CONFRONTING

PLASMODIUM VIVAX MALARIA
Plasmodium vivax is one of five species of Plasmodium that can cause malaria in human beings. Although P. falciparum is responsible for the majority of cases and deaths from malaria, P. vivax has a wider geographical range and is responsible for almost half the cases of malaria outside Africa.

In May 2015, the World Health Assembly endorsed the most ambitious targets for malaria control since the eradication era – namely to eliminate malaria from 35 countries and reduce case incidence and mortality rates by 90% globally.¹ P. vivax presents a major challenge to achieving these targets; in 2013, it was responsible for 16 million cases globally. It predominates in countries that are prime candidates for elimination, accounting for more than 70% of cases in countries with fewer than 5000 cases of malaria each year. Not only does P. vivax present a barrier to elimination, it can also cause severe disease; severe cases and deaths due to P. vivax malaria have been reported from all endemic regions.

More than a third of the world’s population, mostly in Asia and Latin America, is at risk of infection with *P. vivax* malaria.

*P. vivax* is by far the most widespread of the five malaria parasites that infect people. In 2013, it was estimated to be responsible for more than one million malaria cases in four countries (Ethiopia, India, Indonesia and Pakistan).

Despite tremendous progress in reducing *P. vivax* malaria since 2000, there were 16 million cases globally in 2013.

Even though the number of *P. vivax* malaria cases fell by 35% compared to 2000, *P. vivax* is still responsible for almost half the number of malaria cases outside Africa.

*P. vivax* malaria predominates in countries that are prime candidates for elimination.

The parasite accounts for more than 70% of malaria cases in countries with fewer than 5000 cases each year.
PERCENTAGE OF MALARIA CASES DUE TO *PLASMODIUM VIVAX*, BY AVERAGE NUMBER OF CASES, 2000–2013

**ESTIMATED NUMBER OF *PLASMODIUM VIVAX* CASES BY COUNTRY, 2013**

**DOWNWARD TREND IN *PLASMODIUM VIVAX* MALARIA CASES IN AND OUTSIDE SUB-SAHARAN AFRICA, 2000–2013**

**PERCENTAGE OF MALARIA CASES DUE TO *PLASMODIUM VIVAX*, BY AVERAGE NUMBER OF CASES, 2000–2013**
*P. VIVAX MALARIA POSES MULTIPLE CHALLENGES*

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*P. vivax* malaria can be more difficult to control than *P. falciparum* for several reasons related to its biology or the behaviour of mosquitoes that carry it.
• **It can survive in cooler climates.**
Whereas *P. falciparum* is confined to tropical zones, *P. vivax* can develop and survive in the relatively cooler climates of more temperate countries and therefore has a wider geographical range.

• **It is less responsive to conventional methods of vector control.**
In many of the areas where *P. vivax* is common, mosquitoes bite early in the evening, obtain blood meals outdoors and rest outdoors. Thus, tools such as insecticide-treated mosquito nets (ITNs), which work well against night-biting and indoor-feeding mosquitoes, can be less effective in reducing *P. vivax* malaria.

• **It is more difficult to detect using current diagnostic techniques.**
Compared to *P. falciparum*, the number of parasites circulating in the blood of a person infected with *P. vivax* malaria is typically low. Therefore, *P. vivax* infections may be missed, even if a patient presents for treatment. The parasite also has a dormant liver stage that cannot be detected by current diagnostic tools. Hence, there may be a large reservoir of people who are infected with *P. vivax* but are unaware of their condition.

• **A single infection can give rise to multiple episodes of malaria.**
Even in the absence of another mosquito bite, in those infected with *P. vivax*, the dormant liver stage can awaken and can trigger multiple episodes of malaria. These relapses not only cause further illness to the individual, they also provide an opportunity for the parasite to be picked up by mosquitoes and transmitted to others.

• **Treatment of liver-stage parasites requires a 14-day course of primaquine.**
Only one drug, primaquine, is effective against dormant liver parasites. The treatment for this stage of the disease involves the patient taking tablets every day for 14 days, even though the person may no longer be experiencing symptoms of disease. In resource-poor areas where *P. vivax* prevails, many patients have difficulty complying with such a lengthy treatment regimen.

• **Primaquine treatment can produce serious side-effects.**
Patients who have a severe deficiency of the enzyme glucose-6-phosphate dehydrogenase (G6PD) are susceptible to potentially life-threatening destruction of blood cells while taking primaquine. However, current tests for G6PD deficiency are complex and relatively expensive; thus, many clinicians are reluctant to prescribe primaquine to patients whose G6PD status is unknown. In addition, primaquine cannot be used in pregnant women and infants because of the risk of G6PD deficiency. In the absence of treatment, these populations are prone to multiple relapses.
WHAT SHOULD BE DONE AGAINST *P. VIVAX*?

Successful control and elimination of *P. vivax* requires action on three fronts: strengthening malaria programmes, developing new tools, and enhancing financing and political commitment.
STRENGTHENED MALARIA PROGRAMMES

Many of the strategies to control *P. vivax* malaria are the same as those used with *P. falciparum* malaria; for example, using vector control to reduce transmission by the mosquito vector (from humans to mosquitoes, and from mosquitoes to humans); using chemoprevention to prevent establishment of infections in humans; and providing accessible health services that can rapidly detect, diagnose and treat malaria infections. However, successful control of *P. vivax* malaria calls for additional interventions; in particular:

- **targeting outdoor-biting and outdoor-resting mosquitoes**, where such mosquitoes represent the main source of transmission;
- **ensuring that microscopy services are able to detect low-density *P. vivax* infections**, or that bivalent rapid diagnostic tests are used in areas where both *P. falciparum* and *P. vivax* are found;
- **treating liver stages as well as blood stages**; and
- **testing all patients for G6PD deficiency** before administering primaquine (where possible).

Consideration of *P. vivax* needs to be reflected in global, regional and national plans for malaria control. These plans should be monitored at regular intervals through *P. vivax*-specific indicators on programme coverage and disease incidence.

DEVELOPMENT OF NEW TOOLS

A more effective response to *P. vivax* will require new tools that will help to reduce *P. vivax* transmission, and increase the ability of malaria programmes to detect and treat infections. There is a particular need for tools against the dormant liver (hypnozoite) stage, such as:

- **a test that is both sensitive enough to confirm the presence of hypnozoites** in a patient’s liver and specific enough to confirm their absence; such a test could inform decisions about the management of a *vivax* malaria, and be used for epidemiological assessment of the prevalence of *P. vivax* infection in a given area;
- **a test for G6PD deficiency that can be used where patients seek treatment**, to break down a significant barrier to treatment with primaquine; and
- **a drug against the liver stage that is effective**, does not have significant side-effects and is suitable for use in all population groups.

A MORE EFFECTIVE RESPONSE TO *P. VIVAX* WILL REQUIRE NEW TOOLS THAT WILL HELP TO REDUCE *P. VIVAX* TRANSMISSION AND INCREASE THE ABILITY TO DETECT AND TREAT INFECTIONS.

ENHANCED FINANCING AND POLITICAL COMMITMENT

There is a need for international donors and domestic governments to invest in the additional measures required for control of *P. vivax*, and to continue investment even when malaria is reduced to low levels or eliminated. Also, those funding research will need to prioritize investments in *P. vivax* malaria research, to reduce the obstacles to *P. vivax* malaria elimination.
WHAT CAN BE GAINED BY TAKING ACTION AGAINST P. VIVAX?

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A comprehensive response to *P. vivax* malaria will relieve some of the most vulnerable populations of a significant illness that disrupts schooling and work, and can be fatal. Such a response will strengthen health systems, boosting their capacity to improve the treatment of other febrile illnesses and their ability to respond to future public health threats.

Malaria interventions are highly cost effective, and provide one of the highest returns on investment in public health. They help to alleviate poverty, improve equity and contribute to overall development. If *P. vivax* malaria is conquered, not only will international targets to eliminate malaria from 35 countries by 2030 be achieved, but a pathway will be set for the eventual eradication of this ancient disease.
For further information, please refer to *Control and elimination of Plasmodium vivax malaria – A technical brief* published by the WHO Global Malaria Programme in July 2015 and available at http://www.who.int/malaria/publications/atoz/9789241509244/en/.

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