Estimating the distribution of malaria in Namibia in 2009

Assembling the evidence and modelling risk

Ministry of Health and Social Services

Republic of Namibia

&

Malaria Atlas Project

http://www.map.ox.ac.uk

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FURTHER INFROMATION

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Abbreviations

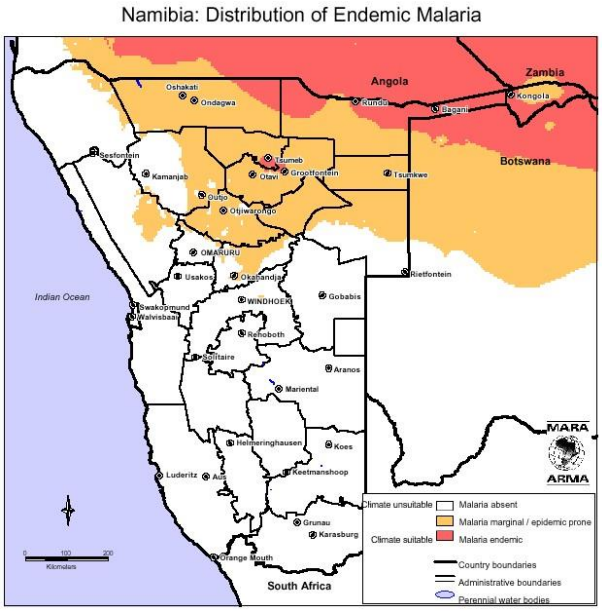
DHS	Demographic & Health Survey
EA	Enumeration Area
EIR	Entomological Inoculation Rate
EVI	Enhanced Vegetation Index
GMAP	Global Malaria Action Plan
GRUMP	Global Rural Urban Mapping Project
HIS	Health Information System
IPTp	Intermittent Presumptive Treatment in pregnancy
IRS	Indoor Residual Spraying
ITN	Insecticide Treated Nets
LCCS	Land Cover Classification System
MAP	Malaria Atlas Project
MARA	Malaria Risk in Africa
MBG	Model-Based Geo-statistics
MCMC	Markov Chain Monte Carlo
MERG	Monitoring & Evaluation Reference Group
MIS	Malaria Indicator Survey
MODIS	MODerate-resolution Imaging Spectroradiometer
MoE	Ministry of Education
MoH	Ministry of Health
MoHSS	Ministry of Health & Social Services
MPHEG	Malaria Public Health & Epidemiology group
NMS	National Malaria Strategy
NVDCP	National Vector-borne Diseases Control Programme
PCR	Polymerase Chain reaction
PSU	Primary Sampling Unit
QA	Quality Assured
RBM	Roll Back Malaria
RDT	Rapid Diagnostic Test
R_O	Basic Reproduction Rate of Infection
UN	United Nations
VCT	Voluntary Counselling & Testing (HIV)
WHO	World Health Organization
ZI	Zero-Inflated

Introduction

The National Malaria Strategy was developed in 2002 covering the period up to 2008 (MoHSS, 2005). At the time the strategy was developed, malaria accounted for over 600,000 clinical cases each year and was thought to contribute to 15% of all childhood deaths. Case burdens have varied between years with important epidemics in 1996/97 and 2000/01. The strategy largely followed recommendations made by the Roll Back Malaria movement, focussing on effective, prompt treatment of clinical episodes, the prevention of risks through the use of combined vector control methods including insecticide treated nets (ITN) and indoor residual house-spraying (IRS) and the promotion of intermittent presumptive treatment of infections among pregnant women; and the detection and prevention of epidemics.

There has historically been a large within country variation in malaria risk. Since 1996 malaria case reporting from health facilities located in Kara, Hardap, Khomas, Omaheke and Erongo were less than 10 cases per 1000 population per year (WHO, MoHSS, 1996). In the development of the national malaria strategies for Namibia in 2002 the MARA climate suitability model was used to highlight the unsuitability for transmission in these five most southerly provinces (Figure 1). This fuzzy logic suitability model however does not rule out transmission, it only provides an estimate of the likelihood that transmission will occur in a given location using various biological priors based on rainfall and temperature (Craig et al., 1999) and for the southern provinces it was "least" likely.

Figure 1: MARA malaria risk map used to delineate risk areas in the Namibian National Malaria Strategy

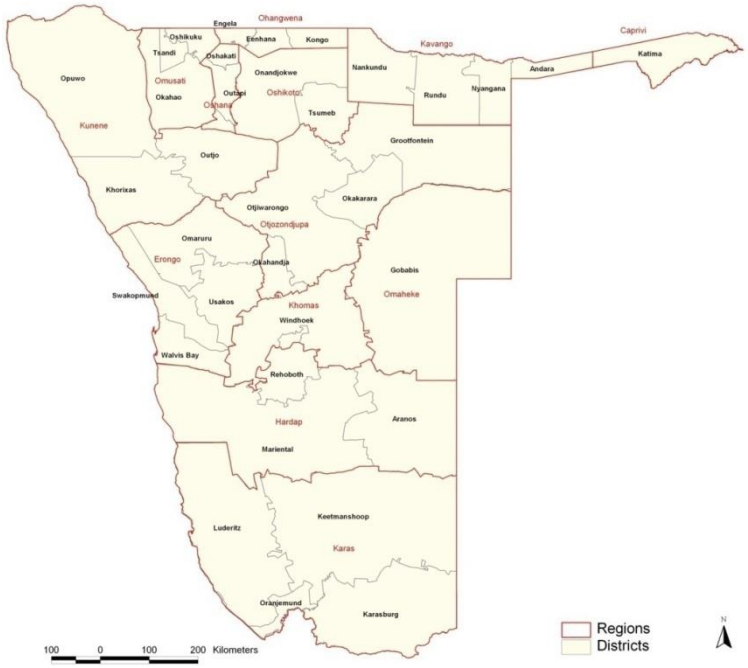


The main rainy season in Namibia runs from November to April and peaks in February-March. However, the total precipitation is extremely variable from year-to-year. Consequently the incidence of malaria in Namibia is acutely seasonal and rainfall patterns affect within and between year variations in malaria disease burden. All three dominant African vectors exist within Namibia: *Anopheles arabiensis, An. gambiae* s.s and *An. funestus;* however *Anopheles arabiensis* is the most ubiquitous and both *An. gambiae ss* and *An. funestus* are thought to have declined in their contribution to transmission following the wide-scale use of IRS.

In recent years there has been a decline in malaria case incidence and Namibia has joined neighboring southern African countries in considering a sub-regional effort to aim for elimination. In planning for a revised national ambition from a stated goal in 2002 "*… to prevent deaths and reduce illness, social and economic losses due to malaria through progressive improvement and strengthening of local and national response capabilities*" (MoHSS, 2005) to one encompassing *elimination* demands a very careful understanding of the spatial extents and intensity of transmission today. The purpose of the present report is to use all available evidence to provide an informed delineation of possible malaria risks nationwide and use these data to guide immediate and medium term priorities for malaria risk mapping to support revised national control ambitions.

There are 34 health districts across 13 regions of Namibia (Figure 2). These health reporting units are used in this report as part of health information system assemblies and definitions of risk. Because Omaheke has only one health district and is large we have split this across the middle for purposes of data assembly – see Section x.

Figure 2: Health regions and districts in Namibia



Defining human settlement and population density

Imperative to any malaria risk modeling exercise is an appreciation of where the human population lives in relation to transmission risk. The MAP team have worked with others in recent years to develop higher resolution human settlement maps as part of the Global Rural Urban Mapping Project (GRUMP) (http://sedac.ciesin.org/gpw/). Since 2008 MAP has continued this work by using multiple sources of national land surface use, census and point settlement data to improve the resolution of population mapping in Africa (http:// www.afripop.org). Through the provision of more spatially configured data on where people live it has been possible to combine interpolated modeling techniques to improve the

spatial population mapping of Namibia as part of the current malaria mapping exercise. The approaches, input data and results of this work are described below.

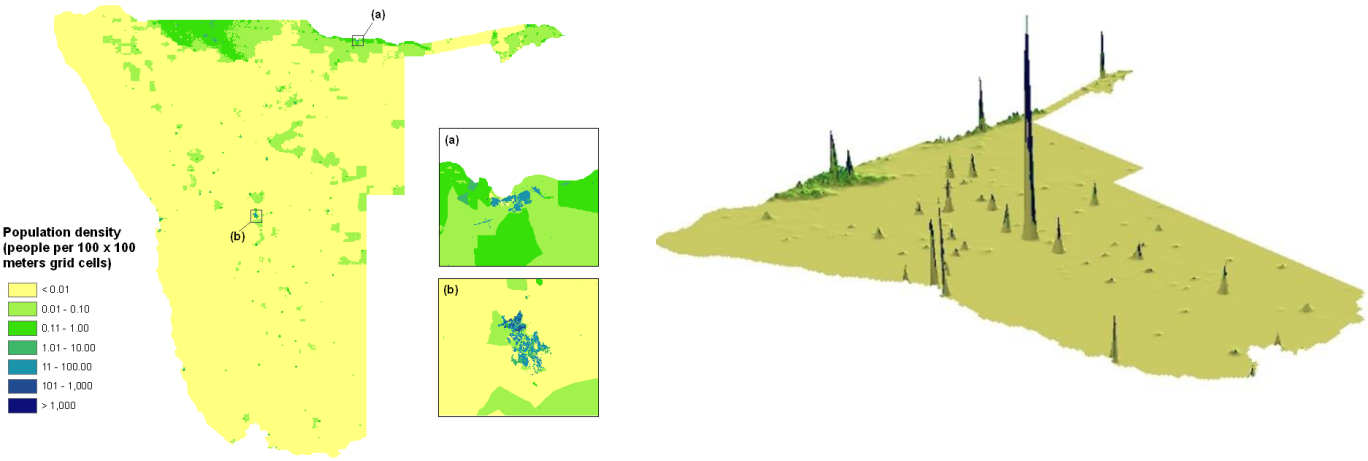
The GlobCover Land Cover product (GlobCover) was downloaded from the European Space Agency website (http://ionia1.esrin.esa.int/). This 300 meters resolution land cover dataset was derived from a time-series of Medium Resolution Imaging Spectrometer (MERIS) images acquired from December 2004 to June 2006 (Arino et al., 2007; 2008). GlobCover is compatible with the UN Land Cover Classification System (LCCS). This allows easy aggregation of LC classes based on a hierarchy of LC class detail, and allows comparison of LC classes across countries and regions. The 47 individual classes were aggregated to a more generic 10 classes. In addition, various other spatial datasets such as administrative boundaries, towns and settlements point locations, health facilities and schools locations, transport networks, etc. were obtained to aid testing and accuracy assessment. A classification of the finest administrative units (enumeration areas) into urban or rural categories was used in combination with a dataset depicting urban and settlement polygon outlines from detailed imagery provided by GeoTerraImage Consultancy. This dataset was principally derived from 2005 Landsat imagery, developed using conventional on-screen interpretation and hierarchical clustering techniques, often involving the use of area-specific geographic masks. The GeoTerraImage Consultancy also provides industrial area delimitations for the main cities.

2001 census data were available for 4072 enumeration areas (EA) level across with an average spatial resolution of 14.3 km^2. The census population count data were adjusted forward to estimated 2010 levels using separate UN urban and rural growth rates taken from the UN World Urbanization Prospects Database, 2007 version: http://esa.un.org/unup/.

The GlobCover dataset was 'refined' to accommodate the more accurate information on settlements extent derived from Landsat. GlobCover was first re-sampled to 100 m spatial resolution. The urban class, which typically overestimates settlement extent size, was then removed and the surrounding classes expanded equally to fill the remaining space. The Landsat-derived settlement polygons were then overlaid onto the 'urban class deprived' land cover map and land covers beneath were replaced. Newly defined settlement pixels belonging to the EAs classified as 'urban' were added as 'urban' class, whereas other settlement pixels were classified as 'rural settlement'. The Landsat-derived industrial area delimitations were also overlaid onto land cover data to define an industrial land cover class. This produced a refined 100 x 100 m land cover dataset.

The refined land cover data and 2001 enumeration area census data were then used to define per land cover class population densities. The average population density of one specific land cover class was calculated based on EAs that record this land cover class for the majority of their pixels. These per land cover class densities were then used as weightings to re-allocate populations within Namibian EAs. Per-pixel population densities were adjusted to match the 2001 census data. In one EA, the sum of per-pixel population counts is therefore equivalent to census population data. An estimate of population in 2010 was produced based on UN rural and urban growth rates for the 2001-2010 period: 0.63% for rural areas for 2001-2005 and 0.40% for 2005-2010, and 3.04% for urban areas for 2001-2005 and 2.91 for 2005-2010. The 100x100m gridded population data produced are not projected, but are referenced by geographic WGS84 coordinates. The resulting modelled 100x100m interpolated maps of the human population settlement and density are shown in Figures 3a and angle planed in Figure 3b.

Figure 3a: **Population distribution map for Namibia showing numbers of people residing in each 100 x 100 metre grid square**. Close-ups show detail around (a) Rundu and (b) Windhoek.; Figure 3b = planed version



Defining unstable transmission in Namibia

As part of global mapping work we have presumed that outside of Africa *unstable* malaria is represented by an incidence of confirmed *P. falciparum* or *P. vivax* malaria cases of < 1 per 10,000 population p.a. (Hay et al., 2009; Guerra et al., 2008; 2010). This is 10-fold more conservative than the metric used by WHO in their schema for countries transitioning from stable endemic control to elimination (<1 per 1000 people p.a.; RBM, 2008). MAP has elected to use a stricter criterion recognizing the difficulties ensuring precision of reliable case-incidence recording between countries and following the revisions adopted in later years of the Global Malaria Eradication Program that also recognized the health system inaccuracies and errors in defining 1 per 1000 cases (Swaroop et al., 1966; Ray & Beljaev, 1984; Yekutiel, 1960). At a global level MAP additionally uses aridity to down-regulate areas where reported case incidence is ≥ 1 case per 10,000 population p.a. to unstable conditions and those where case incidence is < 1 case per 10,000 population p.a. to malaria free. This approach has proven valuable in areas where deserts bisect administrative areas and where populations are located on the margins of an administrative area in less arid areas, thus improving the resolutions of risk across the Sahelian regions of Africa, the Middle East, Northern Asia and the Atacama region in the Americas (Guerra et al., 2008; 2010). We have therefore attempted to apply these approaches to the Namibian context using combinations of Health Information System (HIS) data and remotely sensed measures of aridity derived from earth orbiting satellites.

Malaria HIS data 2005-2009

It is important first to define come of the caveats of using routine malaria health statistics. Malaria case-reporting data often suffer a number of problems for defining risk. With few exceptions across malaria endemic countries, fevers or other malaria-like syndromes are often self-medicated and may resolve regardless of cause before reaching formal health systems. Inaccurate diagnoses might be used to report disease rates, often inflating risks (Chandramohan et al., 2002; Amexo et al., 2004; Koram & Molyneux, 2007). These diagnosis errors may be compounded through inadequate and incomplete

national reporting systems (Chilundo et al., 2004; Gething et al., 2006). However, health service use in Namibia is thought to be high relative to other sub-Saharan African countries (Unger et al., 2006). Nevertheless, until recently most cases of malaria are diagnosed on clinical grounds alone (MoHSS, 2005). Both poor diagnosis (over-reporting) and poor use of services (under-reporting) may compound to provide errors and bias in the use of routine statistics. Despite these caveats MAP and WHO default to using these data in the cartography of malaria risk worldwide and often without any appreciated on the scale or sources of bias and error. Here we have an opportunity to be more precise in the estimation of case-incidence despite incompleteness in the data sources from all reporting facilities, something not possible for other countries.

Assembling routine Health Information System (HIS) data

We have assembled monthly out-patient reports from health facilities across Namibia provided as part of routine reporting between January 2005 and December 2009. Of the 458 health facilities available on the national health facility database that provide out-patient services (i.e. excluding VCT clinics), 126 (27.5%) did not submit any returns to the HIS database between 2005 and 2009 (Table 1). Of those submitting any return during this period five (1.5%) could not be spatially positioned. Of the remaining 327, a total of 5,200 (27%) months of information was not available from a possible 19,620 facility-months and 36 (11%) facilities did not provide information for more than 30 months for the observation period. For those facilities reporting ≥ 12 months of data (371) we have computed the total numbers of "positive" months, i.e. where malaria cases were reported, as a proportion of all reporting months for each facility. The range of percentage months between 2005 and 2009 where presumed clinical cases of malaria were reported are shown in Table 1 and Figure 4. There was a strong secular trend in the data with evidence of declining suspected clinical malaria since 2005 and most marked in 2008 and 2009 (data not shown).

Table 1: Summary of HIS presumed malaria case reporting 2005-2009

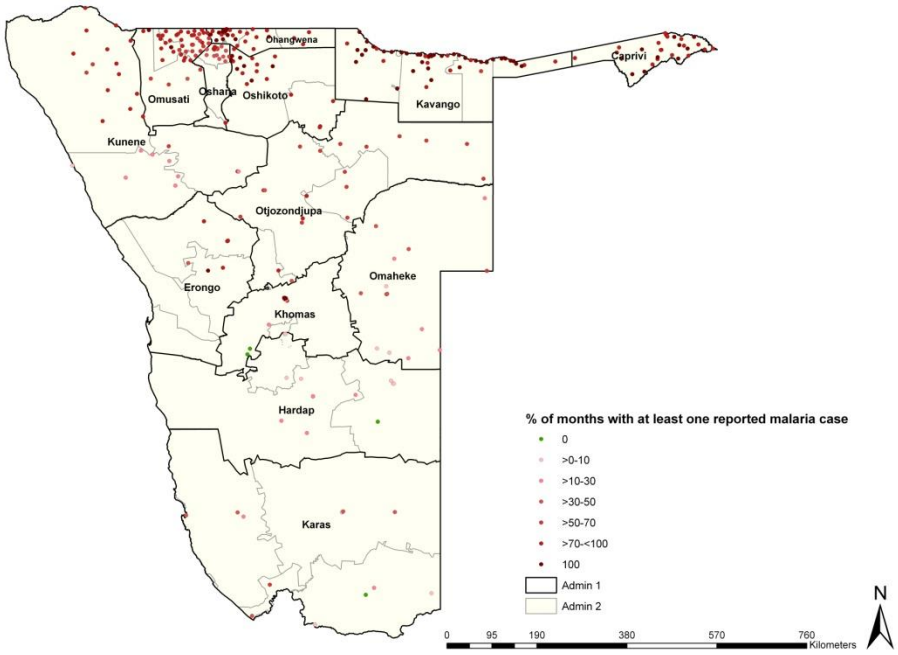
Province	HF; never reporting; reporting but not positioned; reporting and positioned	Number of facilities reporting ≥30/60 months (%of all facilities)	Proportion of months with malaria cases among facilities reporting ≥12/60 months
Karas	31; 13; 0; **18 (58%)**	18 (58%)	42.2% (n=18)
Hardap	21; 5; 0; **16 (76%)**	16 (76%)	37.8% (n=16)
Khomas	43; 31; 1; **11 (26%)**	4 (9%)	100.0% (n=9)*
Erongo	48; 29; 0; **19 (40%)**	4 (8%)	89.1% (n=11)
Omaheke	18; 5; 0; **13 (72%)**	12 (67%)	45.6% (n=13)
Otjozondjupa	30; 9; 0; **21 (70%)**	21 (70%)	66.1% (n=21)
Kunene	31; 2; 0; **29 (94%)**	27 (87%)	81.2% (n=29)
Omusati	54; 5; 1; **48 (89%)**	39 (72%)	79.2% (n=48)
Oshana	26; 8; 1; **17 (65%)**	17 (65%)	59.1% (n=17)
Ohangwena	36; 4; 2; **30 (83%)**	30 (83%)	100.0% (n=30)*
Oshikoto	23; 2; 0; **21 (91%)**	20 (86%)	94.8% (n=21)
Kavango	63; 9; 0; **54 (86%)**	53 (84%)	98.2% (n=54)
Caprivi	34; 4; 0; **30 (88%)**	30 (88%)	97.1% (n=30)
Total	458; 126; 5; **327 (71%)**	**291 (64%)**	**85.8% (n=317)**

*Not an indication of high risk, simply every reporting month was a month with a case

The HIS data on suspected malaria case reporting 2005-2009 demonstrate some of the limitations of using routine health system data; over ¼ of facilities had not submitted any malaria statistics between 2005 and 2009 and reporting facilities did not report all possible months in this interval. The highest

under-reporting rates were in the southern provinces where we are least certain about transmission of malaria. Nevertheless there are some observations that can be made that might help delineate areas of low/unstable transmission. The most southerly provinces reported the largest number of months without a single suspected malaria case (Table 1; Figure 4). Those facilities with cases of suspected malaria every reported every month are those located in the most northern districts along the Angolan border. This broad pattern conforms to national impressions of risk however it should be highlighted that risks of clinical case presentation to facilities across the entire country has been documented.

Figure 4: Distribution of facilities reporting months of cases of suspected malaria as a percentage of reporting months between 2005 and 2009 [Dark red are facilities with every reporting month a malaria case was reported; Green are facilities where no case was reported among all reporting months]



Defining case "incidence"

We computed an "incidence" measure for suspected malaria cases reported between January 2008 and December 2009, to represent a more contemporary measure of risk. This period corresponds to when diagnostic strategies were strengthened and supported as part of improved case-management (NVDCP, 2009) and covers the most recent period that covers the national malaria indicator survey (described in section x). We selected only facilities that reported more than 12 of the 24 month observation period. This resulted in 312 facilities providing records for analysis. We expressed the total number of cases per fraction of a complete year of observation by using the months of reported cases per 24 month time-series. The data series represented a total of 262,595 suspected/and confirmed malaria cases over 24 months (note it was not possible to distinguish confirmed from presumed cases). The longitude and latitude of each facility was then used to identify a 5x5km grid around each facility and extract population totals using the interpolated population density model described in Section x. Evidence from other studies in Africa suggests this is a maximal catchment for out-patient service use (Akin & Hutchinson, 1999; Esnor & Cooper, 2004; Noor et al., 2006). The extracted population denominator was used to compute an annualized incidence of OPD presentations of suspected malaria y multiplying by

the decimal number of years where data were reported to provide a person-years of observation (total across 312 sites = 1,901,483 person years at risk in catchment areas). The summed values for each district within each region are shown in Table 2 (with the adjusted division for Omaheke region) and the categorical ranges of population-adjusted incidence per 10,000 people per annum are shown in Figure 5.

Using a criteria of ≥ 1 case per 10,000 population as indicative of stable transmission, 289 (93%) of the 312 facilities shown in Figure 5 were within this margin of risk and only 23 facilities were less than 1 case per 10,000 population located in Karas, Hardap and Southern parts of Kunene. The averaged incidence from facilities located in Karas and Hardap were < 1 per 10,000 p.a. Using a WHO definition of 1 case per 1000 population encompassed 282 (90%) facility-locations and classified parts of Kunene and Oshikoto provinces as unstable transmission.

Proportion of presumed malaria cases that are parasitologically confirmed

Between February 10th and March 20th 2010 a form was sent to health facilities located in the Northern provinces (Caprivi, Kavango, Kunene, Ohangwena, Omaheke, Oumsati, Oshana, Oshikoto and Otjozondjupa). Staff at each facility were requested to enter how many suspected cases of malaria they had diagnosed by month for 2009, those patients tested for malaria and those who showed evidence of infection. It was not possible to distinguish those who had been tested using microscopy versus the widely distributed Rapid Diagnostic Test (RDT), Paracheck *Pf*®. However it is felt that the majority (>90%) of the diagnostic tests performed were with the RDT. Information was returned for 273 facilities located in these provinces (an estimated coverage of 87%); six facilities did not suspect or test anyone for malaria. Of the remaining 268 facilities a total of 134,366 suspected malaria cases were seen in 2009 and 90,835 (68%) were tested for malaria. Among those tested 9,893 (10.9%) were reported as having a positive test result. Table 3 and Figure 6 show the distribution of tested and positive cases by province and district among the 273 sampled facilities in the north of Namibia.

Figure 5: Distribution of 312 facilities where more than 12 months data between 2008 and 2009 where interpolated case burdens were used to compute incidence within a 5km catchment; dark red = incidence >= 1000 per 10,000 population p.a. through to green = zero incidence (see legend)

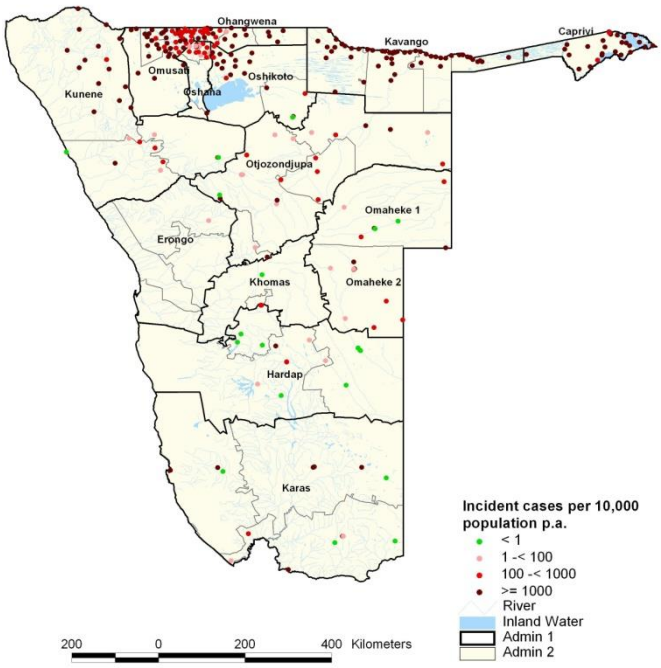


Table 2: Computed incidence of suspected malaria in all age groups per 1000 population p.a. for 312 facilities with semi-complete data 2008-2009

Province / District		HF reporting more than 12 months between Jan 2008 and December 2009	Total cases adjusted for missing months 2008-2009	Total estimated population over two years within 5km of the facilities used to compute case numbers	Overall incidence per facility per 10,000 population within catchment p.a.
Caprivi	Katima	29	33,627	93,598	3,592.7
Erongo	Omaruru	1	47	6,471	72.6
	Swakopmund	NA	NA	NA	NA
	Usakos	NA	NA	NA	NA
	Walvis Bay	NA	NA	NA	NA
Hardap	Aranos	4	0	7,927	0.0
	Mariental	7	28	9,160	30.6
	Rehoboth	5	3	1,238	24.2
Karas	Karasburg	6	17	12,957	13.1
	Keetmanshoop	7	12	43,715	2.7
	Luderitz	6	71	45,921	15.5
	Oranjemund	NA	NA	NA	NA
Kavango	Andara	9	8,842	28,814	3,068.6
	Nankudu	14	21,826	29,301	7,449.0
	Nyangana	10	5,745	21,774	2,638.5
	Rundu	21	85,083	218,023	3,902.5
Khomas	Windhoek	1	0	248,597	0.0
Kunene	Khorixas	8	90	33,766	26.7
	Opuwo	16	2,800	29,689	943.1
	Outjo	4	224	31,896	70.2
Ohangwena	Eenhana	11	5,840	29,400	1,986.4
	Engela	17	27,985	183,562	1,524.6
	Kongo	5	3,406	6,142	5,545.0
Omaheke	Gobabis 1	7	56	4,011	139.6
	Gobabis 2	9	82	41,803	19.6
Omusati	Okahao	11	9,727	35,897	2,709.7
	Oshikuku	28	23,161	139,056	1,665.6
	Outapi	NA	NA	NA	NA
	Tsandi	9	6,036	20,779	2,904.9
Oshana	Oshakati	20	9,529	218,281	436.5
Oshikoto	Onandjokwe	16	16,044	65,773	2,439.3
	Tsumeb	6	794	52,091	152.4
Otjozondjupa	Grootfontein	8	715	87,435	81.8
	Okahandja	3	133	70,911	18.8
	Okakarara	5	321	16,388	195.9
	Otjiwarongo	9	351	67,109	52.3
Total		**312**	**262,595**	**1,901,483**	**1,381.0**

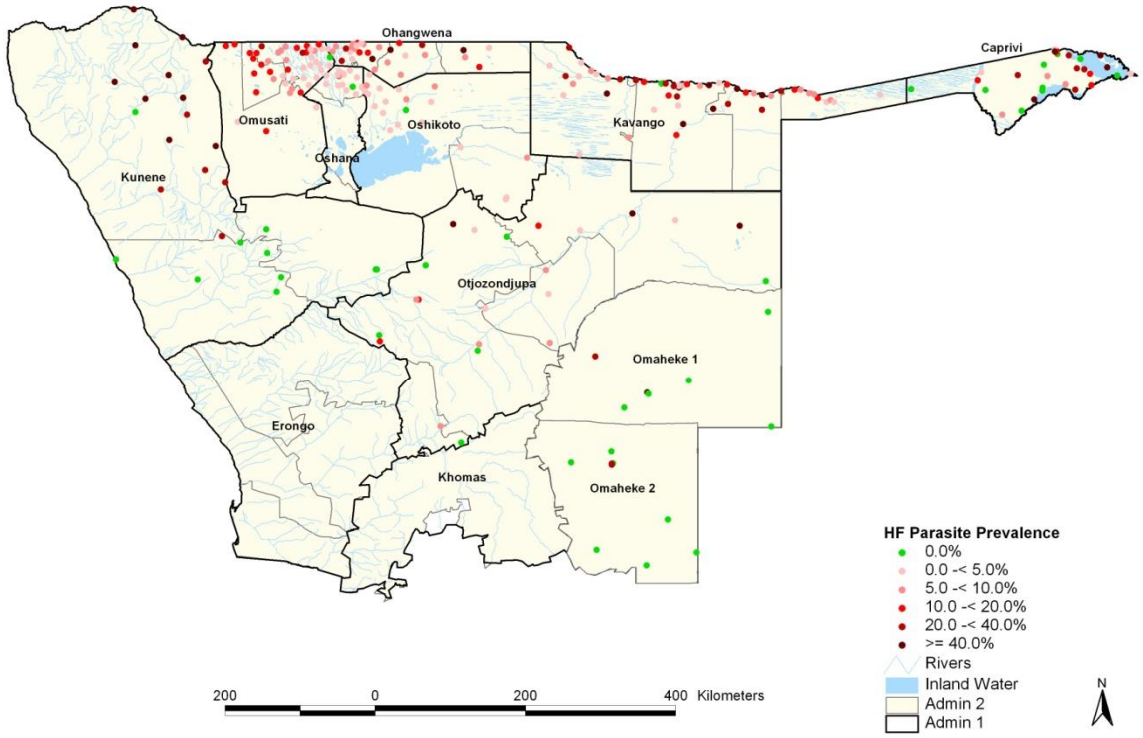
NA = Not Available

For health districts in Omaheke we have spilt Gobabis into two; Gobabis 1 to the North with a total of 7 facilities and Gobabis 2 to the South with 9 facilities and calculated incidence for each region separately

Table 3: Number of suspected, tested and confirmed malaria cases by region in 2009

Province / District		HF returning information in 2009 on malaria case loads and diagnostics	Number tested	Positivity rates among those tested (%)
Caprivi	Katima	29	5,226	18.3
Kavango	Andara	9	3,733	7.4
	Nankudu	13	3,648	6.7
	Nyangana	9	2,428	28.7
	Rundu	23	8,197	14.3
Kunene	Khorixas	8	86	1.2
	Opuwo	16	848	63.6
	Outjo	4	50	2.0
Ohangwena	Eenhana	10	3,748	10.1
	Engela	17	9,749	9.4
	Kongo	4	1,411	37.5
Omaheke	Gobabis	16	96	11.5
Omusati	Okahao	10	6,407	6.7
	Oshikuku	20	6,889	6.4
	Outapi	10	15,740	12.5
	Tsandi	8	5,409	10.4
Oshana	Oshakati	20	9,107	3.9
Oshikoto	Onandjokwe	16	5,970	4.5
	Tsumeb	6	628	4.5
Otjozondjupa	Grootfontein	8	541	10.9
	Okahandja	5	111	2.7
	Okakarara	7	233	7.3
	Otjiwarongo	5	580	6.2
Total		**273**	**90,835**	**10.9**

Figure 6: Distribution of RDT/Slide positivity among the Northern provinces in 2009



Positivity corrected incidence by district

Given that not all suspected malaria cases are true malaria unless confirmed through the use of microscopy or RDTs, the 2009 data (Table 3) re-assembled through a special survey provides an opportunity to correct the averaged data nationwide between 2008 and 2009 (Table 2). At this stage we have made several assumptions to impute neighbouring data to where other data are not available. The assumptions used and corrections made are provided as footnotes to Table 4. Although less than perfect these extrapolations seemed reasonable within the ranges of the data and allow a more complete picture of risk across all the 23 health districts across the 9 malarious regions of Namibia. The one difficult imputation is the assumption that there is no risk in Windhoek district and its surrounds. This may not be true but it seems likely that the urban extent that constitutes Windhoek will have exceptionally low risks of vector breeding and transmission. However, imported cases from neighbouring areas are likely to be seen at clinics in Windhoek.

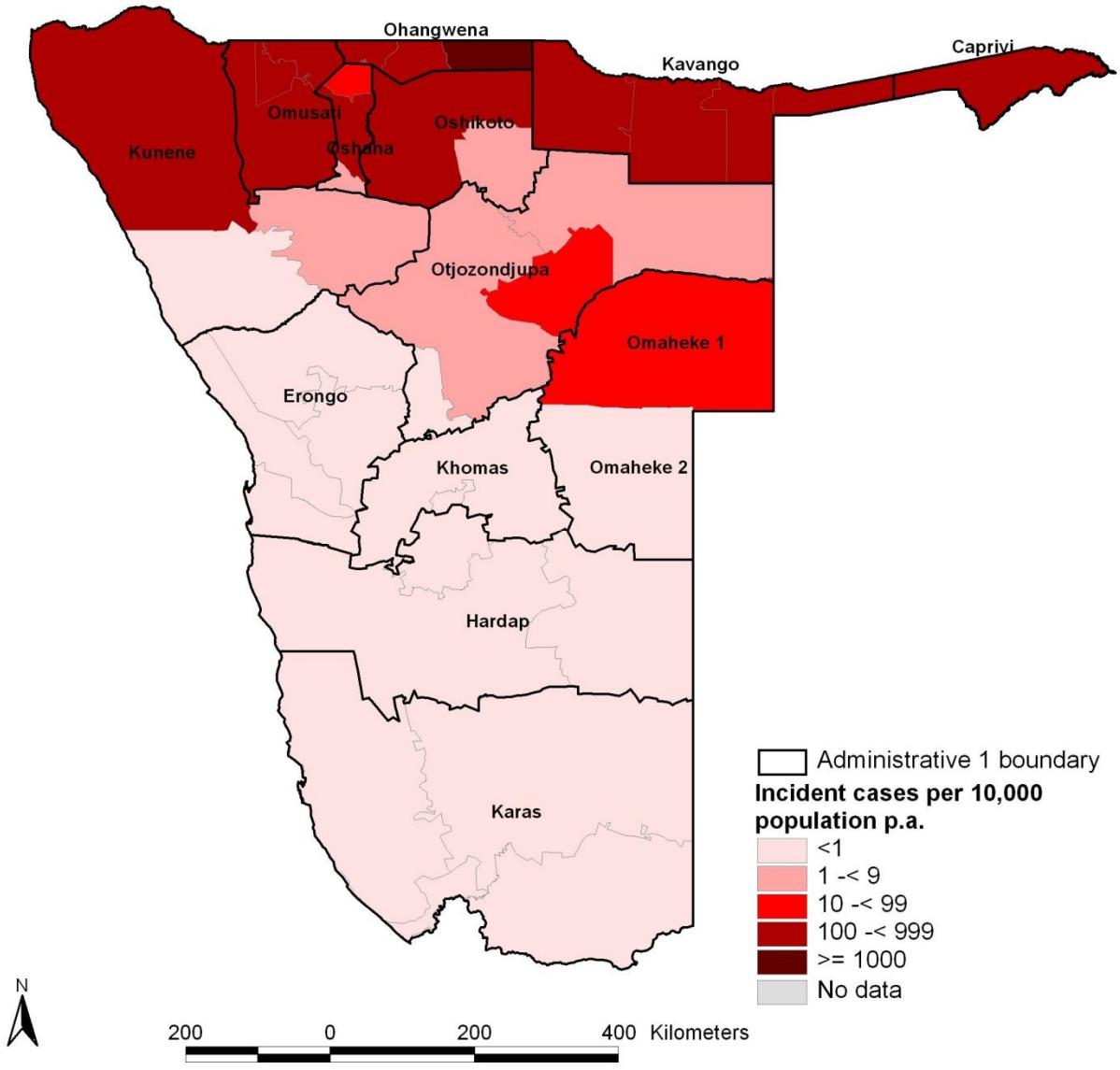
Using a definition of unstable transmission as represented by a case incidence of < 1 per 10,000 population p.a. and under the assumptions described above it seems reasonable to presume that malaria case incidence is unstable in the following regions: Southern Kunene, Khomas, Erongo, Karas and Hardap (Figure 7). This is no surprise to those working on malaria in Namibia and conforms to previous expert opinion, however the approach taken here has a semi-quantitative evidence base using data. Using WHO criteria of <1 case per 1000 population both Otjozondjupa and Omaheke would be classified as unstable. However given the vagaries of the reporting systems and approaches taken we prefer to classify these areas as stable transmission.

Table 4: Computed incidence of suspected malaria in all age groups per 1000 population p.a. per health district

Province / District		Overall incidence per facility per 10,000 population within catchment p.a.	Slide positivity correction	Corrected incidence per 10,000 population p.a.
Caprivi	Katima	3,592.7	0.183	655.8
Erongo[1]	Omaruru	72.6	NA	0.9[1]
	Swakopmund	NA	NA	0.9[1]
	Usakos	NA	NA	0.9[1]
	Walvis Bay	NA	NA	0.9[1]
Hardap	Aranos	0.0	--	0.00
	Mariental[2]	30.6	NA	0.3[2]
	Rehoboth[2]	24.2	NA	0.2[2]
Karas[3]	Karasburg	13.1	NA	0.1[3]
	Keetmanshoop	2.7	NA	0.03[3]
	Luderitz	15.5	NA	0.2[3]
	Oranjemund[4]	10.4[4]	NA	0.1[3]
Kavango	Andara	3,068.6	0.074	228.5
	Nankudu	7,449.0	0.067	498.2
	Nyangana	2,638.5	0.287	756.3
	Rundu	3,902.5	0.143	559.9
Khomas	Windhoek	Presumed risk free	NA	0.00
Kunene	Khorixas	26.7	0.012	0.3
	Opuwo	943.1	0.636	599.5
	Outjo	70.2	0.020	1.4
Ohangwena	Eenhana	1,986.4	0.101	200.9
	Engela	1,524.6	0.094	143.2
	Kongo	5,545.0	0.375	2078.9
Omaheke	Gobabis 1	139.6	0.250	34.9
	Gobabis 2	19.6	0.047	0.9
Omusati	Okahao	2,709.7	0.067	182.7
	Oshikuku	1,665.6	0.064	106.4
	Outapi[5]	2426.7[5]	0.125	303.3[5]
	Tsandi	2,904.9	0.104	303.4
Oshana	Oshakati	436.5	0.039	16.9
Oshikoto	Onandjokwe	2,439.3	0.045	108.7
	Tsumeb	152.4	0.045	6.8
Otjozondjupa	Grootfontein	81.8	0.109	8.9
	Okahandja	18.8	0.027	0.5
	Okakarara	195.9	0.073	14.3
	Otjiwarongo	52.3	0.062	3.2

1. For health districts in Erango we've assumed an average incidence of the Omaruru district (72.6 per 10,000 p.a.) and a suspected positivity rate similar to the southern, neighboring health district in Kunene, Khorixas of 1.2%.
2. The nearest possible corroborating health district for positivity rates among suspected cases is Omaheke, as seen in Figure x those in the southernmost reaches of this district bordering Hardap all had zero infection rates. We have therefore conservatively elected to apply a positivity rate of 1% to those suspected malaria cases in Mariental and Rehoboth districts of Hardap.
3. In the absence of any facility positivity data from Karas region we have applied a positivity rate as done in Hardap of 1% to each of the annualized case incidence estimates for the three health districts in Karas
4. No data on case incidence from Oranjemund so used average of other three health districts in Karas
5. No routine HIS data were available to compute incidence for Outapi health district in Omusati, average of the other 3 districts used

Figure 7: Classifications of stable and unstable transmission based on adjusted case incidence data and assumptions described in the text.



Aridity

Following approaches used at a global level by MAP we now consider the effects of aridity on the administrative region classifications of *stable* and *unstable* case-incidence. Arid conditions restrict *Anopheles* development and survival (Shililu et al., 2004). Limited surface water reduces the availability of water-bodies for oviposition. Moreover, low ambient humidity in arid environments further affects egg and adult survival through the process of desiccation (Gray & Bradley, 2005). The ability of adult vectors to survive long enough to contribute to parasite transmission and their pre-adult stages to ensure minimum population abundance is, therefore, dependent on the levels of aridity and species-specific resilience to arid conditions. To capture the influence of aridity on transmission we used the Enhanced Vegetation Index (EVI) derived from the bidirectional reflectance corrected MODerate-

resolution Imaging Spectroradiometer (MODIS) imagery, available at ~1 km spatial high resolution (Hay et al., 2006). Temporal Fourier processed, monthly EVI images were used to develop an annualized annual surface between 2000-2005 (UNEP, 2006; Figure 8a). Suitability for transmission was defined for each 1x1 km pixel in an average year where EVI was higher than 0.1, used previously by Guerra et al. (2008) to represent biological requirements to complete vector development from egg to adult (Figure 8b). This aridity mask does not completely rule out transmission in areas which have been classified as stable transmission because there may be pockets of very over-dispersed transmission due to man-made water collection points and occasional human population movement transporting vectors and parasites (Bouma et al., 1996; Omer et al., 1968; 1970), but are likely to attenuate completely unstable transmission conditions where case incidence is already very low. Application of the aridity mask to down-regulate stable conditions defined by case incidence to unstable and unstable to risk free therefore provides a more refined criteria of the stable and unstable divide in transmission (Figure 9).

Figure 8: a) EVI 2005-2009; b) selection of binned class of an average annual EVI of < 0.1

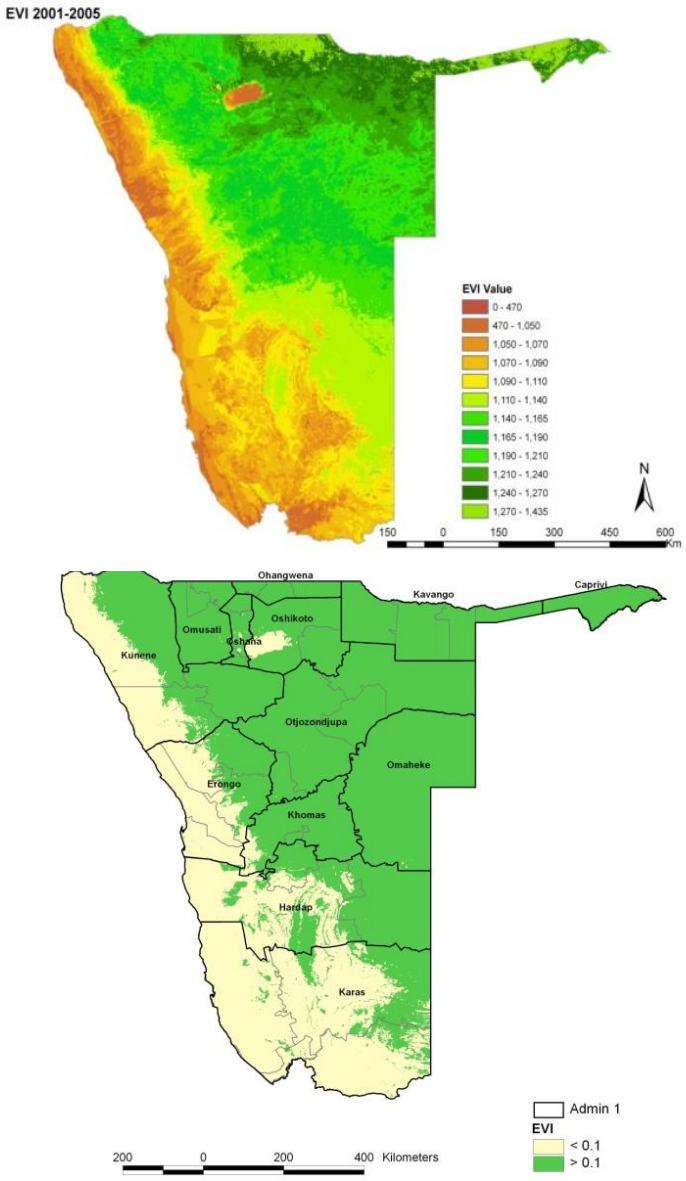
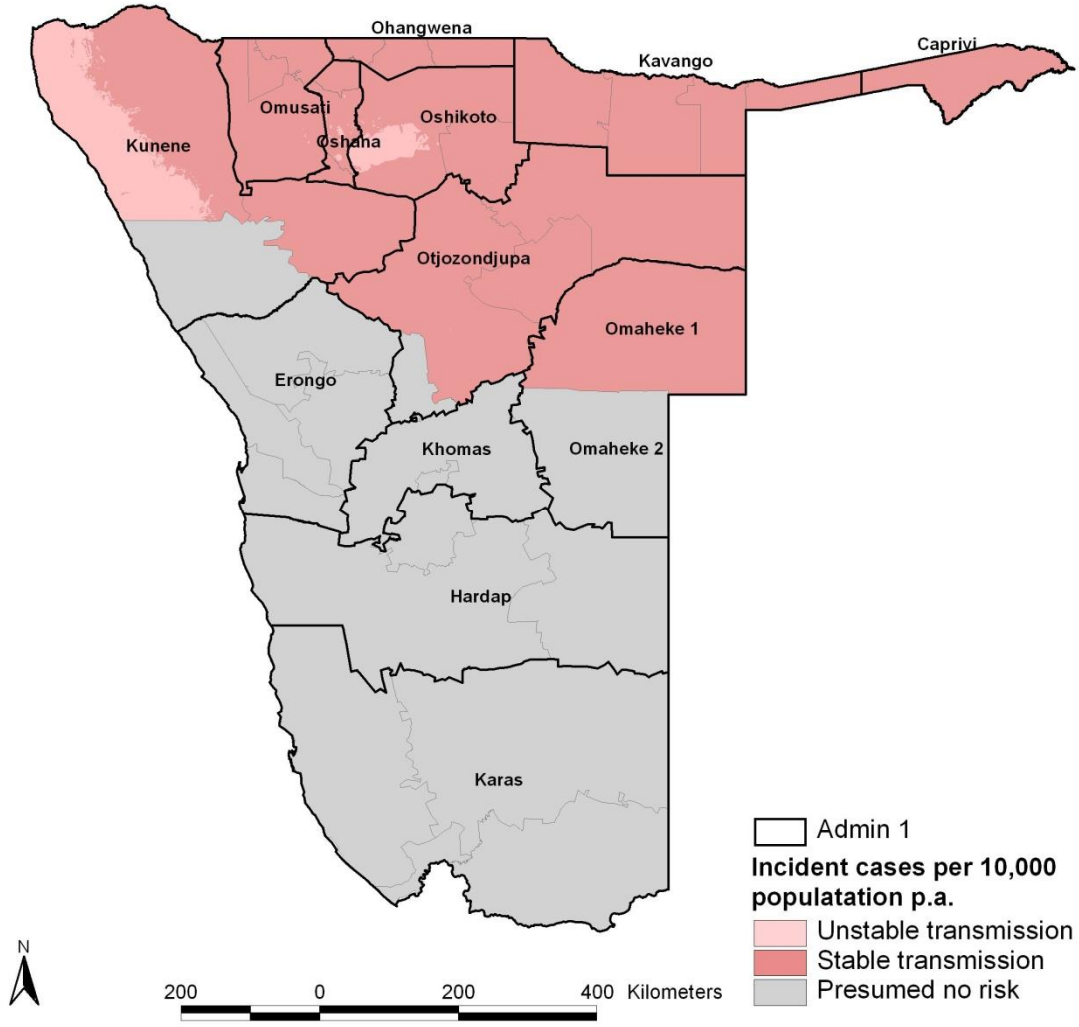


Figure 9: Aridity mask applied to case-incidence definitions of stable and unstable malaria



Modelling transmission intensity within the margins of stable malaria

Within the margins of presumed stable transmission shown in Figure 9, we anticipate a wide range of possible transmission intensities. Defining these ranges of transmission is important in the selection of suites of appropriate interventions (Hay & Snow, 2006). For example one would not promote intermittent presumptive treatment of infection in pregnant women where transmission intensity and subsequent infection prevalence is low. Diagnostics become less cost-efficient the higher the intensity of transmission and the higher the infection risks among fevers attending clinics. Furthermore, in stable endemic settings, where people are constantly exposed to repeated infections from birth, the important characteristic of *P. falciparum* is that only very few new infections result in death and the probability of dying is largely a function of age at first infection (transmission intensity) and age (acquired immunity). These features of immune regulated mortality result in a curvilinear relationship between mortality directly due to *P. falciparum* and parasite transmission intensity (Snow & Marsh, 2002). This form is complex and poorly defined but suggests that the risks of malaria mortality rise sharply with increasing

transmission intensity before reaching a plateau in areas where individuals may receive approximately 10 new infections per year equivalent to parasite prevalence among children of between 40-50%. The implications of this relationship are important for the time-lines and public health ambitions of intervention policies such as treated nets and house-spraying that aim to reduce parasite transmission (Smith et al., 2009) and modeling disease burdens (Snow & Marsh, 2002).

There are several measures of malaria transmission used in malaria epidemiology but by far the most ubiquitous and best understood in the parasite rate (proportion of surveyed individuals at one point in time that harbor malaria infection). This measure has been historically used as a marker of malaria endemicity (Metsellar & van Thiel, 1959), has been mathematically linked to other measures of transmission such as the Entomological Inoculation Rate (EIR) (Smith et al., 2005; 2007a) and the Basic Reproduction Rate of infection (R_0) (Smith et al., 2007a) and has been used to define relationships between disease outcome and transmission intensity (Snow et al., 1997; Snow & Marsh, 2002). Perhaps most importantly models have been developed to infer the projected impact of changes in *Pf*PR with time at varied levels of intervention coverage, notably insecticide-treated nets (ITN) (Smith et al., 2009).

There are several important considerations when undertaking parasite prevalence surveys: a) the most informative age group are children and adolescents above 2 years of age (Smith et al., 2007b). Historically, prevalence was recorded in children aged 2-9 years to provide categorical definitions of risk from hypo- to holo-endemic transmission (Metsellar & van Thiel, 1959); b) Optimized sampling of infection prevalence should be powered by an estimate of point estimates and anticipated between community variance (Design Effect) - most national household sampling for malaria indicators use treated net coverage as the sampling reference point and therefore often result in surveys under-powered to examine infection prevalence; and c) sampling of risk should ideally be repeated in time and space to capture the seasonal nature of transmission but at least sampled at the peak of expected transmission intensity. It is common for national household sample surveys to be conducted during dry seasons when roads are passable and households accessible. These survey times do not always correspond to peak malaria seasons. Other approaches to sub-national and national surveys are discussed in Section x.

Namibian MIS 2009: Sampling and survey procedures

In Namibia it was decided to undertake a Malaria Indicator Survey (MIS) as promoted by the Roll Back Malaria (RBM), Monitoring and Evaluation Reference Group (MERG) among the “malaria” districts in 2009 (UNICEF, 2007). Previous national sample surveys, including the latest 2006 Demographic & Health Survey had not included bio-markers of infection and were undertaken at times of the year when there was little malaria and thus concerns about the reported usage figures for ITN, IPTp and anti-malarial treatment. Sample sizes for the 2009 MIS were defined based on precision around a presumed 40% IPTp and ITN coverage, a design effect of 2 and a 20% non-response rate. The design was a two-stage probability sampling among the nine most Northern provinces, allowing for precision between urban and rural and three MARA-malaria risk strata (Figure 1: malaria absent, epidemic prone and endemic). Multistage sampling within these strata from region, district, constituency to Primary Sampling Unit (PSU) and finally 80% of households within the PSU (c. 25 per PSU) resulted in the selection 120 PSU’s (29 Urban and 91 Rural) and 3,000 households.

The survey was undertaken between April and June 2009. Field teams were trained over 6 days in survey procedures and comprised of two registered nurses, two enumerators and a driver per region, supervised by members of the NVDCP. All data were entered directly in the field using Personal Digital

Assistants. Ethical approval was provided by The Ministry of Health and Social Services Ethical Clearance Committee [Ethical approval number xxxx]. Each household member was asked permission to participate in the survey in a language they were familiar with and given the right to refuse. Finger prick blood samples were taken from every resident child below the age of five years whose parents or guardians provided informed consent located in all the sampled households within each PSU. However, in every fourth household every household member was asked to provide a finger prick blood sample for malaria parasitology. An RDT, Paracheck *Pf*®, was used to record infection at the time of the survey and thick and thin blood smears made for subsequent detailed parasitology. Despite multiple readings of the slides by microscopists at the Namibia Institute of Parasitology, the quality of slide preparation, staining, storage and deterioration of staining in transport limited detailed examination of infection from the field slides; only 11 of 4,582 slides read more than once were regarded as positive and it was decided to ignore the QA slide results. While Paracheck-*Pf*® has a documented false positive rate (Bell et al., 2005; WHO, 2009), due its oversensitive detection of circulating antigens several weeks after active infection, it does provide some indication of parasite exposure and therefore adds some value in particularly low transmission settings for defining community-level exposure.

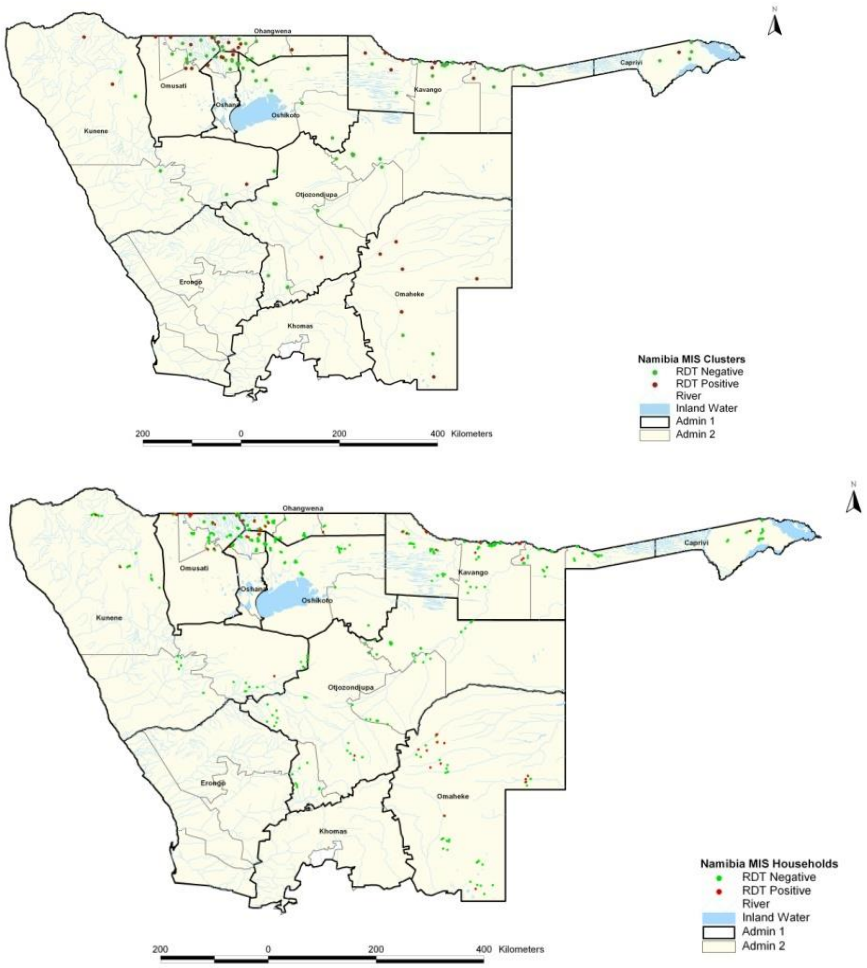
Namibian MIS summary of survey data

Table 5 summarizes the data from the MIS survey. Overall prevalence among all age groups sampled in 1 in 4 households across the 120 PSU's was only 2.93%. More than 70% of PSU's sampled showed no evidence of infection. In Oshikoto no one tested with an RDT showed evidence of infection. Under-five prevalence was similar to the prevalence described when measured in all age groups; no child was positive in Omaheke, Oshikoto and Caprivi regions. For the purposes for the present modelling and mapping work we have focussed on the samples taken among all ages in the 1:4 households sampled within each cluster. The spatial distribution of positive and negative households and aggregated cluster locations for all age surveys are shown in Figures 10a and 10b.

Table 5: Summary of RDT positivity by region for households sampled for examination of all age-groups and households where only children less than five sampled.

Province	Clusters (PSU); households included in all-age testing	RDT positive/Examined (% positive) all ages	Number (%) clusters with no positive cases – all ages	Number (%) of households with no positive cases – all ages	All households sampled for children <5 years Clusters; HH	RDT positive/Number children sampled in all households with an U5 (% positive) under fives only
Omaheke	9; 67	21/249 (8.43%)	3 (33.3%)	54 (80.6%)	9; 56	0/85 (0.00%)
Otjozondjupa	18; 105	1/347 (0.29%)	17 (94.4%)	104 (99.1%)	18; 98	2/167 (1.20%)
Kunene	9; 74	4/231 (1.73%)	6 (66. 7%)	71 (95.9%)	9; 52	1/88 (1.14%)
Omusati	14; 87	28/364 (7.69%)	8 (57.2%)	75 (86.2%)	14; 107	10/151 (6.62%)
Oshana	12; 85	6/297 (2.02%)	8 (66.7%)	80 (94.1%)	12; 81	2/110 (1.82%)
Ohangwena	14; 86	16/390 (4.10%)	8 (57.1%)	77 (89.5%)	14; 127	7/191 (3.67%)
Oshikoto	10; 68	0/313 (0.00%)	10 (100.0%)	68(89.5%)	10; 70	0/97 (0.00%)
Kavango	28; 213	19/926 (2.05%)	20 (71.4%)	201 (94.4%)	28; 228	8/343 (2.33%)
Caprivi	6; 47	1/164 (0.61%)	5 (83.3%)	46(97.9%)	6; 54	0/64 (0.00%)
Urban	**28; 190**	**5/565 (0.88%)**	24 (85.7%)	186 (97.9%)	**28; 159**	**0/218 (0.00%)**
Rural	**92; 642**	**91/2716 (0.34%)**	61(66.3%)	590 (91.9%)	**92; 714**	**30/1078 (2.78%)**
Total	**120; 832**	**96/3281 (2.93%)**	85 (70.8%)	776 (93.3%)	**120; 873**	**30/1296 (2.32%)**

Figures 10a: Clusters sampled in northern 9 regions during the 2009 MIS; Figure 10b: households sampled (all age groups). Green represents absence of infection and red presence of infection.



Modeling spatial interpolated infection prevalence across nine regions covered by the MIS

Novel approaches to mapping malaria infection risk have been developed using principles of model-based geo-statistics (MBG) (Hay et al., 2009; Noor et al., 2008; 2009; Gething et al., 2010; Clements et al., 2006; Vounatsou et al., 2009). These models are computationally complex but allow for the best estimates of infection risk interpolated across space derived from partial data and importantly allow for the definition of uncertainty. The models used for global models of *P. falciparum* infection risk mapping (Hay et al., 2009) we have adapted here to develop risk maps of malaria transmission intensity in the northern parts of Namibia in 2009.

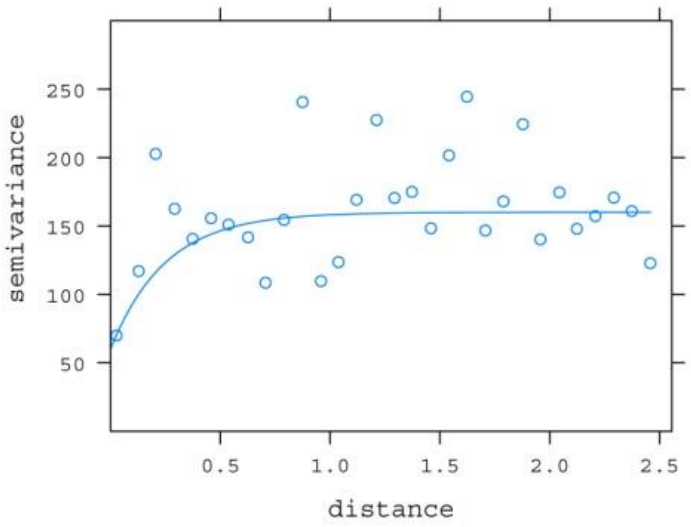
A fundamental concept behind analyzing geographic data is determining the presence of spatial dependence (Tobler, 1970). Spatial dependence simply means co-variation of properties within a geographic space driven by the principle that observations at proximal locations are more correlated (positively or negatively) than those at locations further away. There are a number of reasons for spatial dependence and but all generally relate to factors that lead to spatial correlation, causality or interaction (e.g. people who live in same neighborhood are more likely to be similar than those who live

in communities further away). Spatial dependence in data leads to the statistical problem of spatial autocorrelation which negates the conventional regression wisdom that observations at one location are independent of observations at a neighboring location often yielding unstable parameter estimates and unreliable significance results (Tobler, 1970; Isaacs & Srivastava, 1989).

Geo-statistical techniques overcome this challenge by incorporating the spatial effects in the data analysis. However, not all data from different locations exhibit spatial dependence and before geo-statistical techniques are used the data need to be explored for the presence of spatial structure or autocorrelation. To explore any data for spatial autocorrelation, the variogram, also commonly referred to as the semi-variogram, is used. The variogram is a graphical summary of spatial autocorrelation structure and has three parameters: the *nugget* (*n)* which is the height of the jump of the variogram at the Y-axis and is considered to represent the measurement error; the *sill* (*s)* which is limit of the variogram tending to infinity lag distances; and the *range (r)* which is the distance in which the difference of the variogram from the sill becomes negligible. The semi-variance (half the variance of data pairs) is shown on the Y-axis and increases with increasing separation distances or lag between data pairs shown on the X-axis. For data to be used to construct the variogram, their location must be defined explicitly i.e. they are provided with latitude and longitude coordinates.

Variograms were constructed for the Namibian *Pf*PR data to examine the presence of spatial autocorrelation in the data summarized as clusters (n=120) where all age groups were sampled using the *variogram* function and models were fit using *variofit* function in R (R version 2.10.1, the R foundation for Statistical Computation, http://www.r-project.org/). In all cases, an exponential model was fit to the variogram (Figure 11).

Figure 11: Variogram and model fit for distribution of all cluster level *Pf*PR data where all individuals were examined in each clusters (n=120) The X axis shows distance in degrees latitude and longitude while the Y axis shows semi-variance.



The variograms of the *Pf*PR data showed the presence of spatial structure in clusters with spatial correlation occurring generally up to 0.6 decimal degrees or the equivalent of circa 67 km at the equator.

The relationship of ecological and climatic covariates with *Pf*PR

A set of ecological and climatic covariates have traditionally been used in malaria mapping including temperature, rainfall, vegetation and distance to breeding sites (Craig et al., 1999; Omumbo et al., 2005a; 2005b; Guerra et al., 2008; Noor et al., 2008; Noor et al., 2009). These covariates were identified and assembled from a variety of sources (Annex A) and were then categorized into plausible classes based on the observed statistical distribution of the covariates which were then extracted at each survey location using ArcGIS 9.2 (ESRI Inc., USA). To assess the effects of the covariates on observed *Pf*PR a univariate binomial logistic regression model was implemented for each covariate with *Pf*PR as the dependent variable in Stata/SE Version 10 (Stata Corporation, College Station, TX, USA). The results of the univariate analyses (Table 6) were used to determine an appropriate suite of covariates for inclusion in the Bayesian geo-statistical model. A covariate was considered to have met the inclusion criteria into the model if the Wald's P-value was <0.20 when examined against *Pf*PR as the outcome variable. Urbanization has been shown to limit the availability of optimum environments for the development of the malaria transmitting anopheline populations resulting in reduced vector density, biting rates and transmission intensity in many African countries (Trape & Zoulani 1987; Hay et al., 2005; Omumbo et al., 2005; Wang et al., 2006), therefore the Bayesian geo-statistical model has been set up to implicitly account for this covariate and therefore was not tested independently.

Table 6: Univariate analysis results of urbanization against *Pf*PR

	Number of survey locations	Mean (median) *Pf*PR	Univariate regression*: Odds Ratio (95% CI), P-value
Median annual minimum temperature			
≤14°C	53	2.6 (0.0)	Ref
>14°C	67	3.0 (0.0)	1.17 (0.13, 10.53), 0.888
Median annual maximum temperature			
≤30°C	53	2.1 (0.0)	Ref
>30°C	67	3.4 (0.0)	1.60 (0.16, 15.73), 0.686
Average annual precipitation temperature			
≤40 mm	59	3.7 (0.0)	Ref
>40 mm	61	2.0 (0.0)	0.533 (0.56, 5.04), 0.584
Average annual enhanced vegetation index			
≤0.2	49	3.4 (0.0)	Ref
>0.2	71	2.5 (0.0)	0.72 (0.08, 6.3), 0.767
Median distance to water features			
≤47 km	59	3.0 (0.0)	Ref
>47 km	61	2.7 (0.0)	0.88 (0.10, 7.60), 0.906

From the univariate analysis presented in Table 6 and the detailed description of the data in Annex A, all the covariates explored here did not qualify for inclusion into the Bayesian geostatistical model for predicting *Pf*PR in Namibia. This is not to say these covariates aren't important but probably reflects the overall small sample of clusters upon which to test these adequately. As such we have elected not to include covariates in this iteration of the model development, but with more data in space and time this may become more possible. The MBG therefore simply describes the spatial structure of the data.

Bayesian space-time models and use of covariates

The model used for the modelling of spatial risks in Namibia was a spatial Bayesian generalized linear geo-statistical approach that provides the ability to predict values of a spatially continuous event, in this case *Pf*PR, at un-sampled locations using combinations of the sampled data in space and time, and importantly allow for calculation of robust uncertainty estimates around model predictions. The underlying assumption is that the probability of prevalence at any survey location is the product of two factors: the time and location of the survey, modelled as a transformation of a space-time Gaussian random field. All cluster data were sampled among all age groups so no age-standardization was necessary resulting in predicted surface of *Pf*PR among all ages. The Bayesian spatial-temporal model was implemented in two parts starting with an inference stage in which a Markov Chain Monte Carlo (MCMC) algorithm which was used to generate samples from the joint posterior distribution of the parameter set and the space-time random field at the data locations. This was then followed by a prediction stage in which samples were generated from the posterior distribution of *Pf*PR at each prediction location on a 1×1 km grid which was further classified into the following *Pf*PR categories: *Pf*PR <1%; *Pf*PR 1-4.99%; *Pf*PR ≥ 5%. To provide a measure of uncertainty we developed coincidental maps of the standard deviation from the posterior mean prediction.

Malaria risk classifications and estimations of populations exposed to risk

The product of the MBG simulations for 2009 MIS model run is shown as continuous 1x1 km posterior predictions in Figure xx. These were subsequently binned into the four endemicity classes of *Pf*PR and shown in Figure xx. The raster malaria endemicity maps were then overlaid on the 2010 projected high resolution population map described in detail in Section xx and the number of people in each endemicity class, overall and by region for 2010 was extracted using ArcGIS 9.2 *Spatial Analyst* tool and summarized in Table xx.

Caveats & Recommendations

Here we tackle some more generic recommendations as they apply to the design of new national control ambitions, including elimination, and the more systematic surveillance of risk in Namibia.

1. ***Value added through use of HIS malaria case reporting data***: The data provided through routine HIS since 2005, while not perfect, have enormous value in defining risks of malaria. We have not applied model based geo-statistical techniques to these data, although we presume they will have spatial structure and lend themselves to geo-statistical interpolation (Gething et al., 2006). Combining underlying populations within a presumed catchment enables us to compute rates of suspected malaria clinic presentation and correct these in accordance with expected malaria positivity. It is clear that central reporting is incomplete and rapid surveys of retrospective data assembly were successful in filling in omissions for 2009. It would be valuable to explore these data further with more elaborate, time-space models and covariate assumptions. This is beyond the scope of the present exercise but something that is recommended for future investigation. Meanwhile efforts should be made to extend the retrospective survey to the southern provinces and include 2008 and the first half of 2010 and complete missing facilities and values in the areas further north. Omaheke region appears to have only one health district and this is a very large region with obvious differences in case incidence and fever positivity north to south; the result is that the entire region is weighted in favor of "stable" transmission by northerly facilities. It would be useful during future iterations of this risk model to divide this region into two. Using model based geo-statistical interpolation may be another approach that would use similarities between facilities to model case incidence in space without reference to regional or district boundaries. One caveat not included in the computation of case-incidence is the possible differences in formal health sector use for fevers. These data are available in various forms including the Namibian DHS in 2006-7 and the more recent MIS in 2009. Additional assemblies of service use patterns and semi-qualitative measures of catchment distances to different levels of the health system would add precision to the refined modeling of these data.

2. ***HIS reporting of malaria in southern provinces***: While case incidence is low in Karas, Hardap and Khomas suspected cases have been reported since 2005 and it would seem appropriate to begin to strengthen malaria case-reporting in the southern half of Namibia as an officially notifiable disease and each case investigated in more detail (including travel histories, precise residence and use of prevention and curative interventions). We mention this in the light of possible ambitions to systematically eliminate malaria in Namibia. Should this ambition continue to gain political traction the health systems will need to respond to enhanced surveillance of low risk, sporadic locally acquired infections - even within areas traditionally regarded as low transmission risk. It would seem appropriate to begin to build these systems of surveillance of rare infections in the south as soon as possible before migrating experience to the more Northern provinces as transmission intensity declines in these areas through effective control.

3. ***Challenges for malaria elimination in Northern Namibia***: Despite the caveats of the data presented and analyzed in this report there is one clear observation that will present challenges for an elimination agenda: the concentration of risks along the Angolan border. A recent adaptation of approaches taken here for Northern Namibia to model the distribution of malaria risk in Angola suggest that risks along the Namibian-Angolan border are low, parasite prevalence in children aged < 5 years below 15% (Gosoniu et al., 2010). However this model cam with much

uncertainty as there were only six clusters of data within 100 km of the border. Conversely from the Namibian side there is much more data and risks relative to the rest of Northern Namibia are high along the border. Future surveys of infection prevalence, whether school or community-based, should consider extending sampling either side of this border to more uniquely define the risks in this region. Human population movement is high across the border and *An. arabiensis* may travel up to 2km for a blood meal, both combine to suggest that while there is a national boundary this may be irrelevant for malaria transmission and the possibilities of either country reaching an elimination state.

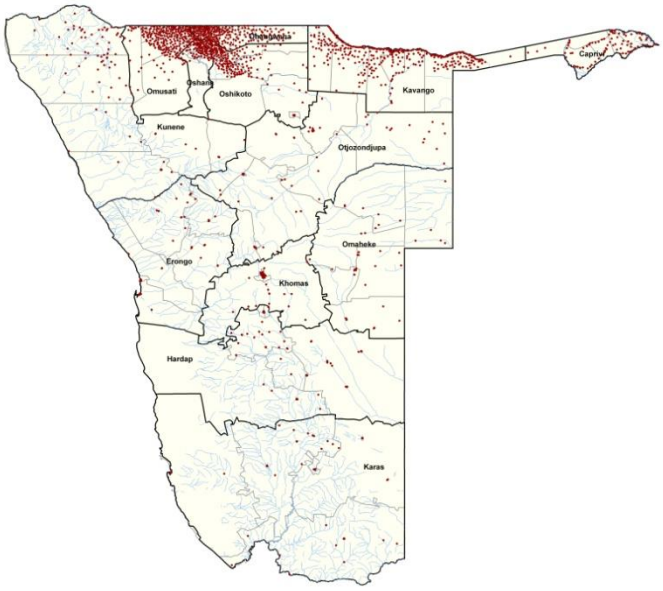
4. ***Limitations of MIS 2009***: As the mapping exercise described in this report suggests large areas of Namibia where empirical data on the point prevalence of infection exist show zero prevalence. We need to be cautious in interpreting these data and some of these reservations are discussed here and in the following bullets. The sample sizes selected for the MIS were small relative to the prevalence of infection (the MIS was powered to detect between area differences in ITN use not infection). Inevitably the reports of zero prevalence by cluster and by household aggregates may well reflect the sample sizes used, 25 households per PSU and only 120 PSU's. The sampling frame was conditional on providing enough power to show differences in intervention coverage by urban and rural classes and basic perceived malaria strata. The sample was not optimized for spatial weighting to provide sufficient spatial coverage of risk – this requires a different population-to-space sampling frame not traditionally used in MIS or other household sampling strategies. Inevitably the MIS data are single point estimate of risk, measured using an RDT, do not reflect the seasonal differences in risk but risks only among household members between May and June 2009.

5. ***Measures of transmission intensity and markers of parasite exposure***: RDT's are useful contributions to household surveys. They are not perfect and tend to have a high false positive rate (WHO, 2009), particularly the Paracheck-*Pf*® (Bell et al., 2005; WHO, 2009). Attempting to reconcile true parasite presence using slides prepared in the field has proved difficult in various countries that have recently completed an MIS including Kenya, Liberia, Djibouti and Sudan. The staining, fixing and storage of slides demands a level of expertise and experience often not included in the staff recruited and trained for household surveys. An alternative method, that is less demanding and more cost-efficient, is confirming parasite presence among all RDT positives and a random pooled selection of negatives from the same cluster using Polymerase Chain Reaction (PCR) detection methods of species-specific parasite DNA extracted from filter papers. Preparation, labeling and storage of filter paper blood spots does demand some training but is easier than preparation of slides and can be automated in appropriately tooled laboratories (Corran et al., 2008). In addition these same filter papers can be used to define historical exposure to infection, important when reaching low levels of transmission intensity. Measurement of anti-malarial antibodies in exposed populations integrates serological definitions of malaria exposure over time, when plotted by age (Drakeley et al., 2005). Species-specific antibodies can be detected in blood from a finger prick, and samples can be assayed quickly in large numbers. Sero-prevalence rates have been used to define malaria endemicity (Corran et al., 2007); used to track the progress of elimination in Maurtius (Bruce-Chwatt et al., 1973); and importantly within the Namibian context distinguish between areas of differential exposure when RDT and reliable slide parasite rates are zero (Bouesma et al., 2010). In areas of very low parasite exposure sero-epidemiological methods can identify residual or potential foci of infection using geo-spatial analysis of individual or household level antibody response (Bouesma et al., 2010). Future household or other sample surveys of risk should consider the

inclusion of filter papers for confirmatory PCR in all areas and serology in low risk marginal areas.

6. ***Alternatives to household sampling***: National household sample surveys are logistically complex and expensive and defining their principle aims and objectives is fundamental before beginning the surveys. If their intention is to define parasite exposure for risk mapping their designs are currently flawed by being only population weighted samples and powered to define intervention coverage (MACRO, 1996; UNICEF, 2007). Migrating from these survey designs to those powered to define low levels of parasite exposure and are population-plus-spatially weighted samples will make these surveys more, rather than less expensive. School children provide a community easy to sample and resident within a definable catchment of the sampling point and represent the optimal age range for parasite prevalence description (Brooker et al., 2009). Conducting school malaria surveys is not a new approach in malariology. School surveys were a regular part of malaria reconnaissance and control during the elimination control strategies of the Global Malaria Eradication Programme (Boyd et al., 1949; Russell et al., 1946). For example, during the 1920-40s, large-scale school parasite surveys were frequently conducted in the United States: during 1942-43, for example, blood films were collected from 104,613 school children in seventeen states, with only 201 (0.2%) found to be infected (Faust, 1949). In the then Southern Rhodesia, school surveys formed part of malaria risk surveillance between 1937 and 1948 (Alves, 1958) and during the 1970's the Blair Institute in Zimbabwe continued the tradition of regular school-based malaria surveillance. In Botswana during the 1960's school surveys were a common measure of malaria risk. Kenya has also had a long history of routine school surveys of malaria infection prevalence as part of responsibilities of the Division of Vector Borne Diseases, MoH, since the 1950's. Kenya has recently resurrected this approach to malaria risk mapping to form an integral part of long-term surveillance of the impact of scaled intervention nationwide and identification of priority areas for tailored suites of intervention (Gitonga et al., 2010). Examining the distribution of 1672 schools in Namibia that provide schooling for over 577,000 children (MoE, 2008) shows an obvious congruence with where people live (Figure xx). Primary school attendance is high across the country and these children are likely to represent the communities surrounding the schools. With the appropriate collaboration between MoHSS and MoE a rapid schools based survey could be considered in Namibia to improve our understanding of risk. As evidenced in Figure xx spatial over-sampling of most schools in the south would add much needed information to existing prevalence data and should probably include serology. This is a good example of why spatial weighting of survey data is important for mapping infectious disease risks. In the north were most people and most schools are located more traditional approaches to population weighting sampling are advised. Inclusion of serology in the most southerly parts of the Northern provinces may be advisable while in the areas defined so far as more stable transmission this may not be necessary. We mention this option for surveillance for two reasons: a) the MIS was inadequately powered to provide enough spatially configured data on risk and more data is needed; b) the MIS did not consider risks in the south and c) school-based survey are increasingly considered a means to indentify foci of infections rapidly and may be useful in focused efforts toward end-game elimination ambitions. More discussion is obviously needed around this possibility but raised here as an option for future malaria mapping and surveillance to improve upon what has been possible to-date.

Figure x: Distribution of schools in Namibia in 2008 (MoE, 2008)



7. ***Non-Gaussian models of risk***: Dealing with many zero infection prevalence survey estimates within the present MBG Bayesian modeling approaches presents a number of limitations. Our approaches assume a normal Gaussian distribution of risks and clearly with a major over-dispersion of risk skewed to zero these models lose some skill. The variance in prevalence is greater than the mean (Vounatsou et al., 2009) and a number of techniques have been used to model data with many zeros. The techniques come under the umbrella of zero-inflated (ZI) models (Mullay, 1986; Lambert, 1992) and could take the form of negative ZI binomial (Denwood et al., 2008) or Poisson ZI (Agarwal et al., 2002; Rodrigues, 2003) models. New work at the MPHEG-MAP labs in Nairobi aims to explore these techniques to develop Bayesian geo-statistical approaches over the next 2 years and will offer new suites of modeling tools for mapping malaria transmission from community prevalence data from low risk areas such as Namibia where data is dominated by very low or zero prevalence.

8. ***Inclusion of multiple data types and sources***: Despite zero risks being defined through the household prevalence surveys, health facility data show evidence of infected fever presentations during 2009 from the same areas. Integrating two types of different data into a single platform of risk assessment presents a number of challenges. First, the similarities and differences in spatial structure between facility and community-level data would need to be explored more elaborately. Second there may be possibilities of using facility-level data as a covariate of risk may be possible within the MCMC stage of the modeling work. Third, it may be possible to use two levels of modeling that provide two different outputs related to clinical incidence and parasite prevalence in the community at the inter-section of very low community prevalence. This is all work that should be explored more imaginatively within different zero-inflated MBG suites.

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Annex A

The relationship of ecological and climatic covariates with *Pf*PR

Maximum and minimum temperature

Temperature has a significant influence on the malaria vector and parasite (Molineux 1988; Craig et al., 1999; Snow & Gilles 2002). Monthly average temperature raster surfaces at 1×1 km resolution were downloaded from the WorldClim website (http://www.worldclim.org/download.html) from which annual averages were derived. These surfaces were produced from global weather station temperature records gathered from a variety of sources for the period 1950-2000 and interpolated using a thin-plate smoothing spline algorithm, with altitude as a covariate, to produce a continuous global surface (Hijmans et al., 2005). For Namibia, the histograms (Figure 1) of both average annual minimum and maximum temperatures showed a negative skew and as a result the median instead of the mean was used to construct categories of temperature. Minimum temperature was classified into areas of median ≤14°C and >14°C; while maximum temperature was classified into ≤30°C and >30°C (Figure 2).

Figure 1: Histograms of a) average annual maximum; and b) average annual minimum temperature. Both covariates are negatively skewed.

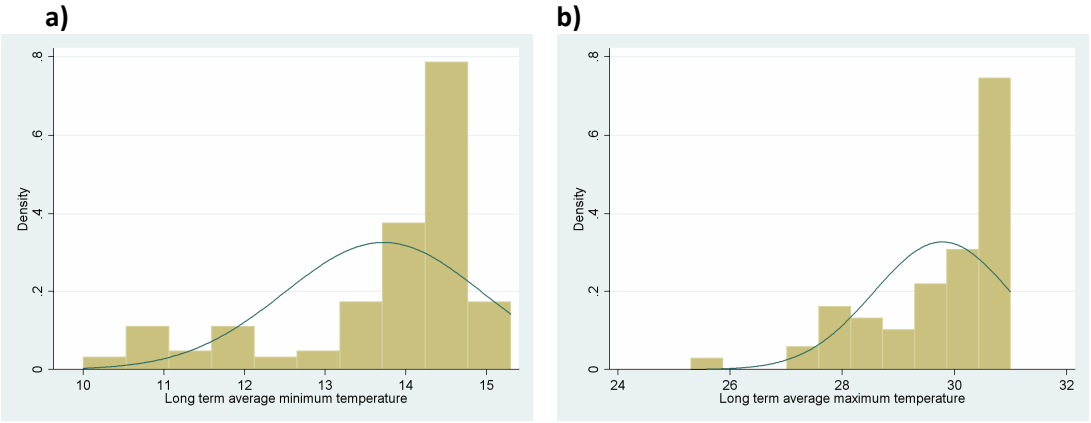
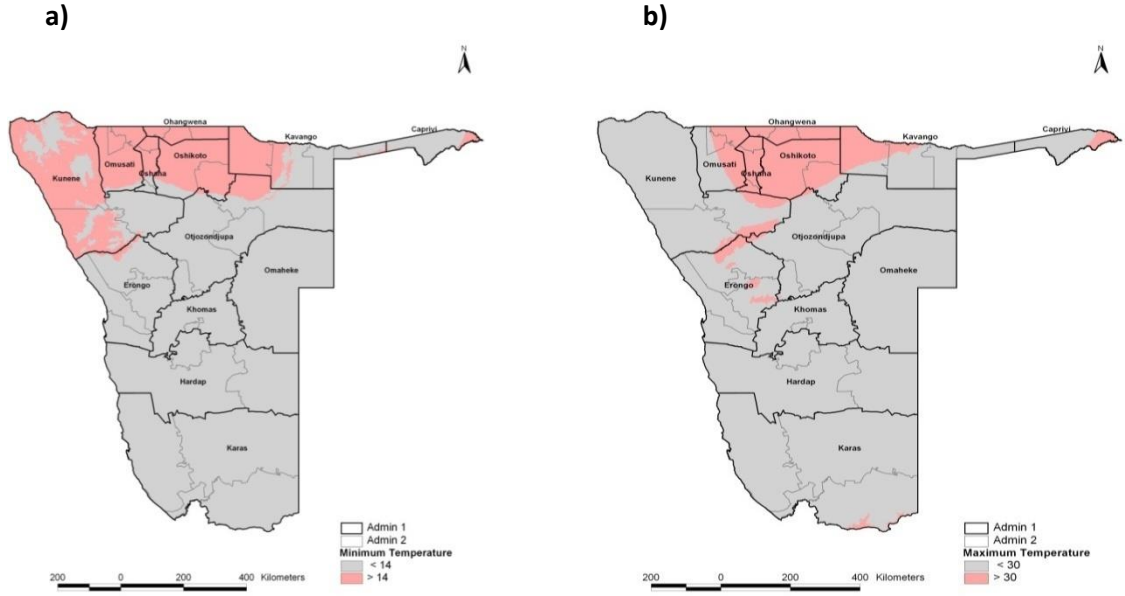


Figure 2: Maps of: a) categories of average annual maximum; and b) average annual minimum temperature.



The box plots (Figure 3) show that most of the infections are concentrated in areas where median temperatures are greater than a minimum of 14 and a maximum of >30°C. The regression results,

however, show that the effects of both these temperature covariates are not significant with P-values of 0.888 and 0.686 respectively (Table 1).

Figure 3: Box plots of *Pf*PR by categories of average annual minimum and maximum temperature

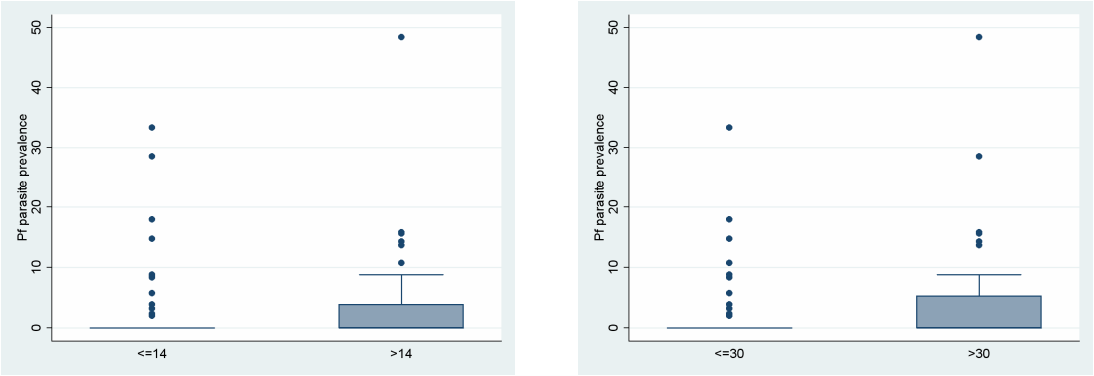


Table 1: Univariate analysis results of categories of minimum and maximum temperature against *Pf*PR

	Number of survey locations	Mean (median) *Pf*PR	Univariate regression*: Odds Ratio (95% CI), P-value
Median annual minimum temperature			
≤14°C	53	2.6 (0.0)	Ref
>14°C	67	3.0 (0.0)	1.17 (0.13, 10.53), 0.888
Median annual maximum temperature			
≤30°C	53	2.1 (0.0)	Ref
>30°C	67	3.4 (0.0)	1.60 (0.16, 15.73), 0.686

Precipitation

Rainfall, combined with suitable ambient temperatures, provides potential breeding environments for *Anopheles* vectors while humidity is associated with vector longevity (Gill 1920; Dutta et al., 1978). Monthly mean precipitation raster surfaces at 1×1 km resolution were downloaded from the WorldClim website (http://www.worldclim.org/download.html) and used as a proxy for rainfall. The monthly means were used to generate a long term average annual precipitation surface which showed a near-normal distribution (Figure 4) with a mean of 40 mm average annual precipitation. This mean was then used to generate a precipitation surface of two classes <= 40 mm and >40 mm of rainfall and a box plot of *Pf*PR by these classes was constructed (Figure 5).

There was no significant association between *Pf*PR and precipitation as demonstrated by the box plot (Figure 6) and the univariate regression results with a P-value of 0.584 (Table 2).

Figure 4: Histogram of average annual precipitation showing a near-normal distribution

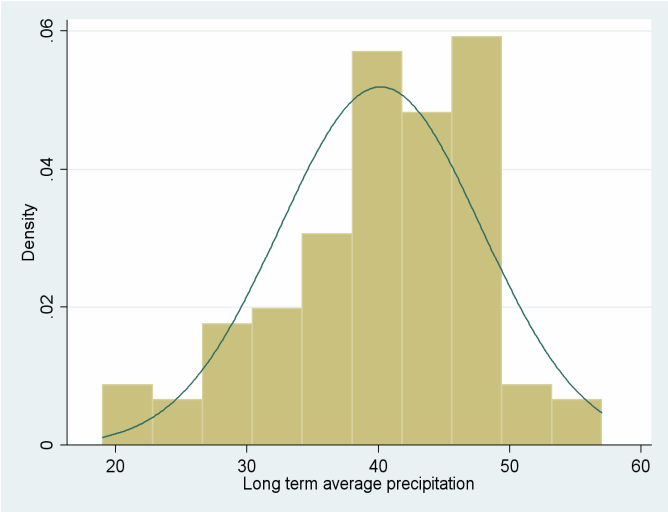


Figure 5: Maps of categories of precipitation shown as areas ≤40 mm and those >40 mm annual average precipitation

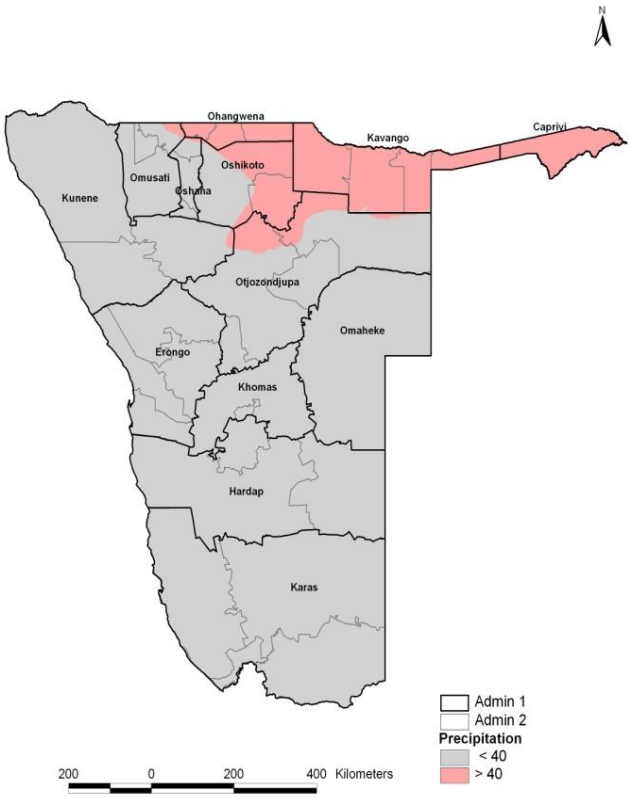


Figure 6: Box plots of *Pf*PR$_{2-10}$ by categories of sets of three continuous months in a year with precipitation >60 mm; sets of three continuous months in a year with precipitation >80; and areas of precipitation of 0-1000mm; 1001-1500mm; and >1500 mm.

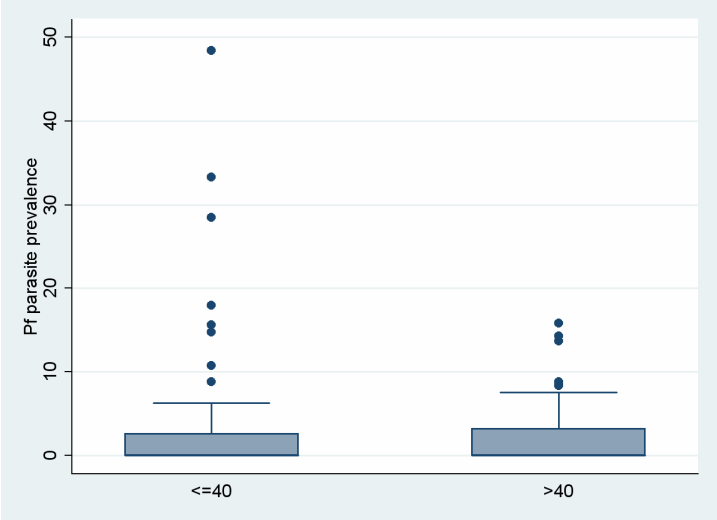


Table 2: Univariate analysis results of categories of precipitation against *Pf*PR

	Number of survey locations	Mean (median) *Pf*PR	Univariate regression*: Odds Ratio (95% CI), P-value
Average annual precipitation temperature			
≤40 mm	59	3.7 (0.0)	Ref
>40 mm	61	2.0 (0.0)	0.533 (0.56, 5.04), 0.584

Enhanced vegetation index (EVI)

EVI is an index of intensity of photosynthetic activity (Tucker et al., 2005; Scharlemann et al., 2008). Traditionally, this index has been used in malaria risk mapping as a proxy of rainfall (Craig et al., 2009; Noor et al., 2009) and a measure of aridity that limits larval growth and vector survival (Guerra et al., 2008). EVI ranges from 0 (no vegetation) to 1 (complete vegetation). Monthly EVI surfaces have been derived from the global Moderate Resolution Imaging Spectroradiometer (MODIS) satellite imagery for the period 2001-2005 and subjected to temporal Fourier analysis at 1×1 km spatial resolution (Scharlemann et al., 2008). To define malaria-relevant EVI a category, a histogram of its distribution was constructed (Figure 7) which showed a near-normal distribution with a mean of 0.2. The EVI surface was then classified to those areas of less or equal to 0.2 and those greater than 0.2 EVI. Although the mean of 0.1 does not correspond to accepted definitions of aridity based in a country like Namibia of 0.1 (Guerra et al., 2008) all the *Pf*PR point had values of >0.1 and this cut-off could not be implemented on the data. A box plot of *Pf*PR against the two classes of EVI was constructed (Figure 8). The results of the univariate analysis showed that EVI was not as significant predictor (P=0.767) of infection prevalence in Namibia (Table 3).

Figure 7: Histogram of average annual enhanced vegetation index showing a near-normal distribution

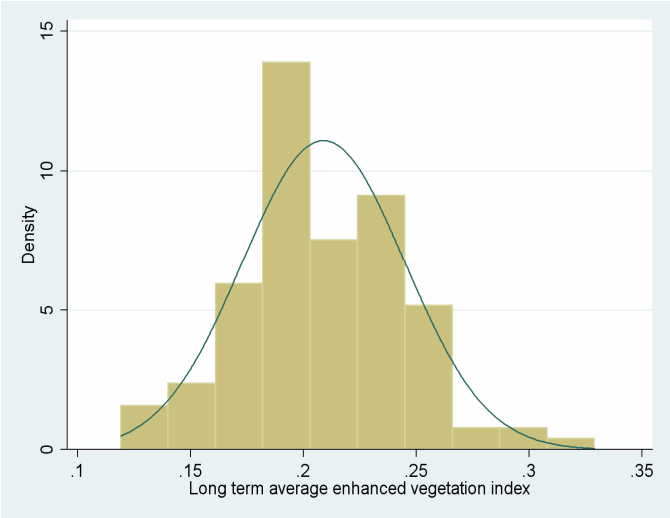


Figure 8: Map of categories of enhanced vegetation index (EVI)

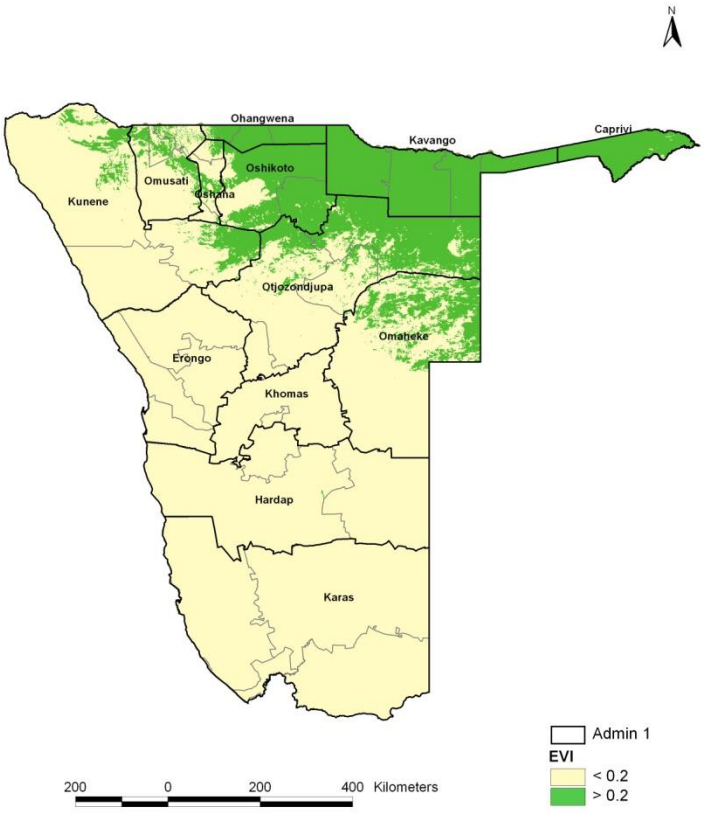


Figure 9: Box plot of *Pf*PR by categories of EVI.

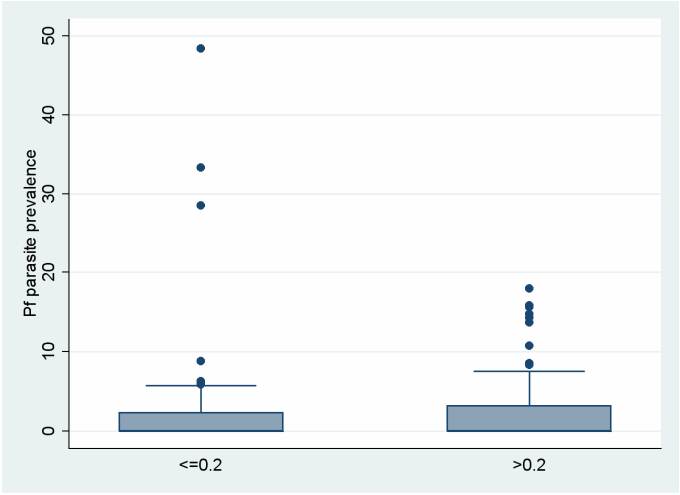


Table 3: Univariate analysis results of categories enhanced vegetation index against *Pf*PR

	Number of survey locations	Mean (median) *Pf*PR	Univariate regression*: Odds Ratio (95% CI), P-value
Average annual enhanced vegetation index			
≤0.2	49	3.4 (0.0)	Ref
>0.2	71	2.5 (0.0)	0.72 (0.08, 6.3), 0.767

Distance to water features

Distance to permanent and temporary water features has previously been used in malaria mapping as a proxy for availability of potential breeding sites for the *Anopheles* vector [Omumbo et al., 2005; Noor et al., 2008; Kleinschmidt et al., 2000). For Namibia a digital rivers file (GIS shapefile format) was downloaded from the digital atlas of Namibia project facilitated by the directorate of Environmental affairs, Ministry of Environment and Tourism, 2002 (http://209.88.21.36/Atlas/Atlas_web.htm). This dataset shows rivers which are perennial and those which are non-perennial mainly in Kavango region. It also categorizes the drainage channels as streams, rivers, inland and their respective catchment regions. Distances were extracted using ArcView 3.2 (ESRI Inc., USA) GIS extraction tools and thereafter used in subsequent analysis. Because the distribution of the distance was skewed (Figure 10) the median distance of 47 km was used instead of the mean to produce a categorical map of areas less than equal to and those greater than the mean distance (Figure 11). A box plot of *Pf*PR against the two classes of distance to water was constructed (Figure 12). Table 10 shows that distance to water was not a strong predictor of infection prevalence in Namibia (P= 0.906).

Figure 10: Histogram of distance to water features showing a mild positive skewed distribution

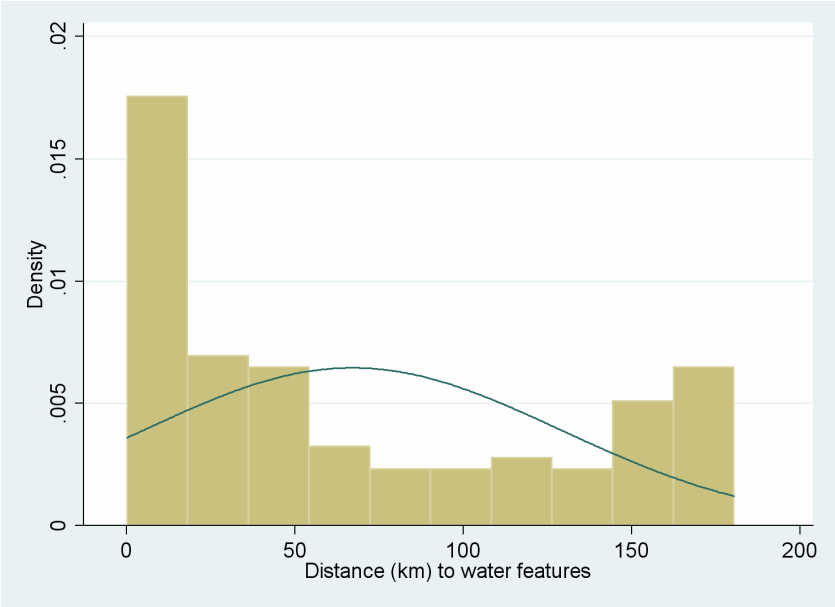


Figure 11: Map of main water features against and map of Euclidean distances to these water features

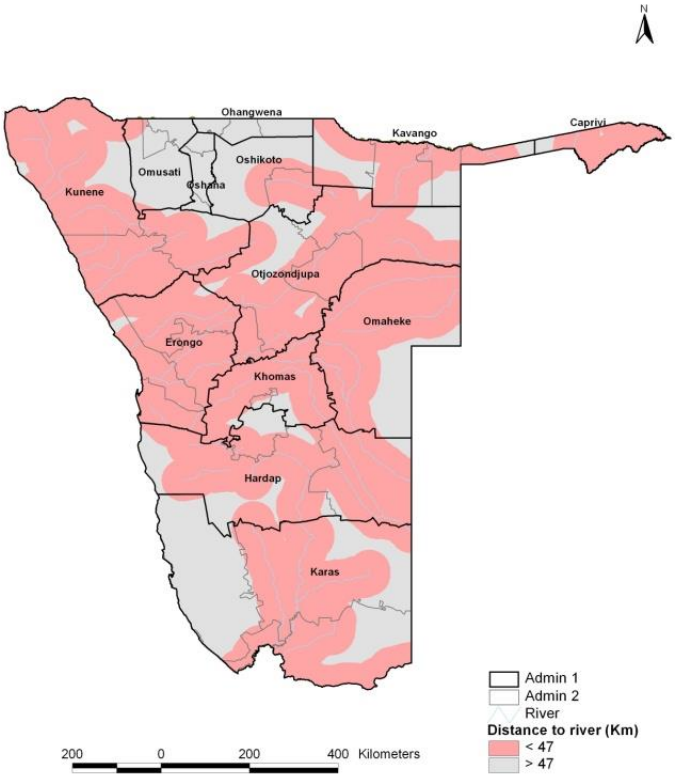


Figure 12: Box plots of *Pf*PR$_2$ by distance categories based on the median (47 km)

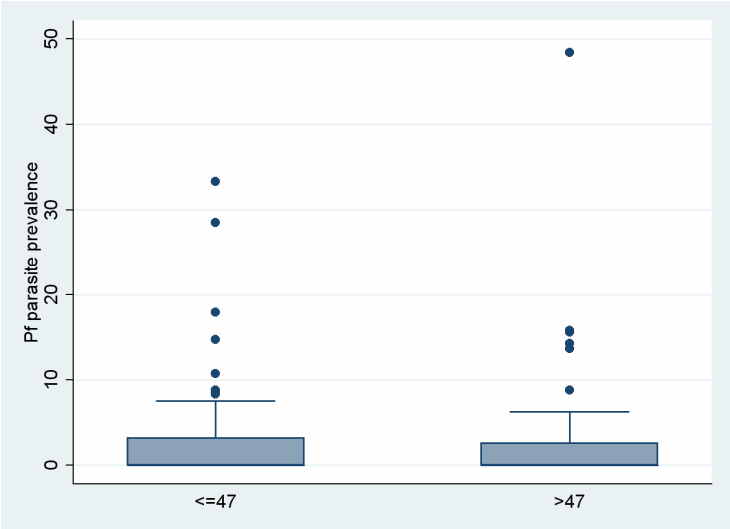


Table 4: Univariate analysis results of categories distance to water features against *Pf*PR

	Number of survey locations	Mean (median) *Pf*PR	Univariate regression*: Odds Ratio (95% CI), P-value
Median distance to water features			
≤47 km	59	3.0 (0.0)	Ref
>47 km	61	2.7 (0.0)	0.88 (0.10, 7.60), 0.906

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