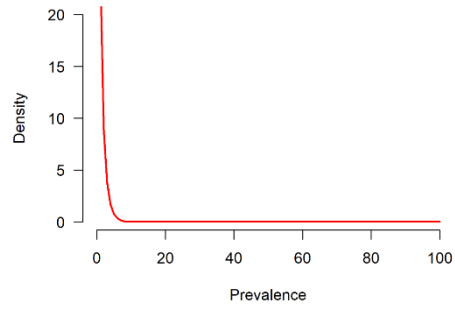
Mozambique - 2007 - Gaza - 0081



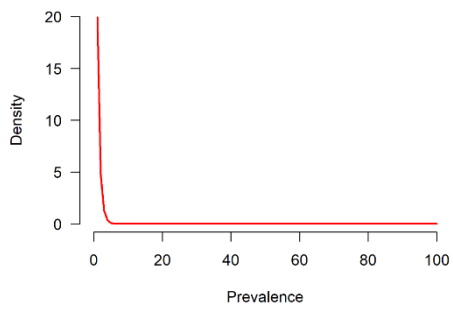
Mozambique - 2008 - Gaza - 0082



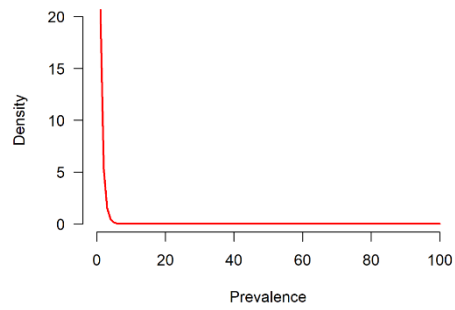
Mozambique - 2008 - Gaza - 0083



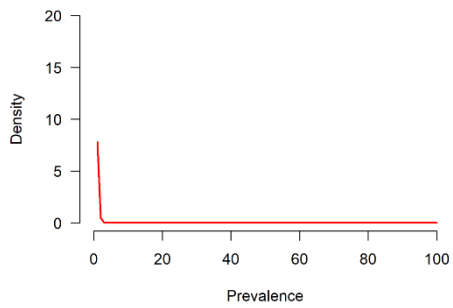
Mozambique - 2008 - Gaza - 0084



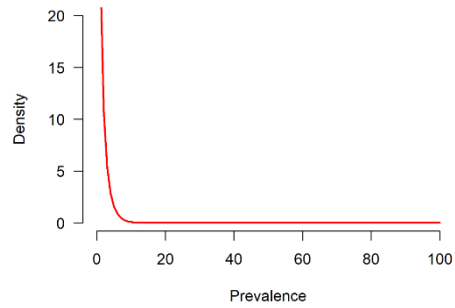
Mozambique - 2008 - Gaza - 0085



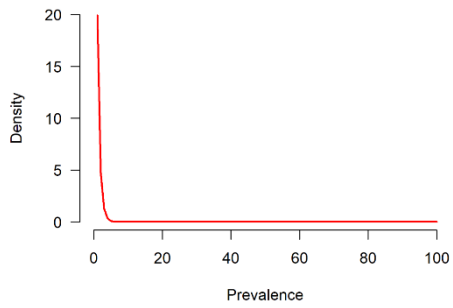
Mozambique - 2009 - Gaza - 0086



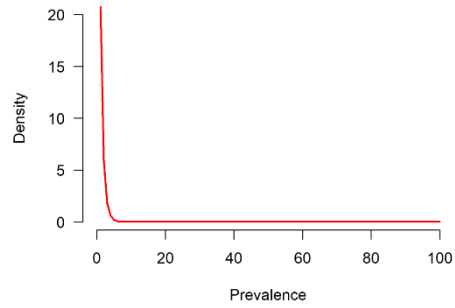
Mozambique - 2009 - Gaza - 0087



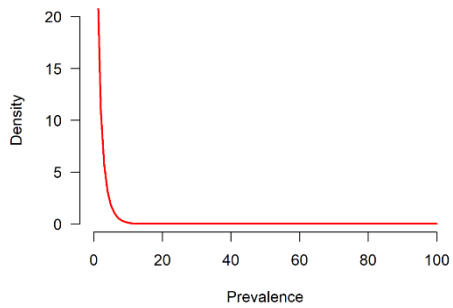
Mozambique - 2009 - Gaza - 0088



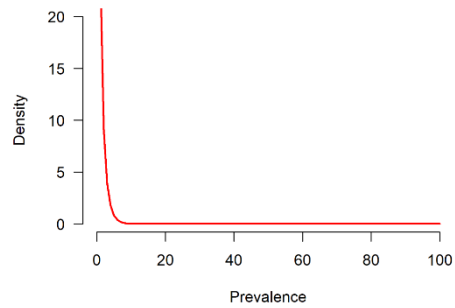
Mozambique - 2009 - Gaza - 0089



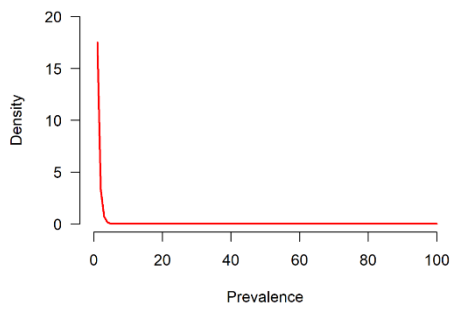
Mozambique - 2010 - Gaza - 0090



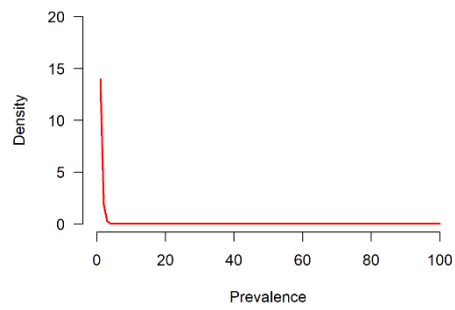
Mozambique - 2010 - Gaza - 0091



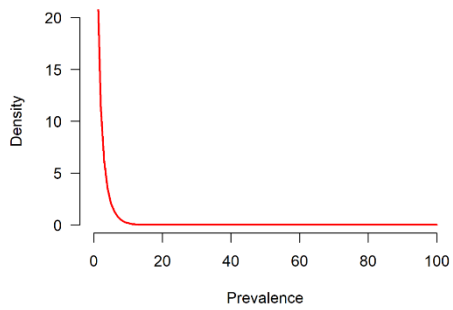
Mozambique - 2010 - Gaza - 0092



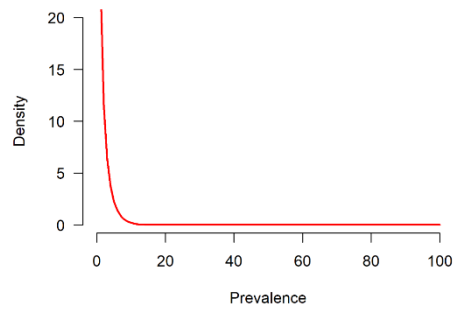
Mozambique - 2010 - Gaza - 0093

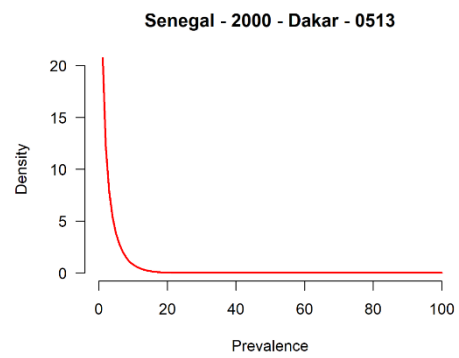
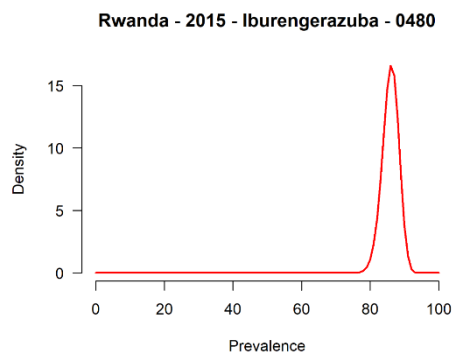
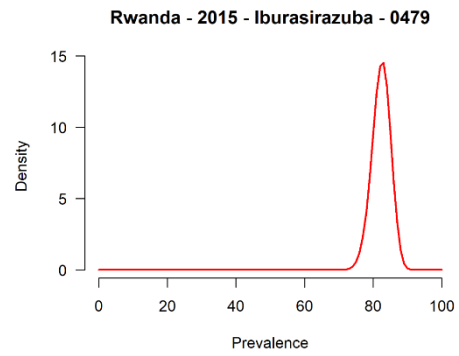
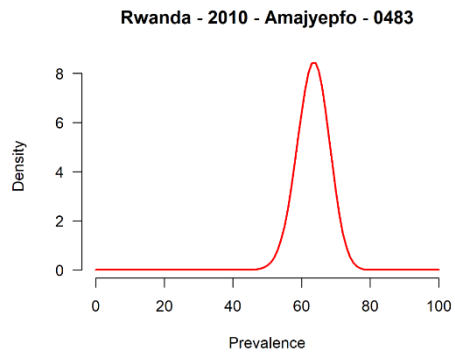
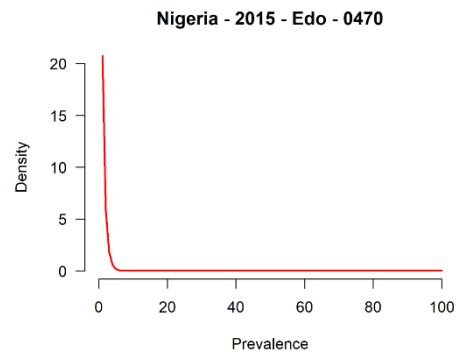
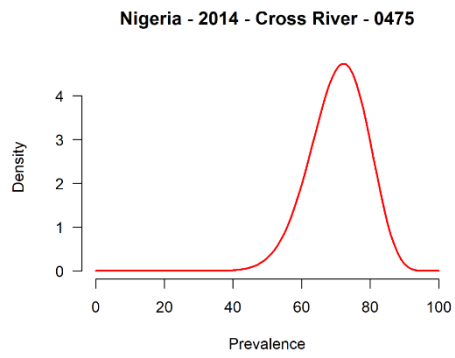
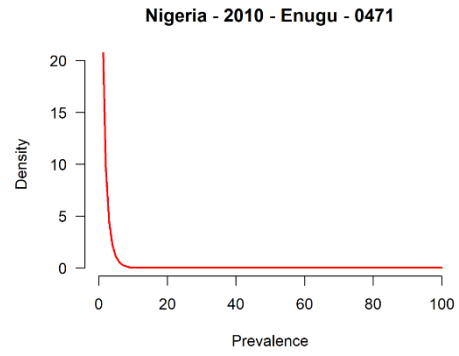
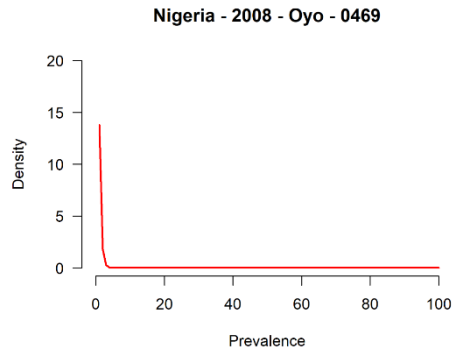


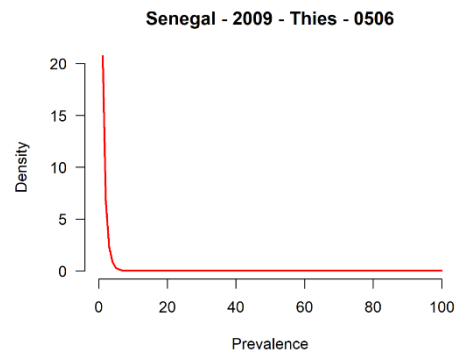
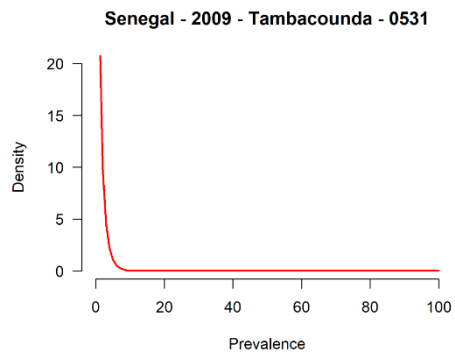
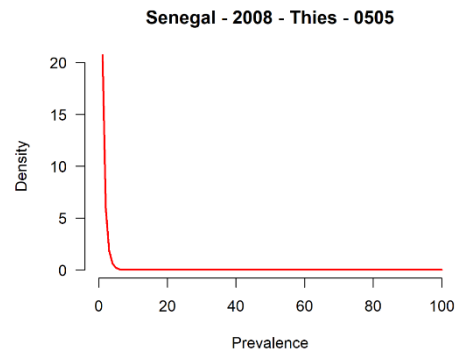
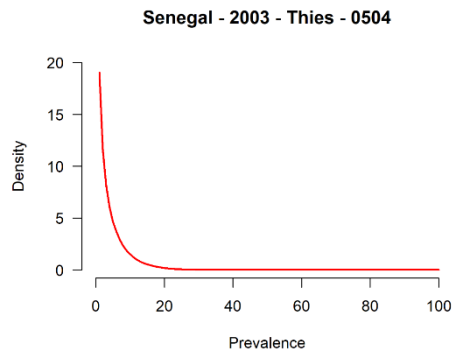
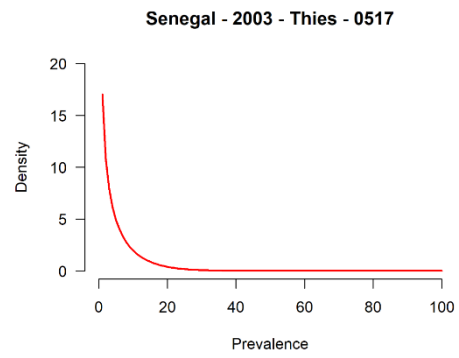
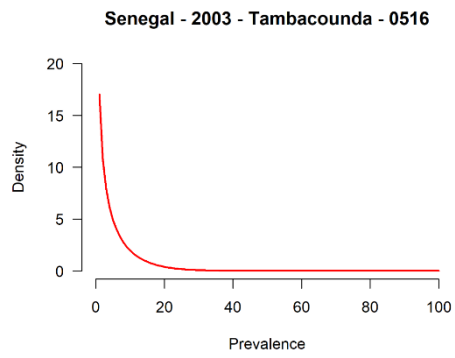
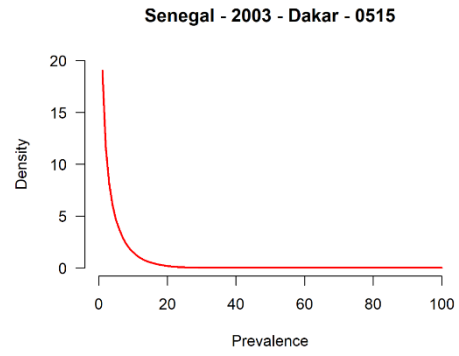
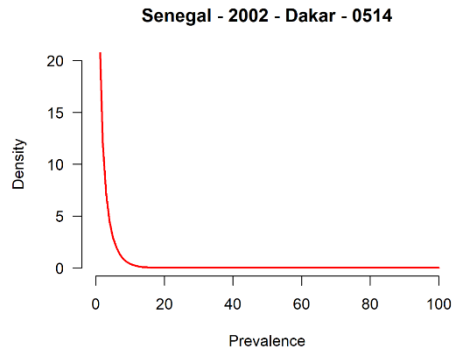
Niger - 2003 - Niamey - 0464



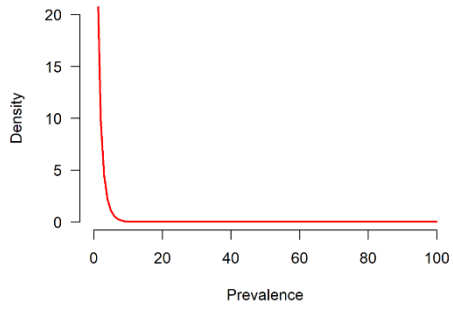
Nigeria - 2003 - Oyo - 0468



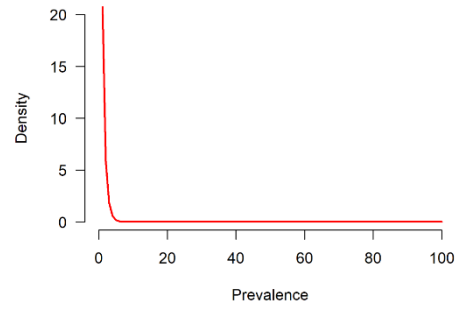




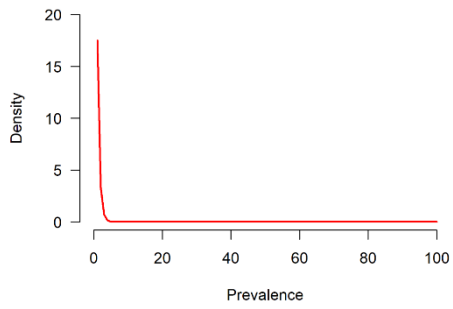
Senegal - 2010 - Tambacounda - 0532



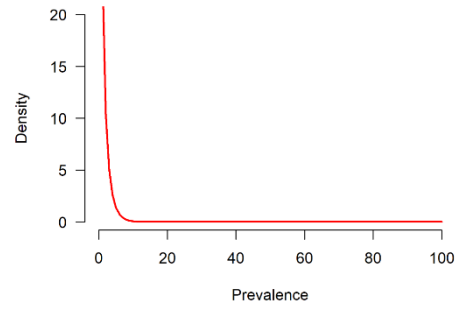
Senegal - 2010 - Thies - 0507



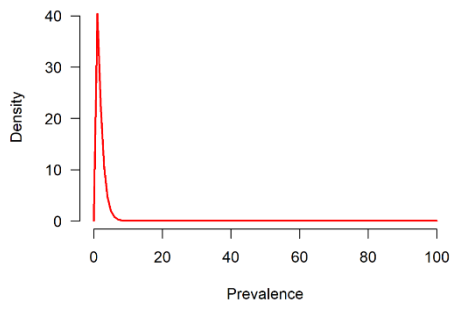
Senegal - 2011 - Thies - 0508



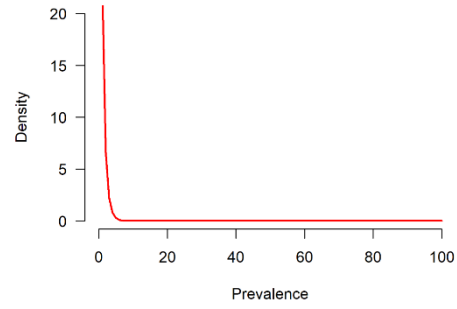
Senegal - 2011 - Thies - 0510



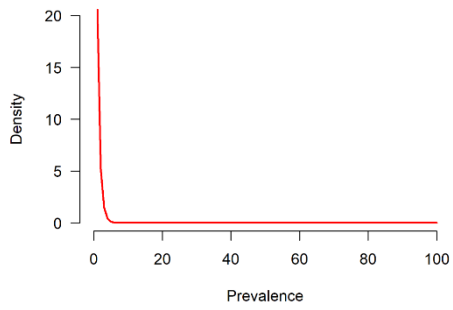
Senegal - 2014 - Dakar - 0511



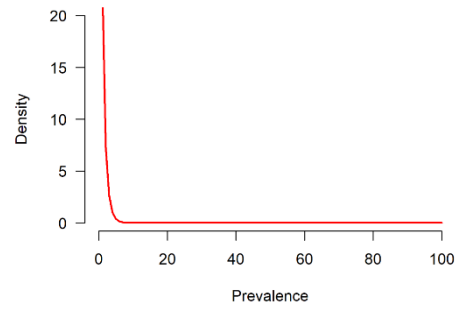
Somalia - 2011 - Jubbada Hoose - 0537

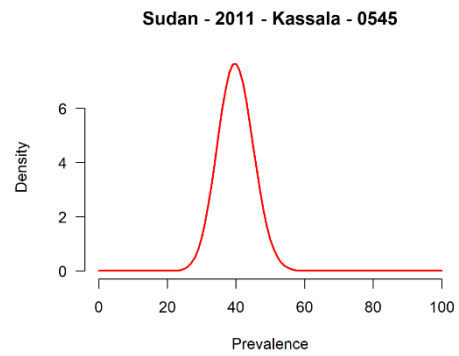
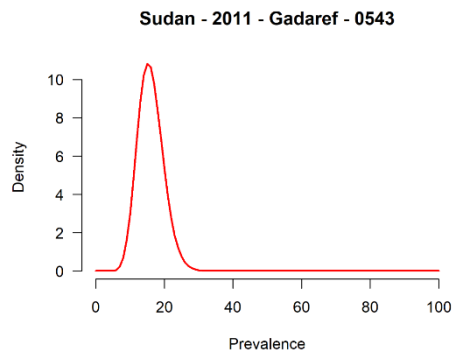
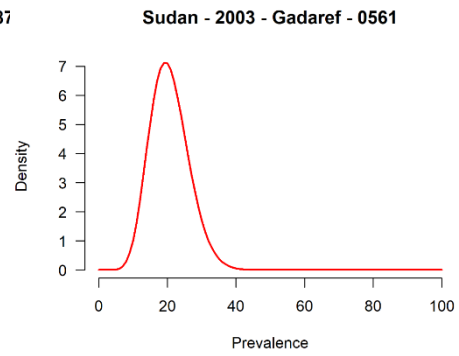
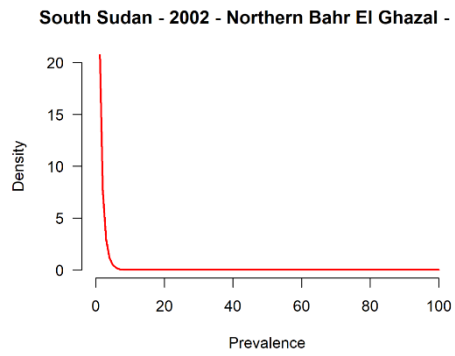
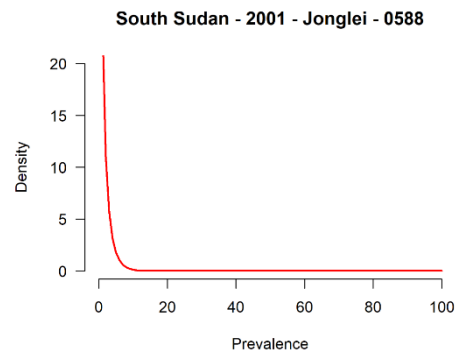
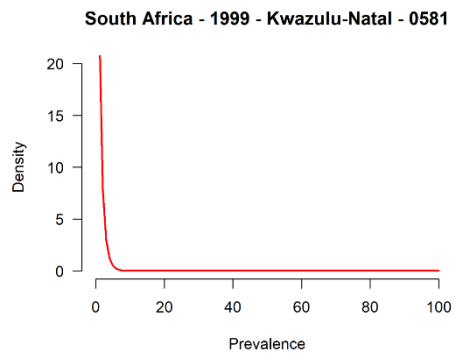
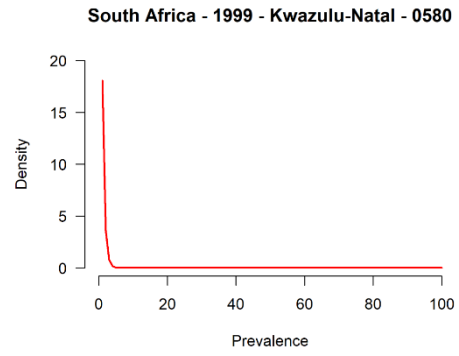
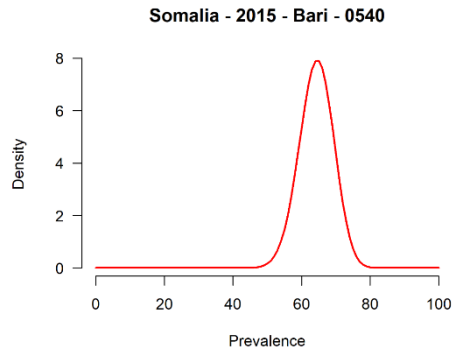


Somalia - 2011 - Shabeellaha Dhexe - 0539

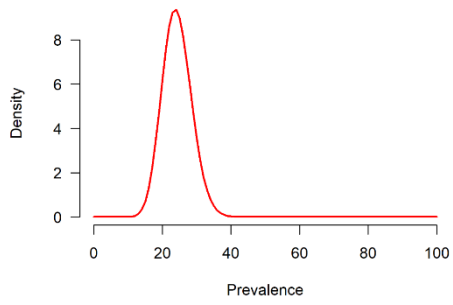


Somalia - 2011 - Shabeellaha Hoose - 0538

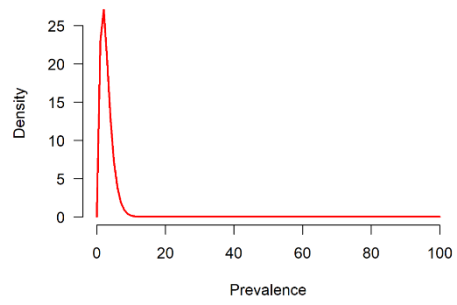




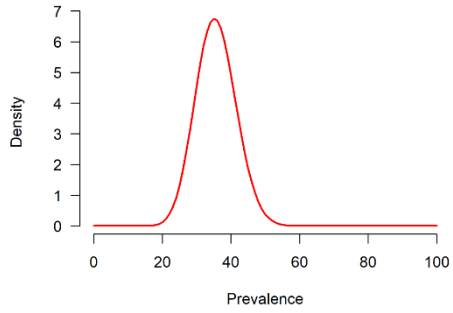
Sudan - 2011 - Sennar - 0542



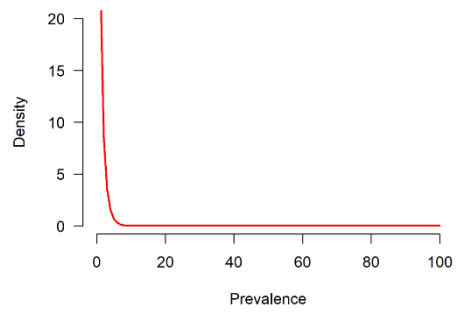
Sudan - 2011 - White Nile - 0544



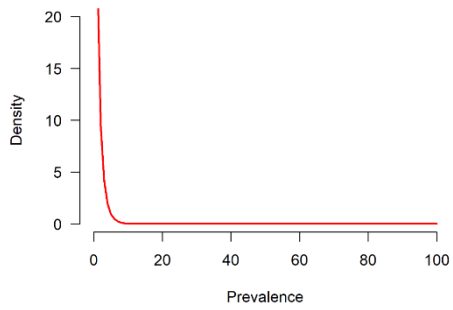
Sudan - 2012 - Kassala - 0546



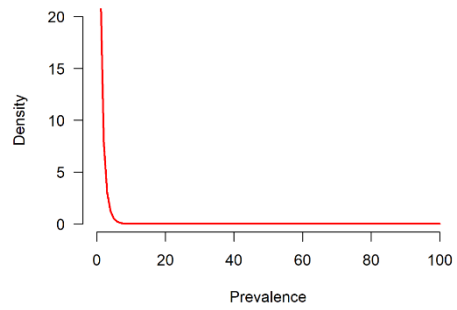
Tanzania - 1999 - Mbeya - 0636



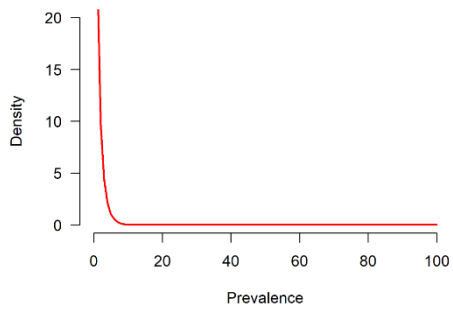
Tanzania - 1999 - Morogoro - 0638



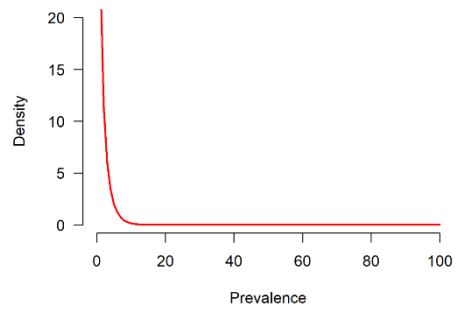
Tanzania - 1999 - Mtwara - 0637



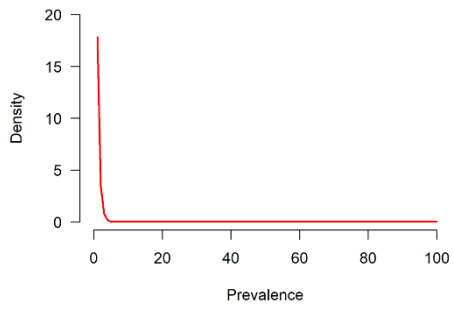
Tanzania - 1999 - Mwanza - 0635



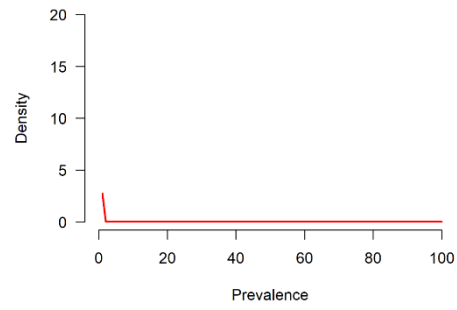
Tanzania - 1999 - Tanga - 0640



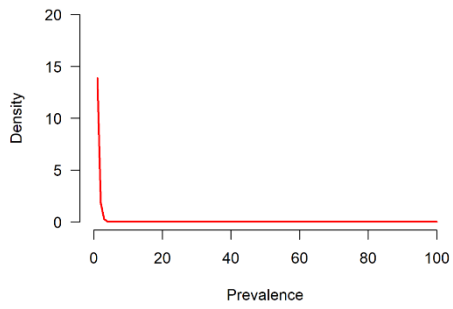
Tanzania - 1999 - Tanga - 0634



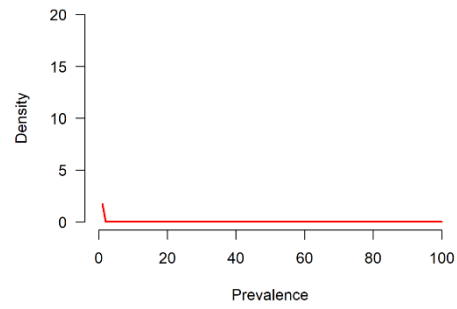
Tanzania - 2000 - Morogoro - 0645



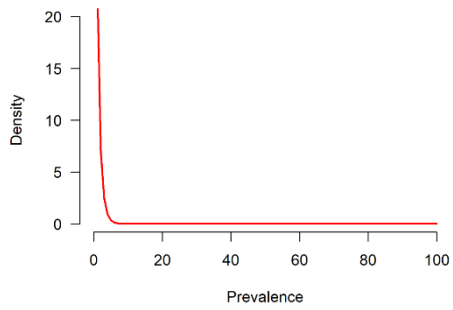
Tanzania - 2000 - Morogoro - 0674



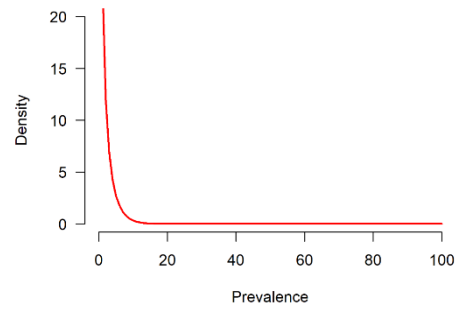
Tanzania - 2000 - Pwani - 0648



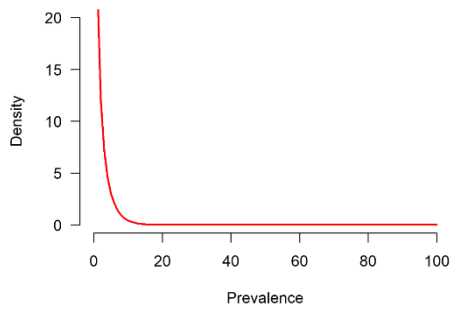
Tanzania - 2001 - Kilimanjaro - 0651



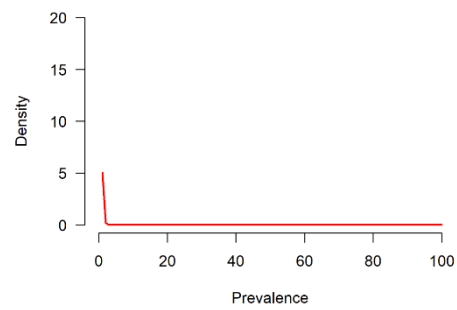
Tanzania - 2001 - Kilimanjaro - 0652



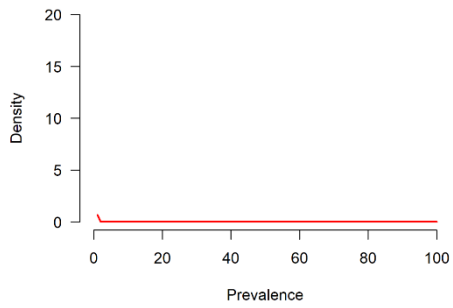
Tanzania - 2001 - Kilimanjaro - 0653



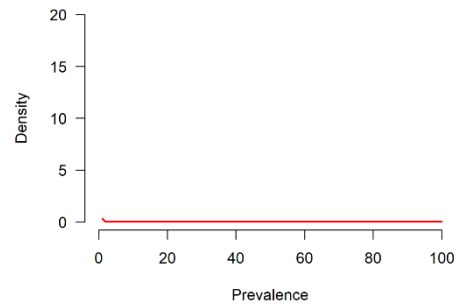
Tanzania - 2001 - Morogoro - 0646



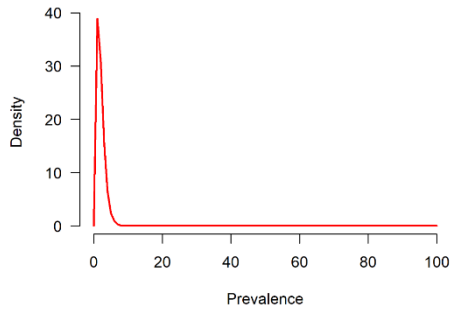
Tanzania - 2001 - Pwani - 0649



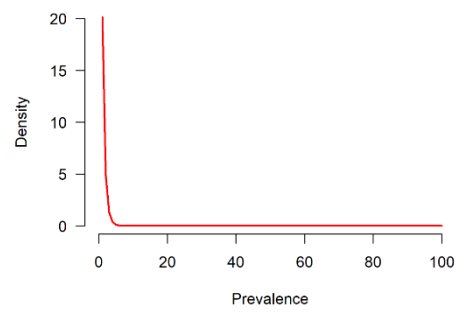
Tanzania - 2002 - Morogoro - 0647



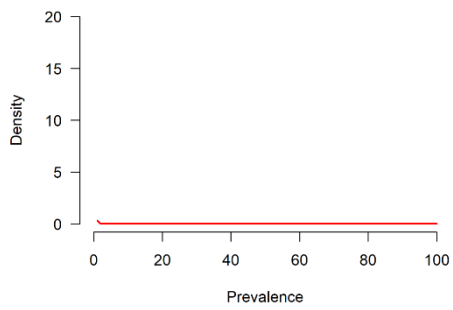
Tanzania - 2002 - Morogoro - 0681



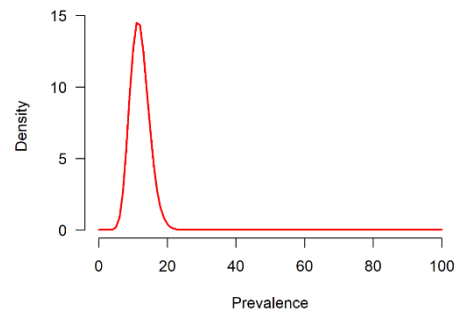
Tanzania - 2002 - Pwani - 0680



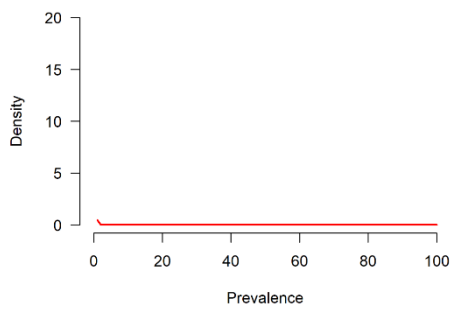
Tanzania - 2002 - Pwani - 0650



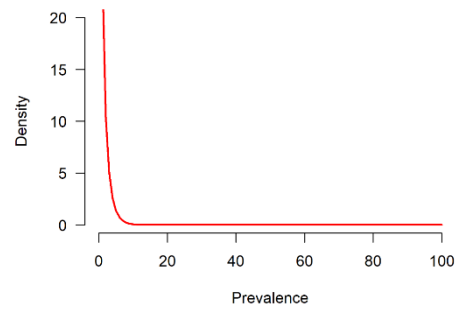
Tanzania - 2003 - Tanga - 0654



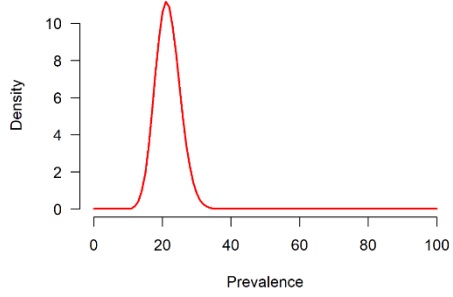
Tanzania - 2004 - Morogoro - 0676



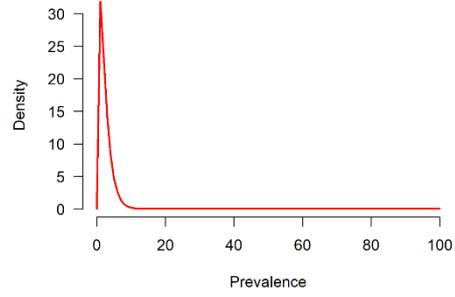
Tanzania - 2004 - Pwani - 0623



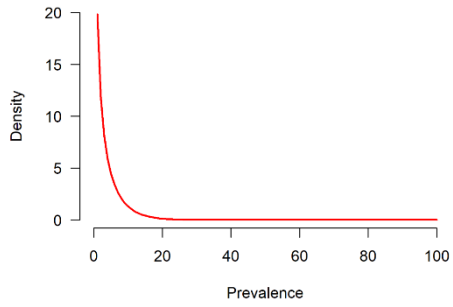
Tanzania - 2004 - Tanga - 0655



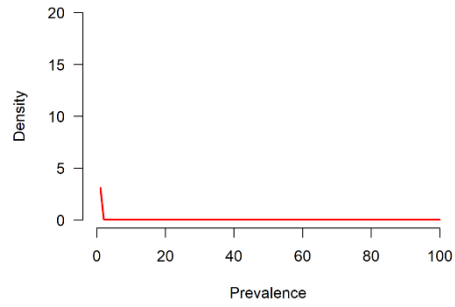
Tanzania - 2005 - Mbeya - 0684



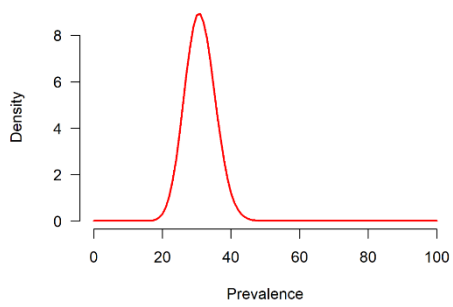
Tanzania - 2005 - Mbeya - 0685



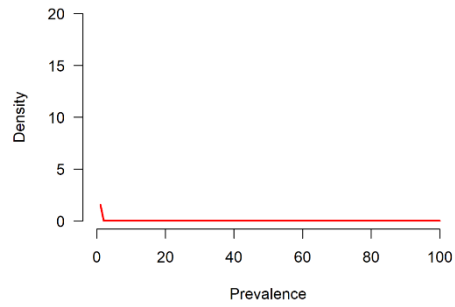
Tanzania - 2005 - Morogoro - 0677



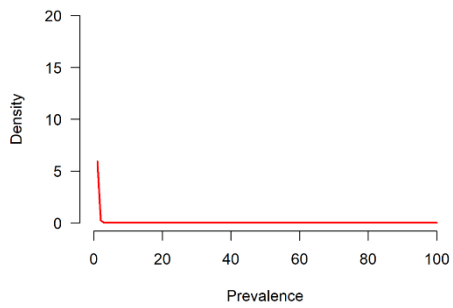
Tanzania - 2005 - Tanga - 0682



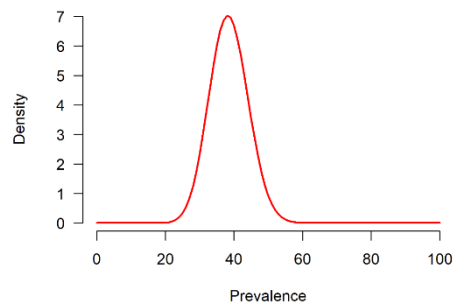
Tanzania - 2006 - Morogoro - 0675



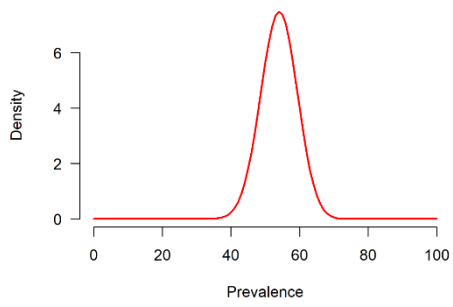
Tanzania - 2006 - Morogoro - 0678



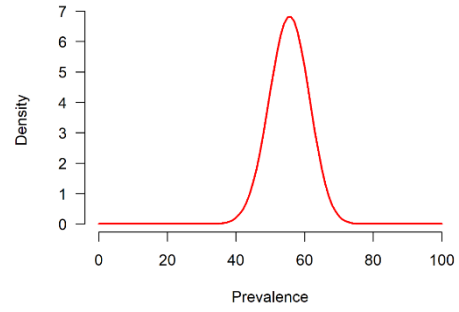
Tanzania - 2006 - Tanga - 0656



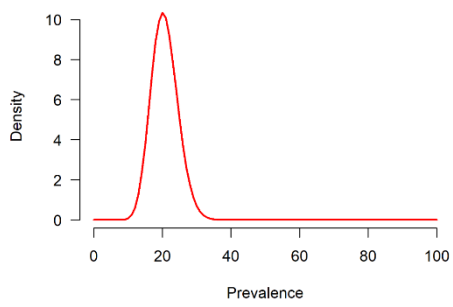
Tanzania - 2006 - Tanga - 0658



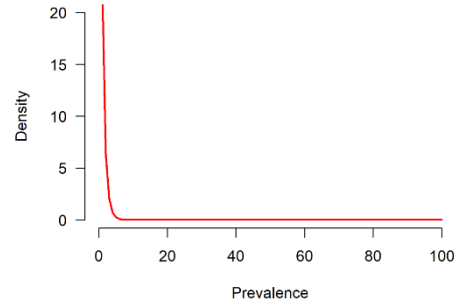
Tanzania - 2007 - Tanga - 0657



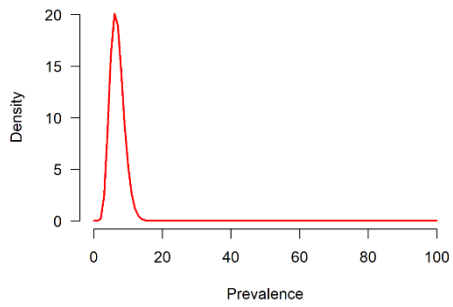
Tanzania - 2011 - Kagera - 0596



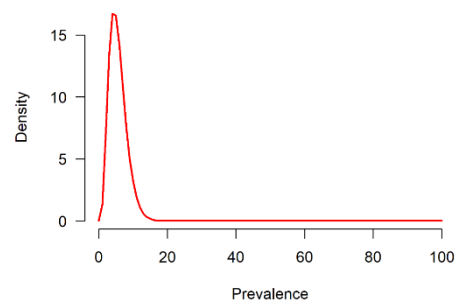
Tanzania - 2011 - Lindi - 0597



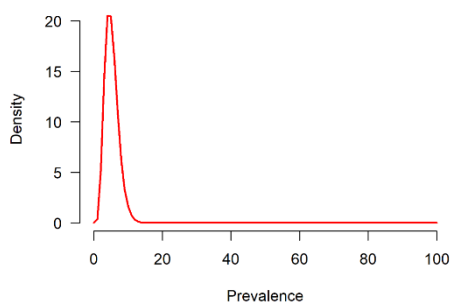
Tanzania - 2011 - Mbeya - 0598



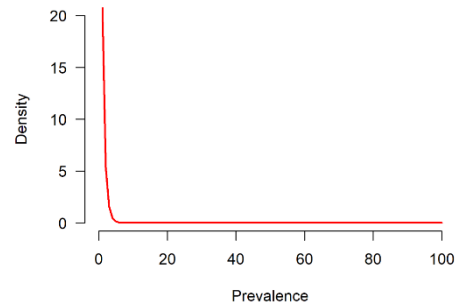
Tanzania - 2011 - Mtwara - 0599



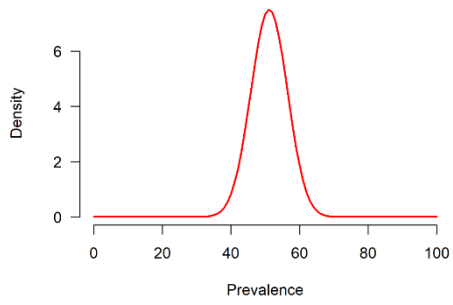
Tanzania - 2011 - Mwanza - 0600



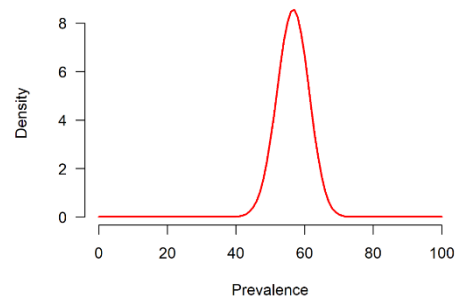
Tanzania - 2011 - Pwani - 0601



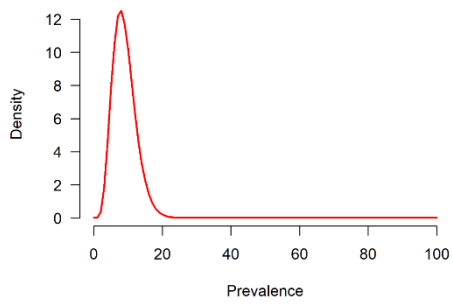
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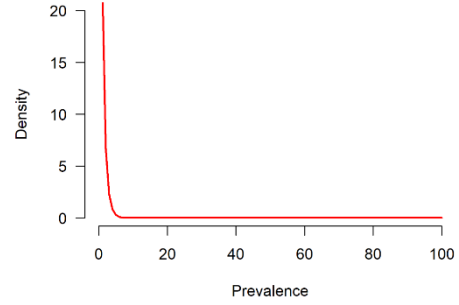
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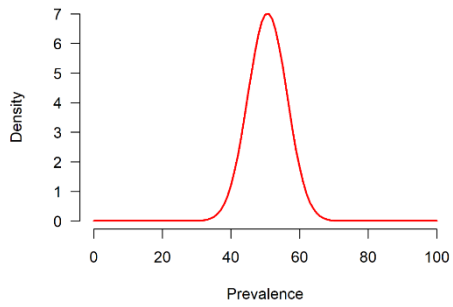
Tanzania - 2013 - Kagera - 0593



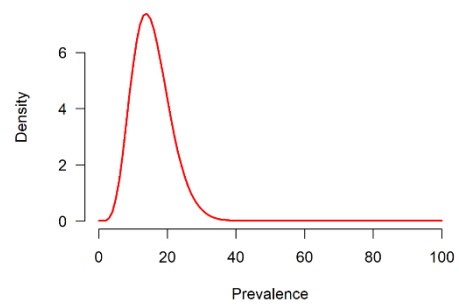
Tanzania - 2013 - Lindi - 0594



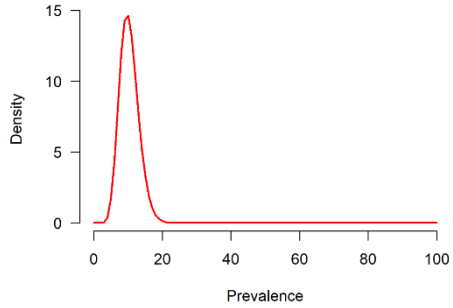
Tanzania - 2013 - Tanga - 0595



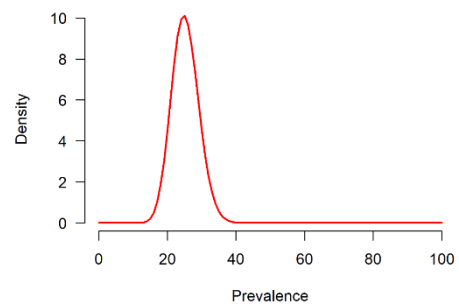
Tanzania - 2014 - Tanga - 0622



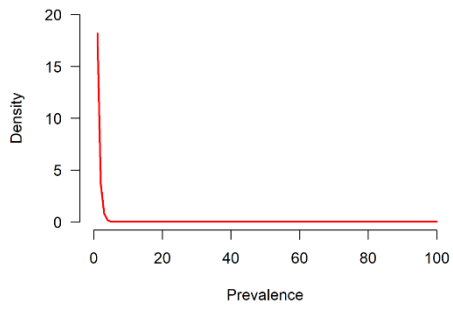
Tanzania - 2015 - Kagera - 0609



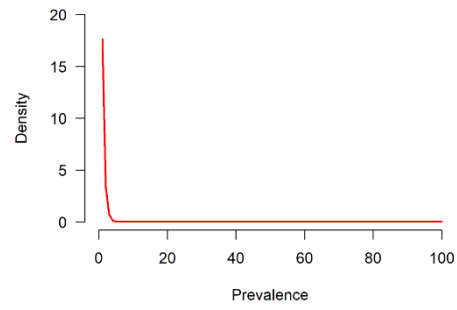
Tanzania - 2015 - Kagera - 0610



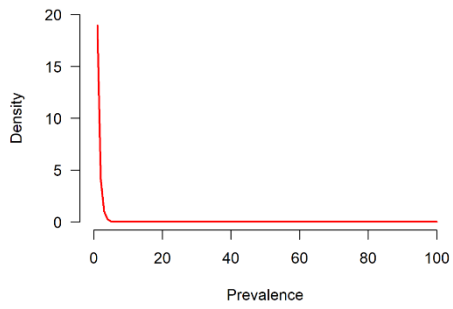
Tanzania - 2015 - Lindi - 0611



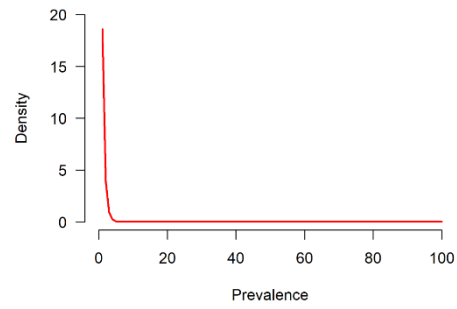
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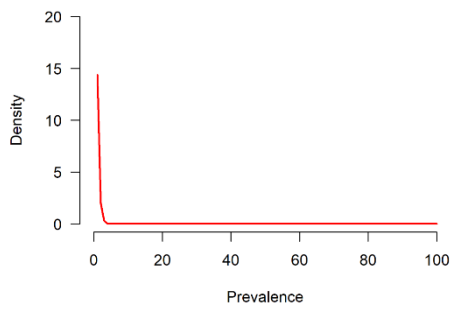
Tanzania - 2015 - Mara - 0613



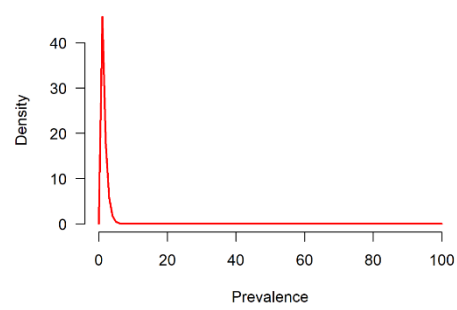
Tanzania - 2015 - Mara - 0614



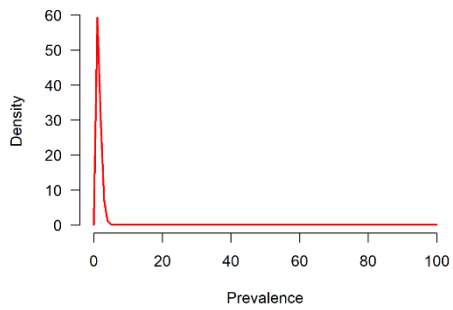
Tanzania - 2015 - Mtwara - 0615



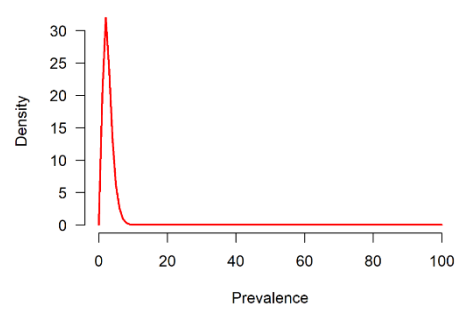
Tanzania - 2015 - Mtwara - 0616



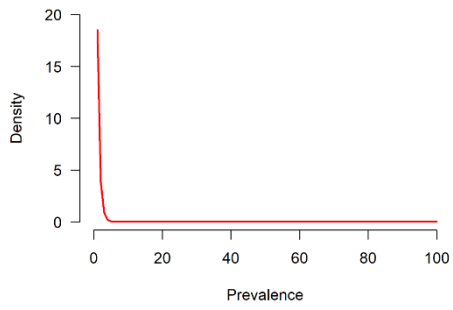
Tanzania - 2015 - Mwanza - 0617



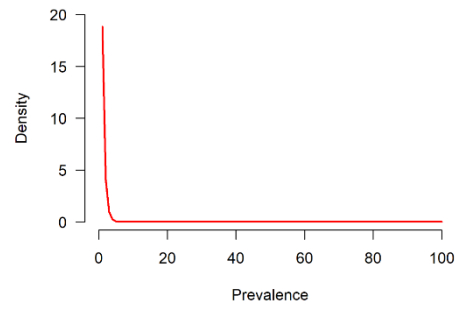
Tanzania - 2015 - Mwanza - 0618



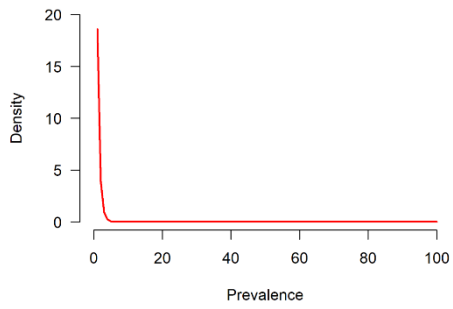
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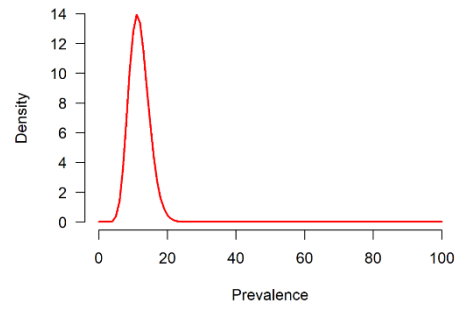
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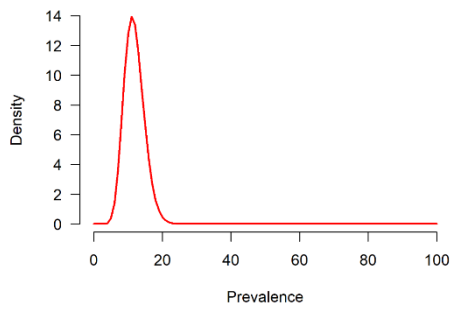
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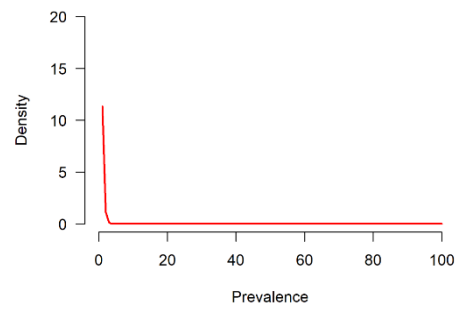
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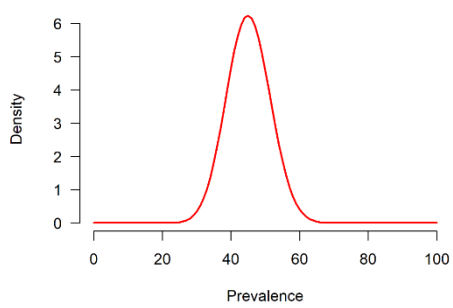
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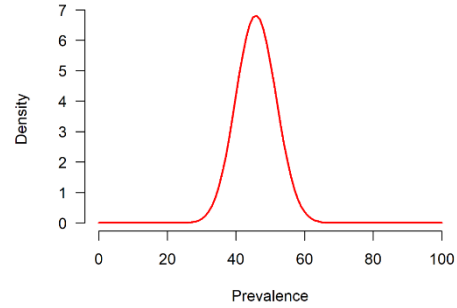
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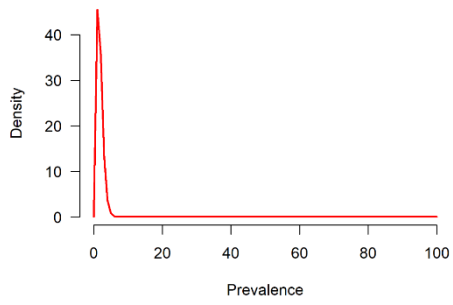
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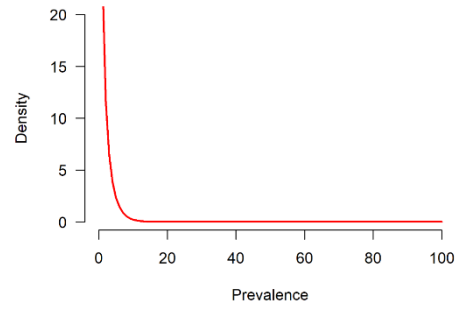
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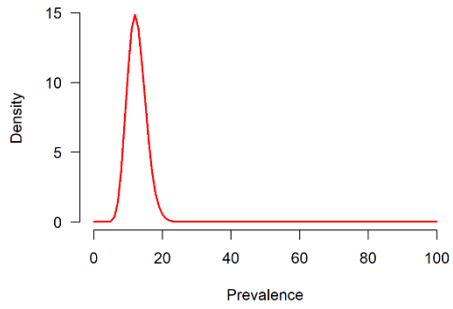
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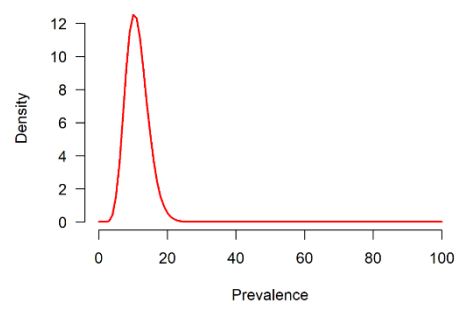
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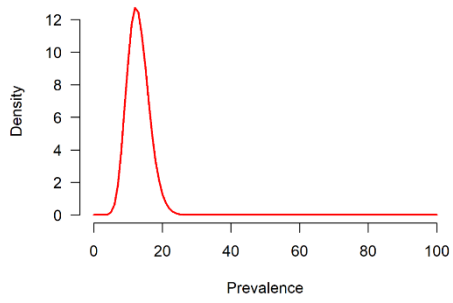
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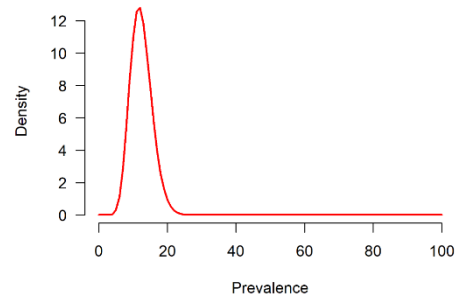
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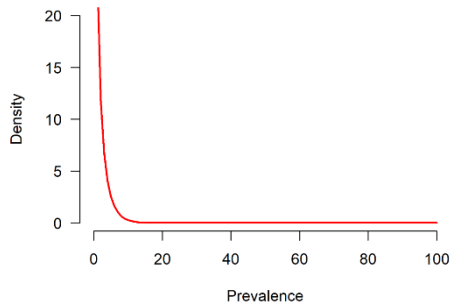
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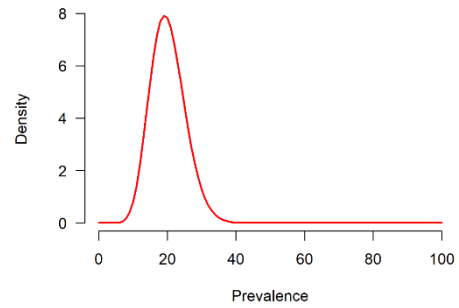
Uganda - 2011 - Tororo - 0717



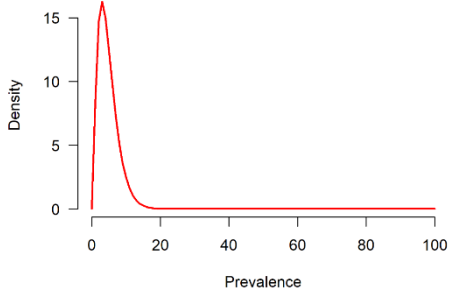
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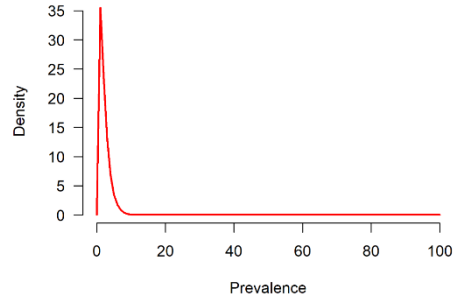
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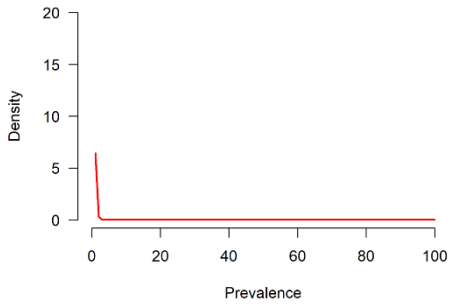
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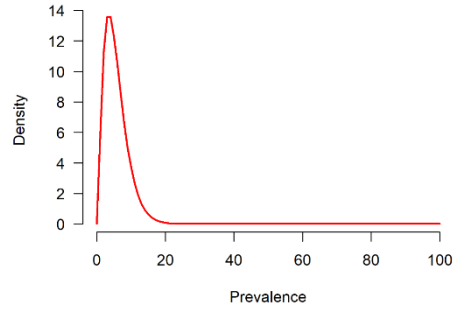
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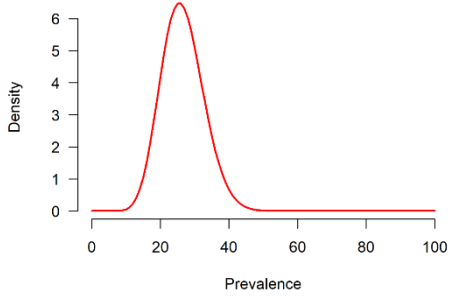
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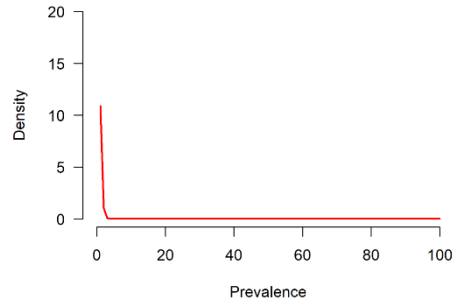
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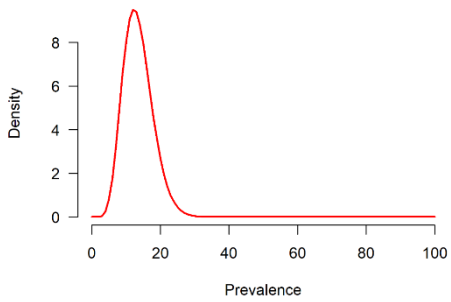
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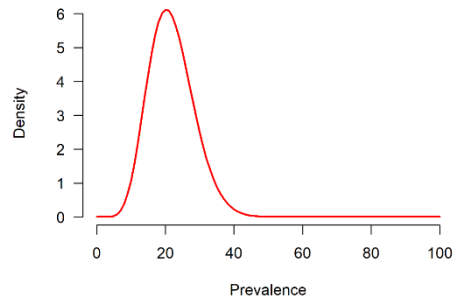
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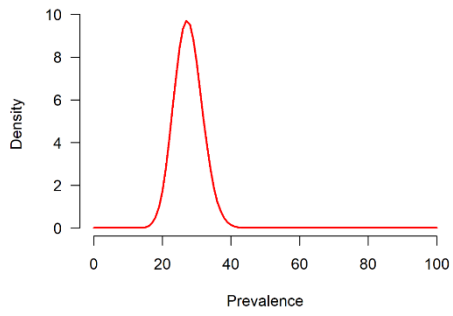
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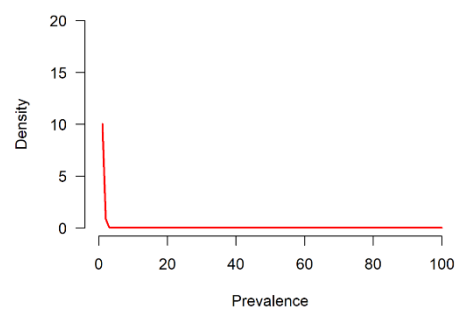
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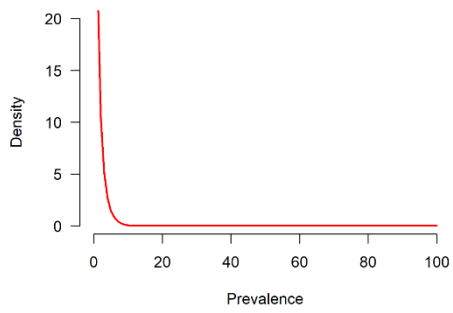
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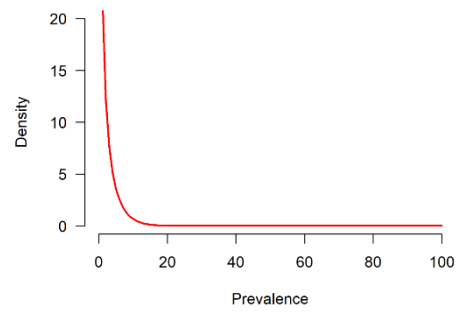
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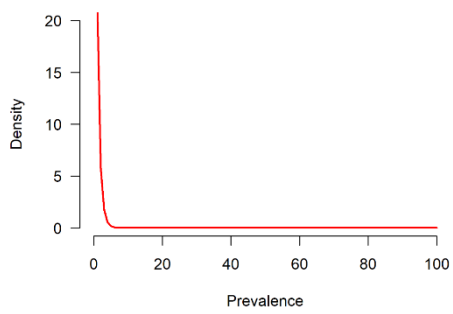
Zambia - 2000 - Southern - 0759



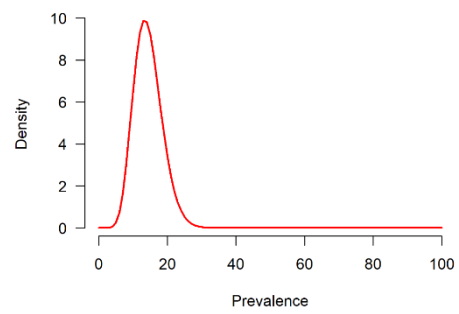
Zambia - 2003 - Southern - 0760



Zambia - 2006 - Southern - 0761



Zambia - 2013 - Luapula - 0756



Supplement 3.6

Table S10: Effectiveness of Sulfadoxine-Pyrimethamine for Intermittent Preventive Treatment in Pregnancy and in Infancy per Country-Year. For each policy, the values in each country-year are posterior probability reflecting the amount of evidence that each intervention is effective under the current WHO frameworks. For IPTp, the WHO thresholds for withdrawal of policy are pfdhps540E >95% and pfdhps581G >10%. For IPTi, the WHO threshold for withdrawal of policy is pfdhps540E >50%. For each intervention, I consider the drug effective in those country-years whose posterior probability >95%. For South Africa, the data is not sufficient to generate evidence on drug effectiveness for IPTp. NA denotes data not available.

Country	Policy	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Angola	IPTp	0.95	0.95	0.95	0.95	0.95	0.94	0.94	0.94	0.94	0.93	0.93	0.92	0.92	0.91	0.91	0.90	0.89	0.88	0.88	0.87	0.86
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Benin	IPTp	0.95	0.95	0.95	0.95	0.95	0.94	0.94	0.94	0.94	0.93	0.93	0.92	0.92	0.91	0.91	0.90	0.89	0.88	0.88	0.87	0.86
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Burkina Faso	IPTp	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.98
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Cameroon	IPTp	0.95	0.95	0.95	0.95	0.95	0.94	0.94	0.94	0.94	0.93	0.93	0.92	0.92	0.91	0.91	0.90	0.89	0.88	0.88	0.87	0.86
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Congo	IPTp	0.95	0.95	0.95	0.95	0.95	0.94	0.94	0.94	0.94	0.93	0.93	0.92	0.92	0.91	0.91	0.90	0.89	0.87	0.86	0.84	0.80
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.99	0.99	0.98	0.95	0.90	0.77	0.51	0.26	0.12	0.06	0.03	0.02
Democratic Republic of the Congo	IPTp	0.95	0.95	0.95	0.95	0.95	0.94	0.94	0.94	0.94	0.93	0.93	0.92	0.92	0.91	0.91	0.90	0.89	0.88	0.88	0.87	0.86
	IPTi	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.92	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91	0.91
Equatorial Guinea	IPTp	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.06	0.44	0.94	0.99	1.00	1.00	1.00	1.00	1.00
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.99	0.99	0.99	0.98	0.97	0.96	0.93	0.89
Ethiopia	IPTp	0.61	0.59	0.60	0.58	0.58	0.56	0.56	0.55	0.55	0.54	0.52	0.53	0.52	0.52	0.52	0.51	0.52	0.52	0.53	0.53	0.54
	IPTi	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.04	0.04	0.04	0.04	0.04	0.04	0.05	0.05	0.05

Gabon	IPTp	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Ghana	IPTp	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.98
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Kenya	IPTp	1.00	0.99	0.99	0.97	0.94	0.90	0.85	0.80	0.77	0.77	0.79	0.84	0.89	0.92	0.96	0.96	0.96	0.94	0.91	0.86	0.80
	IPTi	0.24	0.12	0.06	0.03	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.03	0.07	0.17	0.36	0.59	0.77	0.88
Malawi	IPTp	0.78	0.73	0.66	0.58	0.49	0.38	0.27	0.17	0.10	0.06	0.03	0.02	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	IPTi	0.02	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mali	IPTp	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.98
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Mozambique	IPTp	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.99	0.99	0.98	0.97	0.94	0.91	0.88	0.84	0.81	0.78	0.76	0.76	0.76
	IPTi	0.92	0.91	0.89	0.86	0.81	0.74	0.65	0.54	0.42	0.31	0.21	0.14	0.09	0.06	0.04	0.03	0.03	0.02	0.02	0.03	0.03
Nigeria	IPTp	0.67	0.68	0.68	0.68	0.67	0.67	0.67	0.67	0.67	0.67	0.67	0.67	0.67	0.67	0.67	0.66	0.66	0.66	0.66	0.66	0.65
	IPTi	0.90	0.92	0.95	0.96	0.97	0.98	0.99	0.99	0.99	0.99	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Senegal	IPTp	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
South Africa	IPTp	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	IPTi	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.95	0.94	0.94	0.94	0.94	0.94	0.94	0.93	0.93	0.93	0.93	0.92	0.92	0.92
Sudan	IPTp	0.92	0.90	0.89	0.86	0.83	0.79	0.75	0.73	0.72	0.72	0.73	0.73	0.73	0.72	0.72	0.71	0.71	0.71	0.71	0.72	0.73
	IPTi	0.96	0.80	0.46	0.19	0.08	0.04	0.02	0.02	0.02	0.02	0.03	0.06	0.14	0.33	0.63	0.85	0.95	0.98	0.99	1.00	1.00
Tanzania	IPTp	0.99	0.99	0.98	0.98	0.96	0.95	0.93	0.90	0.86	0.83	0.79	0.76	0.75	0.74	0.74	0.75	0.76	0.78	0.79	0.80	0.80

	IPTi	0.93	0.86	0.75	0.61	0.45	0.31	0.20	0.13	0.08	0.06	0.04	0.04	0.03	0.03	0.04	0.05	0.06	0.09	0.13	0.18	0.26
The Gambia	IPTp	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.99	0.98	0.98	0.98	0.98
	IPTi	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Uganda	IPTp	0.25	0.24	0.23	0.23	0.22	0.21	0.20	0.19	0.18	0.18	0.17	0.17	0.16	0.17	0.17	0.18	0.19	0.20	0.20	0.21	0.22
	IPTi	0.03	0.03	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.01	0.01
Zambia	IPTp	0.70	0.70	0.70	0.69	0.69	0.69	0.69	0.69	0.68	0.68	0.68	0.67	0.67	0.67	0.66	0.66	0.65	0.64	0.63	0.63	0.62
	IPTi	0.48	0.48	0.48	0.47	0.47	0.47	0.47	0.48	0.48	0.48	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47	0.47

Supplement 4:

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