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Research paper

# The Pan African Vivax and Ovale Network (PAVON): Refocusing on *Plasmodium vivax*, *ovale* and asymptomatic malaria in sub-Saharan Africa

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ABSTRACT

The recent World Malaria report shows that progress in malaria elimination has stalled. Current data acquisition by NMCPs depend on passive case detection and clinical reports focused mainly on *Plasmodium falciparum* (*Pf*). In recent times, several countries in sub-Saharan Africa have reported cases of *Plasmodium vivax (Pv)* with a considerable number being Duffy negative. The burden of *Pv* and *Plasmodium ovale (Po)* appear to be more than acknowledged. Similarly, the contribution of asymptomatic malaria in transmission is hardly considered by NMCPs in Africa. Inclusion of these as targets in malaria elimination agenda is necessary to achieve elimination goal, as these harbor hypnozoites.

*The* Pan African Vivax and Ovale Network (PAVON) is a new consortium of African Scientists working in Africa on the transmission profile of *Pv* and *Po.* The group collaborates with African NMCPs to train in *Plasmodium* molecular diagnostics, microscopy, and interpretation of molecular data from active surveys to translate into policy. Details of the mission, rational and modus operandi of the group are outlined.

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**Table 1**
References for some examples of reported *Pv* infections by African country in active and passive surveys and in travelers/migrants as shown on the Map.

| Country | References (country survey reports) | References (travelers/migrant reports) |
|---|---|---|
| Algeria | [a]NR | [8] |
| Angola | [9] | [10–12] |
| Benin | [13] | |
| Botswana | [6,14] | [8] |
| Burkina Faso | | [15] |
| Cameroon | [16,17] | [8,15,18,19] |
| CAR | NR | [8,20] |
| Congo (Brazzaville) | NR | [8,12,21] |
| Cote D'Ivoire | NR | [8,19,21] |
| DRC | [2,22] | [8,10–12] |
| Egypt | [23,24] | [8] |
| Eq. Guinea | [2] | [8,10,12] |
| Eritrea | [2] | [8,15,21,24,25] |
| Ethiopia | [26] | [8,19,21] |
| Gabon | NR | [12,18] |
| Ghana | NR | [10,12,15,19,21] |
| Guinea | [2,27] | [21] |
| Kenya | [2,28] | [8,15,19,21] |
| Liberia | [29] | [10,12,19,21] |
| Madagascar | | [8,15] |
| Malawi | NR | [21] |
| Mali | [30,31] | [12,19,21] |
| Mauritania | [2,32] | [8,15] |
| Mozambique | [33] | [11,12,15,19] |
| Namibia | [7] | NR |
| Niger | NR | [8,12] |
| Nigeria | [34] | [8,12,15,19,21] |
| Senegal | [27,35] | [19] |
| Sierra Leone | NR | [15,19,21] |
| Somali | [33] | [8,19,21] |
| South Africa | NR | [8] |
| South Sudan | NR | [8,15,21] |
| Sudan | [2,36] | [8] |
| Tanzania | [37] | [8,21] |
| Togo | NR | [15,19] |
| Uganda | [27,38] | [8,15,19,21] |
| Zambia | [2,39] | [8] |
| Zimbabwe | [2] | |

[a] NR = Not reported.

**Table 2**
References for some examples of reported *Po* infections by African country in direct surveys and in travelers/migrants as shown on the Map.

| Country | References for direct surveys | References for travelers/migrant infections |
|---|---|---|
| Angola | [30] | [11,18] |
| Benin | [40] | |
| Botswana | [14] | NR |
| Burkina Faso | [41] | [15,19,21] |
| Cameroon | [42] | [10,15,18,21] |
| CAR | [43] | NR |
| Chad | NR | [18,21] |
| Congo (Brazzaville) | [44] | [15,19,21] |
| Cote D'Ivoire | [45] | [15,18,19] |
| DRC | [46,47] | [11,18] [18] |
| Egypt | [48] | NR |
| E. Guinea | [44,49] | [11,18,19] |
| Eritrea | NR | [8,19,21] |
| Ethiopia | [26,50] | [19,21] |
| Gabon | [51] | [8,18,21] |
| Gambia | [30] | [8,19] |
| Ghana | [30,52] | [8,15,18,19,21] |
| Guinea | NR | [15,21] |
| Kenya | [28,53] | [8,15,21] |
| Liberia | [29] | [15,21,19] |
| Madagascar | [54] | [21] |
| Malawi | [54,55] | NR |
| Mali | [30] | [8,21] |
| Mauritania | [56] | NR |
| Mozambique | [57] | [18] |
| Namibia | [7] | NR |
| Niger | NR | [8,19,21] |
| Nigeria | [58] | [8,15,18,21,19] |
| Rwanda | NR | [15,21] |
| Senegal | [54,59] | [8] |
| Sierra Leone | [60,61] | [15,18,19,21] |
| Somali | NR | NR |
| South Africa | [62] | [18] |
| South Sudan | NR | [21] |
| Sudan | NR | [15,18] |
| Tanzania | [63] | [15,18,21,19] |
| Togo | NR | [8,15,19] |
| Uganda | [38,64] | [8] |
| Zambia | [39] | [8,15,18] |
| Zimbabwe | [65] | [8] |

## 1. Introduction

The WHO Global technical strategy (GTS) on Malaria is eradication through elimination [1]. Over the past decade malaria mortality has decreased in all regions by >60% (WHO, World Malaria Report; https://www.who.int/publications/i/item/9789240015791, Assessed January 7, 2021). However, this progress has levelled off since 2017, and a new motivation is needed, in the acquisition of high-quality surveillance data and in innovative solutions to move the GTS agenda forward [1]. Innovations in surveillance data must be active, inclusive of all human *Plasmodium* species and asymptomatic infections. There is conclusive evidence that *Plasmodium vivax* (*Pv*) is present on the African continent as are other non-falciparum *Plasmodium* species [2]. Considering the unique biology of *Pv* and *Po (Plasmodium ovale curtisi and Plasmodium ovale walikeri)* with regards to the hypnozoite stage, and early gametocyte stage for *Pv,* which preclude the use of the same interventional strategies as are applied in *Pf* infections [3], these parasites should not be neglected in National Malaria Control Program (NMCP) planning strategies. Asymptomatic *Plasmodial* infections are established to constitute reservoirs for transmission in both high and low endemic areas [4,5]. A paradigm shift in the approaches that have been used to date to mitigate the burden of malaria disease is relevant. The sole focus of malaria elimination efforts in Africa on *Pf* and passive cases from clinical infections need to change to include at least *Pv* and *Po* and active detection of asymptomatic infections. A medium of change is necessary, and the Pan African *Vivax* and *Ovale* Network (PAVON), is positioned to be such a medium as described subsequently.

## 2. Rational, mission and modus operandi of Pan African *Vivax* and *Ovale* Network (PAVON)

To address the palpable missing link in *Pv* and *Po* transmission focus in Africa, and on asymptomatic *Plasmodium* infections, a group of African scientists working in 13 African countries comprising seven English speaking (Ghana, Botswana, Namibia, Ethiopia, Sudan, South Sudan, Niger and Zambia) and 6 French speaking countries (Cameroon, Burkina Faso, Mali, Benin, Democratic Republic of Congo) congregated in Accra, Ghana, in August 2019, to found the PAVON consortium. The group seeks to form the bridge between NMCPs, regional elimination blocks such as Elimination 8 (E8) in Southern Africa and the SAHEL Malaria Elimination Initiative, and other researchers to generate data on *Pv* and *Po* infections in sub-Saharan Africa. It also seeks to advance the understanding of the parasites' transmission process, interpretation of data and the importance of molecular tools in the detection of symptomatic and asymptomatic parasites in relation to interventional strategies towards elimination. This collaboration with NMCPS will also coordinate and expand the skills and resource base for research into *Pv* and *Po* in sub-Saharan Africa, through standardized procedures. In this way, NMCPs will be equipped to quickly translate research into policy, while also limiting the potential expansion of *Pv* and *Po* infections in Africa, which can pose a formidable task in malaria eradication efforts.

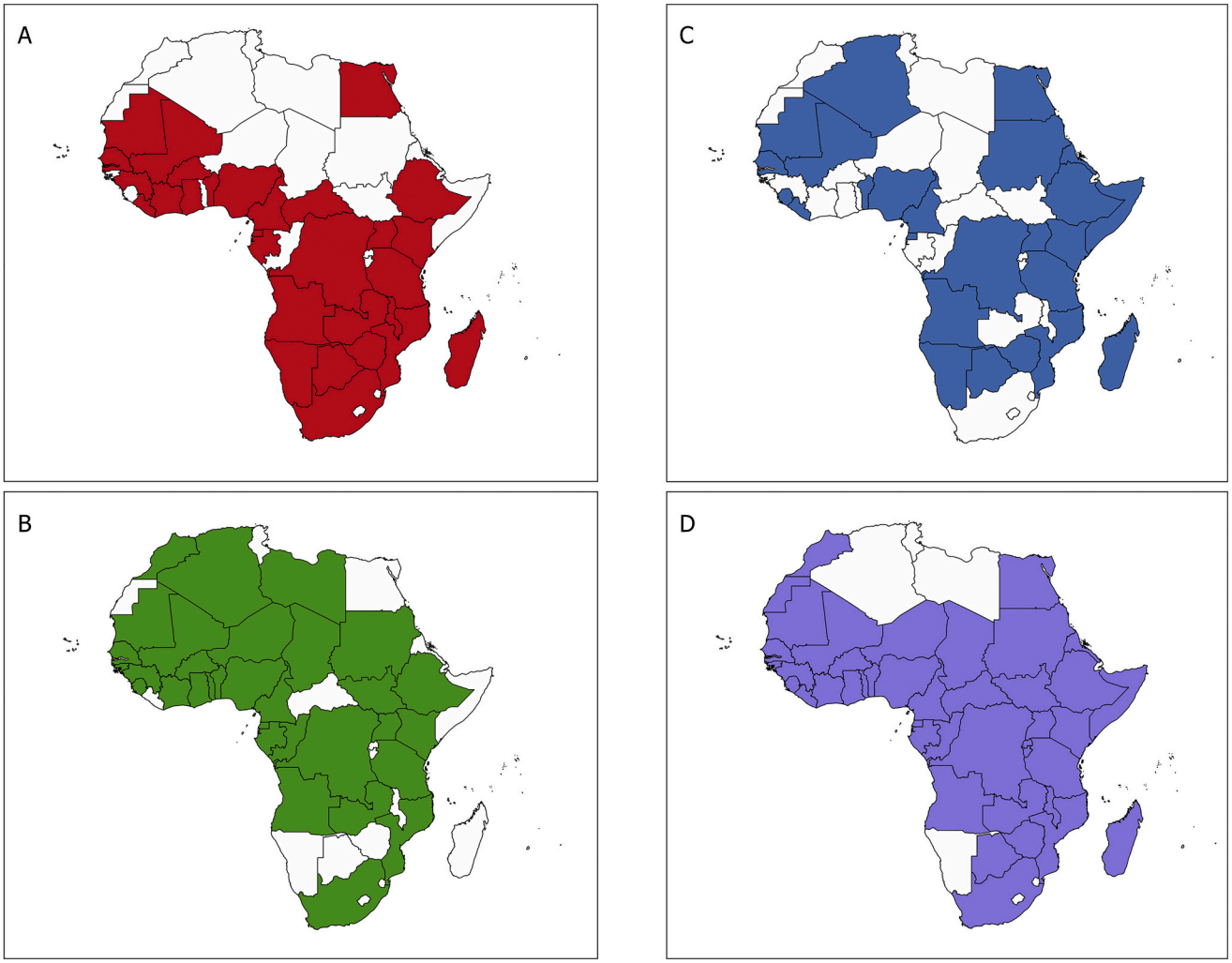


**Fig. 1.** Representative reports of *P. vivax* and *P. ovale* in Africa from direct in-country surveys and traveler/migrant investigational reports.

Represents countries where *P. ovale* was reported in a direct survey: A.

Represents countries where *P. ovale* was found in a traveler/migrant from the country: B.

Represents countries where *P. vivax* was reported in a direct survey: C.

Represents countries where *P. vivax* was found in a traveler/migrant from the country: D.

### *2.1. Mission*

The mission of PAVON is to promote the use of standardized molecular tools in determining the transmission of *Pv and Po* in sub-Saharan Africa and enable NMCPs to understand the molecular data and translate it into policy and practice.

### *2.2. Consortium member composition collaboration*

The network has 14 participating countries from Research Institutions, Academia and the NMCPs currently. The group is open to collaborate with institutions and organizations with similar interests targeting Africa, to enhance *Pv* and *Po* research, build capacity for African countries and closely collaborate with the NMCPs and African regional networks. Our current partners are the Merck Global Health Institute and the A*STAR Infectious Disease Laboratory, Agency for Science Technology and Research (A*STAR), Singapore.

### *2.3. Regulatory requirements, ethical considerations and oversight*

The consortium will comply with all local and international regulations that govern human subject research and data sharing, and develop contractual agreements concerning the execution of projects with the NMCPs and institutions. Where necessary, training initiatives for Institutional Review Boards (IRBs) will be facilitated to improve understanding of data acquisition, processing and sharing engagements with the local NMCPs.

### *2.4. Field work, sample collection, processing and storage*

The consortium has developed standardized procedures for field work activities with modifications to suit in-country specific needs and regulations, subject selection and engagement, and involvement of parents and guardians for consent and assent of children to participate in our projects [6,7]. The group has also standardized field and laboratory protocols for *Plasmodium* species diagnosis by microscopy, PCR and qPCR procedures.

## 3. Evidence for *Pv* and *Po* in Africa

To provide the evidence for *Pv* and *Po,* we searched through Pubmed and Google Scholar to document some examples of reports of *Pv* and *Po* in country surveys and in African migrants to countries outside of Africa spanning the period from 1957 to 2019. The surveys included both passive and active, symptomatic, and asymptomatic cases. These are presented in Tables 1 and 2, and in Fig. 1.

## 4. Impact of PAVON on national, regional and international priority setting towards malaria elimination and eradication

Three key impact areas of the work of PAVON are to generate data on non-falciparum malaria, train graduate students at the Master and PhD levels in Applied Epidemiology and provide standardized materials as references in field and laboratory work in Africa. Nationally, there has been a lack of focus on non-falciparum malaria because of the top to bottom approach where funders lay emphasis on *P. falciparum,* and inadvertently make the NMCPs also consider *P. falciparum* as the sole problem, to the neglect of the others. One main reason is because of the lack of consensus on whether non-falciparum malaria contribute to the data on the passive cases that are collected in national reports in sub-Saharan Africa, as a lot of these are asymptomatic and not easily detected by conventional microscopy. Such data will need to be generated overtime to provide the evidence, although there is already some evidence on this from some countries [16,66] An available evidence can trigger a need for a paradigm shift in the focus. Such a shift will require that the necessary tools including the human resource capacity are available to generate the relevant data for policy. In addition, by initiating the crosstalk with NMCPs, PAVON will directly facilitate openness, trust and the dialogue for targeting research activities on the key elements of the elimination and eradication agenda for the NMCPs. This will open-up further regional and international cross-talks for exchange of data and expertise as well as collaborations that will not only sustain these activities but also revamp the skills and resources that exist, to optimize outcomes.

## 5. Conclusion

PAVON is an African initiative seeking to use its diverse expertise in Malaria research across institutions in Africa, to highlight the importance of data acquisition on *Pv* and *Po, standardized molecular tools and asymptomatic infections* towards malaria elimination in sub-Saharan Africa.

## Declaration of interest

None.

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