Abstract

Background: Identifying areas that support high malaria risks and where populations lack access to health care is central to reducing the burden in Afghanistan. This study investigated the incidence of Plasmodium vivax and Plasmodium falciparum using routine data to help focus malaria interventions.

Methods: To estimate incidence, the study modelled utilisation of the public health sector using fever treatment data from the 2012 national Malaria Indicator Survey. A probabilistic measure of attendance was applied to population density metrics to define the proportion of the population within catchment of a public health facility. Malaria data were used in a Bayesian spatio-temporal conditional-autoregressive model with ecological or environmental covariates, to examine the spatial and temporal variation of incidence.

Findings: From the analysis of healthcare utilisation, over 80% of the population was within 2 hours’ travel of the nearest public health facility, while 64.4% were within 30 minutes’ travel. The mean incidence of P. vivax in 2009 was 5.4 (95% CrI 3.2–9.2) cases per 1000 population compared to 1.2 (95% CrI 0.4–2.9) cases per 1000 population for P. falciparum. P. vivax peaked in August while P. falciparum peaked in November. 32% of the estimated 30.5 million people lived in regions where annual incidence was at least 1 case per 1000 population of P. vivax; 23.7% of the population lived in areas where annual P. falciparum case incidence was at least 1 per 1000.

Conclusion: This study showed how routine data can be combined with household survey data to model malaria incidence. The incidence of both P. vivax and P. falciparum in Afghanistan remain low but the co-distribution of both parasites and the lag in their peak season provides challenges to malaria control in Afghanistan. Future improved case definition to determine levels of imported risks may be useful for the elimination ambitions in Afghanistan.

Background

Since the Soviet invasion in 1979, Afghanistan has experienced prolonged periods of insecurity and political instability. Consequently it has some of the poorest socio-economic and health status indicators globally. The country is ranked the thirteenth lowest on the human development index [1] and has a child mortality rate of 97 deaths before the age of five years for every 1000 children born [2,3]. In Afghanistan, malaria is an important disease with approximately half the population at risk [4,5,6].

Malaria transmission in the country is constrained by altitude, the rugged topography, patchy rainfall and extreme aridity [7]. There is no active malaria transmission in areas greater than 2000 metres above mean sea level [8], while transmission is unstable in
areas with limited annual rainfall. There are at least six malaria vectors in Afghanistan namely: the Anopheles superpictus, An. culicifacies, An. hyrcanus, An. Pulcherinus, An. fluviatilis, and An. stephensi. The latter two are mainly found in the eastern provinces [4,9]. Malaria infections are predominantly due to the Plasmodium vivax parasite although Plasmodium falciparum infections exist [8].

Afghanistan has a long history of malaria control dating back to the formation of the Directorate General of Preventive Medicine and Primary Health Care in 1948 [7]. Earlier vector control efforts focused on spraying using dichlorodiphenyltrichloroethane (DDT) and by 1970 the An. superpictus was almost eradicated [7,10,11]. After the Soviet invasion, the national program gradually weakened and had almost ceased to function [7,12]. Chloroquine resistance and population movement, mainly from returning refugees, contributed to an increase in malaria burden in Afghanistan [12,13,14]. Since 2000, however, substantial resources have been invested in malaria control in Afghanistan with support from the Global Fund to fight AIDS, Tuberculosis and Malaria, the United States Agency for International Development (USAID) as well as other agencies [15]. Despite the insecurity and infrastructure challenges, progress has been made in reducing the burden [5]. A recent malaria indicator survey (MIS) conducted in 2011 showed an average prevalence of less than 1% for both P. vivax and P. falciparum nationally while 76% of household clusters had no residents infected.

In the national malaria strategy of 2008-2013, Afghanistan aimed to reduce, by 60%, the malaria morbidity by 2013 and reduce P. falciparum cases to near zero with the aim of eventually interrupting its transmission [15]. The main interventions were coverage with vector control, parasitological diagnosis and treatment with effective antimalarials. In addition, a cross-border initiative was launched with Tajikistan to reduce the risk of imported infections to Tajikistan and to eliminate P. falciparum malaria in three border districts.

To track progress towards the national targets, the National Malaria and Leishmaniasis Control Programme (NMLCP) and partners established a routine information system to report monthly malaria cases by health facility [16]. The system, however, captured passively detected case data from only the public health system and contained both clinically diagnosed and parasitologically confirmed P. vivax and P. falciparum cases. Passive case detection, usually from HMIS, is hindered by the challenges of the low parasite confirmation rates which inflate reported malaria caseloads. In addition, low reporting rates tend to underestimate disease burdens because of the spatially and temporally incomplete data [17]. To provide more reliable estimates of disease burden, techniques are required that can adjust for these deficiencies by smoothing crude incidence rates; filling in gaps where no health reports have been assembled; and adjusting for the rate of facility utilisation since only a proportion of actual cases present at a facility [18].

In this study, a formal spatial and temporal approach, that incorporates a variety of data sources to estimate malaria incidence by district from 2006-2009 in Afghanistan, was developed. First, nationally representative household survey data from the 2011 MIS were used to characterize the utilisation of public health facilities and subsequently develop the denominator (catchment population) weighted by probability of health facility use for fever treatment. Secondly, malaria cases reported at the health facilities were used to model incidence of P. vivax and P. falciparum spatially and temporally using a Bayesian approach [19]. The clinically reported cases were adjusted using species-specific slide positivity rates observed at the facility and combined with parasite species confirmed cases to calculate the numerator. Slide positivity is the ratio of the number of positive malaria cases to the total number of people examined usually expressed as a percentage (rate). The combination of the adjusted cases and catchment populations were then used to compute the incidence of both P. vivax and P. falciparum.

### Methods

#### Health management information structure in Afghanistan

Afghanistan is divided into 34 administrative provinces. Healthcare is delivered mainly through the Basic Package for Health Services (BPHS) and the Essential Package for Hospital Services (EPHS) constituted in 2002 by the Ministry of Public Health (MoPH) [20,21,22]. In a bid to increase coverage, the BPHS was expanded through the contracting out of services to NGOs and MoPH partners [21,23]. The BHC constitutes clinics, health posts and Maternal Child Health (MCH) centres and Comprehensive Health Centres (CHC). This is linked to EPHS made up of the District Hospitals (DH) (first referral level) and regional or provincial (tertiary) hospitals. At village level community health workers manage the health posts and treat mild conditions and, in some cases, Mobile Health Teams (MHTs) are used [20,24]. In terms of data reports, tally sheets are filled at these lower-tier facilities and aggregated at the next tier facilities (CHC) which are then forwarded to regional directorates [16]. Thus, the health posts serve as a support network for the health centres and sometimes malaria cases are reported at the health centre rather than the individual health unit. The basic health centres link the basic service providers at the community level with the next service tier (the CHC) that are, in turn, linked to district hospitals and regional referral hospitals. Thus, where no regional or tertiary facility exists, district hospitals are the main referral centres. HMIS reports are also compiled the regional level and distributed to the national management level. Inpatient facilities are provided mainly at the tertiary level [20]. Parasitological diagnosis is conducted at higher tier facilities (Hospitals) where laboratory facilities exist while clinical diagnosis is predominantly used at health posts. The 2010 national malaria treatment guidelines outline the scale up of diagnostics at all health facilities to ensure diagnosis prior to treatment.

#### Data

The malaria case data were obtained from HMIS through the Afghanistan National Malaria and Leishmaniasis Control Programme (NMLCP). This consisted of records from 1,629 public health facilities for a 48-month period from 2006 to 2009. Data represented aggregate monthly cases of P. falciparum and P. vivax. Of the 1,629 health facilities, 1,587 had reported malaria cases based on both clinical and parasitology examination. Parasitological diagnosis (microscopy or RDTs) was conducted at higher-tier facilities (hospitals and health centres) where laboratory facilities exist while clinical diagnosis was predominantly used at lower-level facilities such as health posts (File S1). No cases were examined or reported for 228 facilities which were treated as missing data while data for mobile units (n=93) were omitted from the final analysis since they serve as outreach centres from major facilities. The missing spatial and temporal structures of data were imputed as ‘NAs’ and predictions made at missing locations. The spatial coordinates of health facilities were obtained from the Afghan Management Information Systems (AMIS) (http://www.aims.org.af/), which was formerly managed by the United Nations Office for the Coordination of Humanitarian
Affairs (UNOCHA) and the United Nations Development Programme (UNDP) in the early 2000s, but became a national independent Non-Governmental Organisation (NGO) in 2008. These facilities were either mapped using non-differential handheld global positioning systems (GPS) receivers during the assessment surveys or in some cases the longitude and latitude were established using a village or settlement database. For analysis, the facilities were classified into three broad categories that combined: basic facilities made up of health posts (HPs), clinics and maternal health centres (MCH); health centres; and hospitals.

Data for modelling health care utilisation for treatment of fever was obtained from the national MIS carried out between September and October 2011 (n = 15,442 individuals) [25]. The MIS was conducted in 21 provinces, across the diverse malaria strata (medium to high risks; low risk; and very low or potentially malaria free areas) in Afghanistan, but excluded the southern regions for security reasons. A multi-stage probability sampling design was adopted in line with other MIS surveys conducted in sub-Saharan countries [26]. At the first stage clusters or villages were selected randomly in a district via probability sampling while at the second stage, households within the selected clusters were sampled randomly [23]. Self-reported treatment seeking behaviour, disaggregated by healthcare sector, was recorded for all household members that reported an episode of fever two weeks prior, to assess the variance and the standard error of the predictive information criterion (DIC) [35]. This approach simplifies model selection to a single value, which can be easily tabulated for comparison with the remaining hyper-parameters (the unstructured random effects). Inverse Gamma priors \( IG(a,b) \) were assigned to precision hyperparameters for these unstructured effects components \( \theta_{term} \sim N(0,\tau^2) \). The time interaction was modelled as a first-order auto-regressive process, \( \rho Y(s_t, t_{t-1}) \) with the first term coming from a stationary distribution \( N(0,\sigma^2 \sum) \) that depends on past values for \( 0 > \rho < 1 \) [34]. Full details of implementation can be found in File S1.

Prior posterior predictions were made at the district level along with associated standard errors. Four spatio-temporal models were compared to assess the effect of the introduced random effects at province and facility level as well as the inclusion of the covariates. The first two models (referred to as M1 and M2) did not include any covariates with random effects excluded for the first model (M1). The other two models (M3 and M4) included environmental covariates, with M3 excluding random effects at facility and province level. Comparisons were made using the deviance information criterion (DIC) [35]. This approach simplifies model selection to a single value, which can be easily tabulated for comparison with proper Bayesian interpretation. A subset comprising 10% of the data selected randomly was used independently to compare posterior prediction against the crude incidence. Additionally, model checking was implemented by assessing the variance and the standard error of the predictive distribution [36].

**Results**

**Data characteristics and public sector utilisation in Afghanistan**

In modelling healthcare utilisation, a list of the universe of public health facilities was used (\( n = 1,581 \)) from the 34 provinces. There were more health posts (\( n = 754 \)) compared to health centres (\( n = 698 \)) and hospital (\( n = 129 \)). The majority were run by NGOs that work in partnership with the Ministry of Public Health (MOPH). The malaria case reporting rate was low for basic health facilities (an average of 33% for the four years) compared to hospitals and health centres where the reporting rate was >70%. Of the estimated population (32.3 million) in 2011, 27.8 million (85.8%) were estimated to be within 2 hours of travel of a public
health facility; 17.9 million (64.4%) were within 30 minutes. Approximately 13.1 million (47.4%) were within distances where the probability of attendance was ≥80% (SI).

**Posterior predictions of incidence of P. falciparum and P. vivax**

Table 1 lists the four Bayesian spatio-temporal models implemented along with associated model parameters for both *P. vivax* and *P. falciparum*. According to the DIC, the fourth model (M4) provided the best trade-off between model fit and parsimony compared to the other three models, although with more effective parameters \( P_B \). For both *P. vivax* and *P. falciparum*, the standard error in M4 of the predictive distribution was also lower. This model was subsequently selected for analysis of incidence of *P. vivax* and *P. falciparum*. Overall mean error of the crude incidence and the predicted incidence per 1000 population per year, based on a 10% validation set was −0.30 and −0.44 for *P. vivax* and *P. falciparum* respectively showing an overall tendency to under-predict by less than 0.5 incident cases per 1000 population. The Pearson correlation based on the validation set was 0.63 for *P. vivax* and 0.62 for *P. falciparum*.

Table 2 lists the posterior summaries of the parameters representing the fixed effects, the unstructured components, and the temporal and spatial parameters for both *P. vivax* and *P. falciparum* models. None of the covariate parameters were significant at 95% Bayes credible interval (Crl) based on the *P. falciparum* model but temperature suitability (0.123, 95% Crl 0.046–0.202) was significant based on the *P. vivax* model. All other model parameters were significant at 95% Crl.

Figure 1 shows the monthly variation of incidence for *P. vivax* and *P. falciparum* for the four-year period. The incidence of *P. vivax* peaked in August (7.611 95% Crl 4.849–11.721) compared to *P. falciparum* which peaked in November (mean incidence per 1,000 population was 2.403 95% Crl 0.929–5.276). *P. falciparum* was lowest in May (0.830 95% Crl 0.303–1.783). Figure 2 and Figure 3 shows maps of monthly incidence of *P. vivax* and *P. falciparum* respectively, at district level. The incidence of *P. falciparum* was generally very low compared to *P. vivax*. Nangahar, Kabul and Kunar had highest estimated clinical burden of *P. vivax* and *P. falciparum* while lowest estimated burden was in districts bordering Iran in Nimroz and Farah and in northern Afghanistan. The predicted mean incidence in the most recent data year (2009) for *P. vivax* was 5.4 (95% Crl 3.2–9.2) cases per 1,000 population and 1.2 (95% Crl 0.4–2.9) cases per 1,000 population for *P. falciparum*. Comparison between the baseline in 2006 and in 2009 showed small change in incidence (4.9, 95% Crl 3.0–7.8 and 5.1, 95% Crl 3.2–8.1 respectively for *P. vivax*; 1.1, 95% Crl 0.3–2.4 and 1.1, 95% Crl 0.3–2.5 respectively for *P. falciparum*) (Figure 4). However, there was a slight increase in malaria incidence in 2008 for both *P. vivax* and *P. falciparum* as predicted by the model, but, subsequently dropped to the 2006 level in 2009. The mean percentage change in incidence in the 34 provinces between the baseline year and 2009 for *P. vivax* was 3.0 and 5.9 for *P. falciparum* (Table 3). *P. vivax* reduced in 17 of the 34 provinces in Afghanistan while *P. falciparum* reduced in 13 provinces.

Table 3 provides summaries of population at risk by region. Of the 30.6 million people in 2009, the estimated burden of *P. vivax* in 2009 was 165,712 compared to 36,077 for *P. falciparum*. Approximately 32% of the population lived in regions where *P. vivax* was greater than 1 case per 1000 population compared to 23.7% for *P. falciparum*. About 1.3% of the population were estimated to live in districts with <1 case per 1,000 population and the majority (66.7%) in districts of 1 to <5 *P. vivax* cases per 1,000
Table 2. Parameters of the selected Bayesian models (M4) for both *P. falciparum* and *P. vivax* (sequentially as intercept $\beta_0$, EVI, TSI, Precipitation, random effects at (facility, district and province), temporal parameter and spatial CAR prior effect $\phi$, SD is the Standard Deviation).

| Parameter                      | Mean   | SD    | 5%   | 50%   | 95%   |
|-------------------------------|--------|-------|------|-------|-------|
| *P. falciparum*               |        |       |      |       |       |
| Intercept ($\beta_0$)         | 2.3630 | 0.387 | -4.244 | -3.633 | -3.008 |
| EVI ($\beta_1$)               | -0.031 | 0.079 | -0.162 | -0.031 | 0.099 |
| TSI ($\beta_2$)               | 0.164  | 0.127 | -0.042 | 0.163  | 0.334 |
| Precipitation ($\beta_3$)     | 0.008  | 0.051 | -0.077 | 0.008  | 0.091 |
| Facility random effect ($\tau_1$) | 1.940  | 1.903 | 0.192  | 1.380  | 5.534 |
| District random effect ($\tau_2$) | 2.484  | 0.829 | 1.355  | 2.369  | 4.010 |
| Province random effect ($\tau_3$) | 3.668  | 1.164 | 2.040  | 3.521  | 5.838 |
| Rho for the month ($\phi$)    | 0.849  | 0.117 | 0.617  | 0.881  | 0.969 |
| Spatial effect ($\phi$)       | 5.492  | 4.535 | 0.698  | 2.376  | 20.970 |
| *P. vivax*                    |        |       |      |       |       |
| Intercept ($\beta_0$)         | -2.065 | 0.240 | -2.451 | -2.069 | -1.662 |
| EVI ($\beta_1$)               | -0.026 | 0.019 | -0.058 | -0.026 | 0.005 |
| TSI ($\beta_2$)               | 0.124  | 0.048 | 0.046  | 0.124  | 0.202 |
| Precipitation ($\beta_3$)     | 0.013  | 0.011 | -0.005 | 0.013  | 0.031 |
| Facility random effect ($\tau_1$) | 8.383  | 1.778 | 6.095  | 8.057  | 11.750 |
| District random effect ($\tau_2$) | 2.081  | 1.976 | 0.181  | 1.500  | 5.888 |
| Province random effect ($\tau_3$) | 7.972  | 3.953 | 3.897  | 6.922  | 15.530 |
| Rho for the month ($\phi$)    | 0.728  | 0.098 | 0.551  | 0.737  | 0.872 |
| Spatial effect ($\phi$)       | 3.141  | 0.983 | 1.759  | 3.024  | 4.933 |

The betas represent the fixed effects of the covariates.

doi:10.1371/journal.pone.0102304.t002

Figure 1. Time series of two malaria parasites. Plots showing the predicted monthly ($n=48$ months) incidence for (2006–2009) for *P. vivax* (mean as top dash-dot line) and for *P. falciparum* (mean as green dash line) with error bars for each moth showing 95% Bayesian credible interval (Crl). *P. vivax* formed the most burden in Afghanistan and its incidence peaked in July and August compared to *P. falciparum* that peaked later in the year in November.

doi:10.1371/journal.pone.0102304.g001
population. Of the remaining population, only 23.3% were in districts with 5 to 10 cases per 1,000 population, 8.4% in 10 to 20 cases per 1,000 population and 0.3% of the population. The latter comprised of populations in eastern Afghanistan in Kunar and Nangarhar provinces. For *P. falciparum* case incidence, 76.3% of the population lived in districts where annual incidence was <1 per 1,000 population, while 20.9% lived in areas were incidence of *P. falciparum* was 1 to 5 cases per 1,000 population. A minority (2.8%) of the population lived in districts with an estimated annual incidence of 5 to 10 *P. falciparum* cases per 1,000 population.

**Discussion**

In this study we have developed a modelling approach that combines household and routine HMIS data within a Bayesian hierarchical spatial-temporal model, to compute the annual incidence of *P. vivax* and *P. falciparum* malaria across 398 districts in Afghanistan. The findings demonstrate a strong geographic co-distribution of *P. vivax* and *P. falciparum* malaria morbidity in Afghanistan (Figure 2 and Figure 3). There was no significant change in the mean annual incidence between 2006 and 2009. The incidence of *P. vivax* and *P. falciparum* in 2009 were estimated to be 5.4 and 1.2 per 1000 population respectively. The incidence (for both parasites) was higher in the south-eastern and eastern parts of Afghanistan bordering Pakistan and lowest in northern districts. In addition, the analysis showed that malaria in Afghanistan exhibits a strong seasonal peak between July and November. *P. vivax* tended to peak in August (mean incidence of 7.611 95% CrI 4.849–11.721) compared to *P. falciparum* which peaked in November (mean incidence 2.403 95% CrI 0.929–5.276). However, incidence was low in the winter months between January and May for both parasites. Slightly more than 76% of districts in Afghanistan had predicted incidence of <1 per 1000 population for *P. falciparum* which is a threshold for pre-elimination.

Using the 2006 data as baseline estimates, 17 and 13 provinces had already reduced *P. vivax* and *P. falciparum* incidence respectively by 2009. No reduction in incidence was predicted for Nangahar, Balkh, Sari Pul, Khost and Hirat Nangahar and Khost provinces in south-eastern regions of Afghanistan were amongst those with highest predicted incidence for both parasites. A range of malaria control strategies are implemented at a national level in Afghanistan. LLIN, for example, is targeted in the high to medium risk districts in Badakhshan, Badghes, Baghlan, Balkh, Faryab, Herat, Helmand, Kandahar, Khost, Kunar, Kunduz, Laghman, Nangarhar and Takhar. From the MIS undertaken in 2008, Nangahar had an estimated long lasting insecticidal nets (LLINs) coverage of 19% while no LLINs use was observed in Hirat [37]. Sari Pul region, for example, had some of lowest rates of long lasting insecticidal nets (LLINs) coverage and access to treatment of care. In the districts where indoor residual spraying (IRS) is used as the main vector control approach or to complement LLINs, the targeting of this intervention should be informed by the lag in the

---

**Figure 2. Monthly maps of *P. vivax*** Maps showing the predicted posterior mean monthly incidence of *P. vivax* per 1000 population for Afghanistan in 2009 using a Bayesian CAR model with environmental covariates (rainfall, TSI and EVI). Cases comprised of parasitologically confirmed and clinical cases corrected for slide positivity rates at the facility for a four-year period (2006–2009). Random unstructured effects were included at the facility level to account for regional heterogeneity. The highest burden of *P. vivax* (exceeding 15 cases per 1000 population) was in southeastern and the eastern regions bordering Pakistan.

doi:10.1371/journal.pone.0102304.g002
peak season of the two main malaria parasites. *P. vivax* peaks in August while *P. falciparum* peaks in November. IRS campaigns should therefore be planned in such a way that the insecticide are efficacious through the two peak seasons.

Of the 34 provinces of Afghanistan, five (Bamyan, Ghazni, Ghor, Panjsheer and Nuristan) were considered to be malaria free based on altitude thresholds [38]. These provinces, however, accounted for 9.7% of all estimated cases in 2009 indicating a...
### Table 3. Predicted mean malaria incidence per 1000 population for 2009 and estimated population at risk by Province for *P. vivax* and *P. falciparum.*

| Province | Estimated P. vivax clinical burden 2009 | Mean incidence 2009 | Percentage change from baseline 2006 | Estimated P. falciparum clinical burden 2009 | Mean incidence 2009 | Percentage change from baseline 2006 | Population | Population |
|----------|----------------------------------------|---------------------|-------------------------------------|-----------------------------------------------|---------------------|-------------------------------------|------------|------------|
| Kabul    | 19,788                                 | 4.3                 | 1.1                                 | 0.59                                          | 0                   | 4,513,039                          | 98.1       | 72,584     |
| Kapisa   | 2,497                                  | 5.4                 | 0.8                                 | 0.59                                          | 0                   | 215,825                            | 46.8       | 145,913    |
| Logar    | 1,988                                  | 4.4                 | 1.1                                 | -2.01                                         | 0                   | 308,882                            | 68.2       | 145,913    |
| Panjshir  | 777                                    | 5.5                 | 1.5                                 | 1.24                                          | 0                   | 123,418                            | 86.7       | 188,797    |
| Parwan   | 2,806                                  | 3.4                 | 0.9                                 | -4.04                                         | 0                   | 778,082                            | 93.2       | 57,015     |
| Wardak   | 2,439                                  | 3.8                 | 1.1                                 | -1.13                                         | 0                   | 515,633                            | 79.9       | 129,611    |
| Samangan | 2,172                                  | 4.3                 | 1.3                                 | 4.79                                          | 0                   | 465,596                            | 92.2       | 396,33     |
| Day Kundi| 2,280                                  | 4.2                 | 1.5                                 | 0.19                                          | 0                   | 143,333                            | 262        | 403,394    |
| Kunar    | 6,897                                  | 13.3                | 2.0                                 | 2.61                                          | 0                   | 517,421                            | 100        | 57,015     |
| Laghman  | 4,114                                  | 8.1                 | 0.6                                 | 2.91                                          | 0                   | 48,935                             | 9.7        | 456,482    |
| Nangarhar| 23,043                                 | 13.3                | 0.9                                 | 5.48                                          | 0                   | 733,865                            | 42.5       | 993,460    |
| Nuristan | 1,043                                  | 5.9                 | 1.1                                 | 3.20                                          | 0                   | 35,830                             | 20.3       | 112,523    |
| Badakhshan| 6,959                                | 5.4                 | 1.4                                 | 0.59                                          | 0                   | 247,984                            | 19.4       | 785,904    |
| Baghlam  | 3,039                                  | 2.9                 | 1.0                                 | 2.05                                          | 0                   | 1,040,766                          | 100        | 432,258    |
| Kunduz   | 4,639                                  | 4.1                 | 0.7                                 | -0.82                                         | 0                   | 775,118                            | 66.4       | 381,799    |
| Takhar   | 3,452                                  | 3.1                 | 0.7                                 | 1.73                                          | 0                   | 1,128,142                          | 100        | 463       |
| Balkh    | 4,091                                  | 2.9                 | 1.1                                 | 10.56                                         | 0                   | 1,002,618                          | 71.1       | 408,202    |
| Faryab   | 5,209                                  | 4.8                 | 1.3                                 | -0.05                                         | 0                   | 498,575                            | 45.8       | 591,181    |
| Jawzjan  | 2,583                                  | 4.1                 | 1.3                                 | -2.39                                         | 0                   | 521,918                            | 83         | 106,563    |
| Samangan | 1,219                                  | 2.8                 | 1.0                                 | -1.86                                         | 0                   | 441,833                            | 100        | 239       |
| Savi      | 2,548                                  | 3.7                 | 1.0                                 | 3.69                                          | 0                   | 604,845                            | 88.5       | 78,646     |
| Khost    | 5,613                                  | 8.5                 | 1.3                                 | 10.31                                         | 0                   | 57,439                             | 8.7        | 343,942    |
| Paktika  | 3,037                                  | 6.0                 | 1.9                                 | -4.60                                         | 0                   | 25,624                             | 5.3        | 435,431    |
| Paktya   | 4,458                                  | 6.9                 | 1.1                                 | -0.44                                         | 0                   | 115,091                            | 17.8       | 432,258    |
| Ghazni   | 9,033                                  | 6.3                 | 1.2                                 | 2.46                                          | 0                   | 330,263                            | 36.7       | 173,664    |
| Hillmand | 2,859                                  | 2.8                 | 1.1                                 | -0.26                                         | 0                   | 1,039,697                          | 100        | 216,844    |
| Kandahar | 5,644                                  | 4.1                 | 1.2                                 | -0.08                                         | 0                   | 1,161,551                          | 84.2       | 178,308    |
| Nimroz   | 577                                    | 3.1                 | 1.2                                 | -2.38                                         | 0                   | 187,872                            | 100        | 78,646     |
| Uruzgan  | 1,601                                  | 4.0                 | 1.1                                 | -0.88                                         | 0                   | 306,799                            | 75.9       | 97,595     |
| Zabul    | 2,621                                  | 7.5                 | 1.6                                 | -6.88                                         | 0                   | 20,586                             | 5.9        | 144,845    |
Table 3. Cont.

| Province | Estimated P. falciparum burden | Mean baseline P. falciparum incidence per 1,000 population | Mean P. falciparum baseline incidence per 1,000 population | Percentage change | Estimated P. vivax burden | Mean baseline P. vivax incidence per 1,000 population | Mean P. vivax baseline incidence per 1,000 population | Percentage change |
|----------|-------------------------------|----------------------------------------------------------|----------------------------------------------------------|-----------------|----------------------------|---------------------------------------------------|---------------------------------------------------|-----------------|
| Badghis  | 2,257                         | 0.9 [0.8, 1.0]                                           | 0.5 [0.5, 0.5]                                           | 1.82            | 534,183                    | 17,642                                            | 13,607                                           | 1.22            |
| Farah    | 1,459                         | 2.5 [2.3, 2.7]                                           | 2.0 [1.8, 2.2]                                           | -0.28           | 581,449                    | 0                                                 | 0                                                 | 0               |
| Ghor     | 3,141                         | 4.1 [3.9, 4.3]                                           | 3.0 [2.8, 3.2]                                           | 1.07            | 468,819                    | 13,304                                            | 11,077                                           | 0.94            |
| Herat    | 7,532                         | 3.6 [3.4, 3.8]                                           | 2.9 [2.7, 3.1]                                           | 2.41            | 2,098,175                  | 100                                               | 98,175                                            | 0.71            |
| Herat    | 1,655                         | 5.4 [5.2, 5.6]                                           | 4.0 [3.8, 4.2]                                           | 1.32            | 36,077                     | 1,200                                             | 871,194                                           | 2.34            |

SD: Standard Deviation.

The results of our analysis also have important applications to the design and allocation of resources for malaria case management. Mixed infections especially with *P. vivax* and *P. falciparum* present a challenge for treatment [42]. *P. vivax* infections relapse from dormant liver-stage hypnozoites months after primary infections and are often difficult to diagnose and treat and define as true incident infections [43]. Chloroquine is used as first line treatment of *P. vivax* in Afghanistan as recommended for countries where it remains efficacious and where parasites can be isolated [44], while Artesunate + Sulfadoxine-Pyrimethamine (AS+SP) is used for *P. falciparum* [15]. The incidence maps developed in our study can be used to quantify the need for the number of treatment dosages required for both parasites in Afghanistan. The prevalence of Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is estimated to be 8% in Afghanistan [45] which complicates the use of the recommended 14 day regimen of primaquine (PQ) for *P. vivax* [46]. The use of PQ in patients with G6PD deficiency can cause severe haemolysis [47]. To improve the existing information on the prevalence of G6PD deficiency these maps can be used to provide *P. vivax* incidence information that would be useful for the design of G6PD surveys. Where both species are endemic, the use of ACTs has been proposed [48,49] and other clinical studies have shown a faster parasite clearance rate when ACTs were used [50]. Figure 2 and Figure 3 indicates Kunar, Khost, Laghman, Nangarhar, Takhar and some districts in Kunduz could benefit from such a case management approach.

Although HMIS data used in this analysis represent individuals presenting with fever (symptomatic cases) and with a greater chance of detecting an infection, diagnosis was mainly based on either microscopy or Rapid Diagnostic Test (RDT), both of which have varying sensitivities [51]. In low transmission settings, the rate of false positivity rates, when using RDTs, may be higher and the quality of microscopy in routine HMIS data with varying laboratory conditions may also vary [52]. In addition, it was not possible to identify which diagnosis was used at each facility to adjust the sensitivities. A combination of factors might have limited the effect of environmental covariates especially for *P. falciparum*. This relates to assumptions of linearity during modelling even though rainfall was lagged by four months (SI) and given the short time-series of the data (four years). We used an autoregressive time-varying factor in the model assuming that present state evolves from previous values, but modified by the set of spatial and spatio-temporal covariates [34]. Future studies should relax the linearity assumptions of the fixed effects. Another limitation of the data presented here is that the effects of migration or travel between various regions were not incorporated into the modelling
framework. A study in south-eastern Afghanistan showed higher asymptomatic infections in the migrant population [33]. Modeling migration patterns at national level was beyond the scope of this study. It was assumed that individuals would seek treatment at the nearest facility or at least within a district or one of its neighbours. In this study, we have modelled malaria morbidity at the facility level and explicitly modelled healthcare attendance at individual facilities as part of our methodology. Security or conflict remains an important factor affecting utilisation of healthcare facilities. This was not modelled in the study due to lack of data, but future studies should consider accounting for this effect on reported health events. Given the additional spatial precision resulting from the facility-level analysis representing febrile individuals within facility catchments, maps of both malaria species are useful for concerted planning.

Conclusion

This study demonstrates how HMIS and household survey data can be assembled, integrated and interpolated to identify districts with high malaria burden spatially and temporally. Maps were produced at the level of decision-making units, which are potentially useful to the malaria control programme in assessing the changing burden of disease in Afghanistan, targeting malaria interventions at the population most at risk, and planning health resources. The districts identified with high burden should be the focus for targeting vector control. Districts with both P. vivax and P. falciparum and high rates of mixed infections should be investigated and careful case management strategies adopted. Improved case definition to determine levels of imported risks in malaria free areas is necessary for the elimination ambitions in Afghanistan.

Supporting Information

File S1

The analysis of public healthcare utilisation for treatment of fever and Bayesian model specification for modelling incidence is provided in the supplementary information. For healthcare coverage and utilisation, this includes the modelling of probability of attendance for fever treatment and delineation of public health facility catchments to estimate population using public health facilities. For incidence modelling, the supplementary information includes details on model specification, parameter estimation and validation.

(DOC)

Acknowledgments

The authors are grateful to the National Malaria and Leishmaniasis Control Programme (NMCLP) under the Ministry of Public Health in Afghanistan, who provided the health facility data used in this study. We also thank Caroline Kabaria, Viola Oieno, Jacob Ooko for help with geocoding and the assembly of ancillary data sets. We would like to thank Dr Hoda Atta and Dr Ghasem Zamanii of the WHO-EMRO for their comments.

Author Contributions

Conceived and designed the experiments: VAA AMN RWS. Performed the experiments: VAA. Analyzed the data: VAA. Contributed reagents/materials/analysis tools: VAA WB SMN AWS NH. Contributed to the writing of the manuscript: VAA PMA JW AMN RWS.

References

1. UNDP (2013) Human development report 2013. Washington DC: 22 p.
2. Afghan Public Health Institute, Ministry of Public Health [APHI/MoPH] [Afghanistan]; Central Statistics Organization (CSO) [Afghanistan]. ICF Macro, Indian Institute of Health Management Research (IIHMR) [India], et al. (2013) Afghanistan Mortality Survey 2010. Calverton, Maryland, USA: APHI/MoPH, CSO, ICF Macro, IIHMR and WHO/EMRO.
3. Rasooly MH, Govindaasiy AM, Asgari A, Rustein S, Arnold F, et al. (2013) Success in reducing maternal and child mortality in Afghanistan. Glob Health Action.
4. Safi N, Leslie T, Rowland M (2009) Progress and Challenges to Malaria Control in Afghanistan. Afghanistan Annual Malaria Journal: 15–29.
5. World Health Organization (2013) World Malaria Report 2013. Geneva: World Health Organization.
6. World Health Organization (2013) Country profile, Afghanistan. World Health Organization.
7. Kolaczinski J, Graham K, Fahim A, Brooker S, Rowland M (2005) Malaria control in Afghanistan: progress and challenges. The Lancet 365: 1506–1512
8. Brooker S, Leslie T, Kolaczinski K, Moloo E, Mehboob N, et al. (2006) Spatial epidemiology of Plasmodium vivax, Afghanistan. Emerg Infect Dis 12: 1600–1602.
9. Rowland M, Mohammed N, Rewman H, Hewitt S, Mendis C, et al. (2002) Anopheles vectors and malaria transmission in eastern Afghanistan. Trans R Soc Trop Med Hyg 96: 620–626.
10. Dy FJ (1954) Present status of malaria control in Asia. Bull World Health Organ 11: 725–763.
11. Ramachandra T (1953) Malaria control using indoor residual sprays in the Eastern Province of Afghanistan. Bull World Health Organ: 3: 639–661.
12. Rowland M, Hewitt S, Durran N, Banu N, Wirtz R (1997) Transmission and control of vivax malaria in Afghan refugee settlements in Pakistan. Transactions of the Royal Society of Tropical Medicine and Hygiene 91: 232–235.
13. Delini LF (1989) The first case of Plasmodium falciparum resistant to chloroquine treatment discovered in the Republic of Afghanistan. Trans R Soc Trop Med Hyg 83: 316.
14. Shah I, Rowland M, Mehmood P, Mujahid C, Razique F, et al. (1997) Chloroquine resistance in Pakistan and the upsurge of falciparum malaria in Pakistani and Afghan refugee populations. Annals of Tropical Medicine and Parasitology 91: 591–602.
15. Ministry of Public Health [2008] National Malaria Strategic Plan 2008–2015. General Directorate of Preventive Medicine and Primary Health Care, National Malaria and Leishmaniasis Control Programme.
16. Ministry of Public Health [2006] National Health Management Information Systems (HMIS): Procedures manual. Kabul.
17. Gething PW, Noor AM, Gikandi PW, Ogara EA, Hay SI, et al. (2006) Improving imperfect data from health management information systems in Africa using space-time geostatistics. PLoS Med 3: e271.
18. Cibulskis RE, Areogvi M, Williams R, Oaten M, Dye C (2011) Worldwide Incidence of Malaria in 2009: Estimates, Time Trends, and a Critique of Methods. PLoS Med 8: e1001142.
19. Alegana VA, Atkinson PM, Wright JA, Kamruvi R, Usuku P, et al. (2013) Estimation of malaria incidence in northern Namibia in 2009 using Bayesian conditional-autoregressive spatial-temporal models. Spatial and Spatio-temporal Epidemiology 7: 25–36.
20. Ministry of Public Health (2010) A Basic Package of Health Services for Afghanistan, Kabul: Islamic Republic of Afghanistan, Ministry of Public Health.
21. Waldman R, Strong L, Wali A (2006) Afghanistan’s health system since 2001: condition improvement, progress cautiously optimistic.: Afghanistan Research and Evaluation Unit briefing paper series.
22. Ministry of Public Health (2005) A basic package of health services for Afghanistan. Kabul: Islamic Transitional Government of Afghanistan.
23. Steinhardt LG, Aman I, Pakzad I, Kumar B, Singh LP, et al. (2011) Removing user fees for basic health services: a pilot study and national roll-out in Afghanistan. Health Policy and Planning 26: 492–503.
24. Belay T (2010) Building on Early Gains in Afghanistan’s Health, Nutrition and Population Sector: Challenges and Options. Washington (D.C.): World Bank.
25. Ministry of Public Health (2012) The second Malaria Indicator Survey in the Islamic Republic of Afghanistan, 2011. World Health Organization, Health Net TPO, BRAC, HPPO, KEMRI/Wellcome Trust Research Programme.
26. RMB-MERG (2008) A guide to Malaria Indicator Surveys (MIS). 11.
27. Gaughan AE, Stevens FR, Linard C, Jia P, Tatem AJ (2013) High Resolution Population Distribution Maps for Southeast Asia in 2010 and 2015. PLoS One 8: e55882.
28. Alegana V, Wright J, Perinna U, Noor A, Snow R, et al. (2012) Spatial modelling of healthcare utilisation for treatment of fever in Namibia. International Journal of Health Geographics 11: 5.
29. McLeod AL, Xu C (2008) bestglm: Best Subset GLM.
30. Ghosh SK, Mukhopadhyay P, Lu J-C (2006) Bayesian analysis of zero-inflated regression models. Journal of Statistical Planning and Inference 136: 1360–1375.
31. Lambert D (1992) Zero-inflated Poisson regression, with an application to counts of social and economic determinants of malaria in space and time in Viet Nam. International Journal for Parasitology 41: 109–116.
34. Sahu SK, Bakar KS (2012) Hierarchical Bayesian autoregressive models for large space–time data with applications to ozone concentration modelling. Applied Stochastic Models in Business and Industry 28: 395–415.
35. Spiegelhalter DJ, Best NG, Carlin BP, Van Der Linde A (2002) Bayesian measures of model complexity and fit. Journal of the Royal Statistical Society: Series B (Statistical Methodology) 64: 583–639.
36. Neelon BH, O’Malley AJ, Normand SL (2010) A Bayesian model for repeated measures zero-inflated count data with application to outpatient psychiatric service use. Stat Modelling 10: 421–439.
37. Ministry of Public Health (2009) Malaria Indicator Survey. Ministry of Public Health, Islamic Republic of Afghanistan.
38. Ministry of Public Health (2010) National malaria treatment guidelines. Kabul: Islamic Republic of Afghanistan, Ministry of Public Health.
39. Tatem A, Huang Z, Narib C, Kumar U, Kandula D, et al. (2014) Integrating rapid risk mapping and mobile phone call record data for strategic malaria elimination planning. Malaria Journal 13: 52.
40. World Health Organization (2007) Malaria elimination: a field manual for low and moderate endemic countries. Geneva: World Health organization.
41. Feachem RGA, Phillips AA, Hwang J, Cotter C, Wielgosz B, et al. (2010) Shrinking the malaria map: progress and prospects. The Lancet 376: 1566–1578.
42. Douglas NM, Nosten F, Ashley EA, Phaiphun L, van Vugt M, et al. (2011) Plasmodium vivax recurrence following falciparum and mixed species malaria: risk factors and effect of antimalarial kinetics. Clin Infect Dis 52: 612–620.
43. White N (2011) Determinants of relapse periodicity in Plasmodium vivax malaria. Malaria Journal 10: 297.
44. World Health Organization (2012) World Malaria Report: 2012. Geneva: World Health organization.
45. Howes RE, Piel FB, Patil AP, Nyangiri OA, Gething PW, et al. (2012) G6PD Deficiency Prevalence and Estimates of Affected Populations in Malaria Endemic Countries: A Geostatistical Model-Based Map. PLoS Med 9: e1001339.
46. World Health Organization (2010) World Health Organization: Guidelines for the treatment of malaria; Organization WH, editor.
47. Cappellini MD, Fiorelli G (2008) Glucose-6-phosphate dehydrogenase deficiency. Lancet 371: 64–74.
48. Sinclair D, Gogtay N, Brand F, Olilaro P (2011) Artemisinin-based combination therapy for treating uncomplicated Plasmodium vivax malaria. Cochrane Database Syst Rev: CD008492.
49. Douglas NM, Anstey NM, Angus BJ, Nosten F, Price RN (2010) Artemisinin combination therapy for vivax malaria. Lancet Infect Dis 10: 403–416.
50. Dao NV, Caoong BT, Ngpa ND, Thay le TT, The ND, et al. (2007) Vivax malaria: preliminary observations following a shorter course of treatment with artesunate plus primaquine. Trans R Soc Trop Med Hyg 101: 534–539.
51. WHO-FIND (2009) Malaria rapid diagnostic test performance: results of WHO product testing of malaria RDTs: round 1 (2008). Geneva: World Health Organization Special Programme for Tropical Diseases.
52. Hopkins H, Gouachez IJ, Polley SD, Angutoko P, Ategeka J, et al. (2013) Highly sensitive detection of malaria parasitemia in an endemic setting: Performance of a new LAMP kit in a remote clinic in Uganda. Journal of Infectious Diseases.
53. Nateghpour M, Akbarzadeh K, Farivar L, Amiri A (2011) Detection of asymptomatic malaria infection among the Afghani immigrant population in Iranshahr district of southeastern Iran. Bulletin de la Société de pathologie exotique 104: 321–323.