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World Malaria Report 2011 Questions and Answers

Q: Why has mortality from malaria gone down during the past decade?

Mortality from malaria has decreased by over 25% globally since 2000, and by 33% in the WHO African Region. Much of this decrease is due to the increased availability of long-lasting insecticidal nets, indoor residual spraying, and better access to diagnostic testing and effective treatment with artemisinin-based combination therapies (ACTs). Socio-economic improvements in many countries in sub-Saharan Africa have also brought down the number of deaths from all causes among children under 5 and are likely to have also had an impact on the malaria burden.

There were an estimated 655 000 malaria deaths in 2010, which is 36 000 lower than the estimated mortality in 2009 (a 5% year-on-year reduction). While this represents significant progress, the mortality figures are still disconcertingly high for a disease that is entirely preventable and treatable. Mortality estimates in this year's report reflect a downward revision of child mortality estimates for all causes and diseases by the UN Inter-agency Group for Child Mortality Estimation.¹ This revision reduced malaria mortality estimates in the WHO African Region by approximately 11%.

Q: What are the projections for international funding for malaria programmes?

International funds for malaria control reached US\$ 1.7 billion in 2010 and US\$ 2 billion in 2011 but remained significantly below the US\$ 5-6 billion that would be needed annually to achieve global malaria targets. According to projections in the report, despite increased support from the United Kingdom, malaria funding may slightly decrease in 2012 and 2013, and will likely drop further to an annual US\$ 1.5 billion by 2015. This is an optimistic scenario as no firm data is available about possible decreases in funding from bilateral donors and other sources. This projected reduction is due primarily to the shrinking of available funding through the Global Fund to Fight AIDS, Tuberculosis and Malaria, which accounts for approximately 50% of the amounts disbursed in 2011.

¹ The UN Inter-Agency Child Mortality Estimation Group (IACMEG) includes technical experts from WHO, UNICEF, the United Nations Population Division, the World Bank as well as independent experts. It was formed in 2004 to harmonize estimates within the UN system and improve methods for child mortality estimation. For more information, go to: www.childmortality.org.

Q: What is the latest on drug resistance?

Drug resistance is a major concern. *Plasmodium falciparum* resistance to artemisinins, which was confirmed on the Cambodia-Thailand border in 2009, is now suspected in parts of Myanmar and Viet Nam. Since 2008, containment activities have been ongoing to limit the spread of artemisinin-resistant parasites. While these activities have sharply reduced the overall burden of *Plasmodium falciparum* malaria in the containment zone, the proportion of patients with resistant parasites has risen. It is therefore necessary to eliminate all *Plasmodium falciparum* parasites in areas with documented resistance. In 2010, the WHO Global Plan for Artemisinin Resistance Containment (GPARC) called for an urgent and multi-faceted response to this challenge.

WHO has also recommended that all countries ban the marketing of oral artemisinin-based monotherapies, which have been one of the major factors fostering the emergence of drug resistance. Despite a World Health Assembly resolution addressing this issue, 25 countries still allow the marketing of oral artemisinin-based monotherapies and 28 pharmaceutical companies continue to market these products (down from 39 in 2010). Most of the countries that still allow marketing are located in the African Region and most of the manufacturers are in India.

Despite the observed changes in parasite sensitivity to artemisinins, ACTs remain highly effective in almost all settings, so long as the partner drug in the combination is locally effective.

Q: What is the latest on mosquito resistance to insecticides?

The problem of mosquito resistance to insecticides appears to be growing, although it has not generally been linked to a failure of malaria vector control efforts to date. Mosquito resistance to insecticides is caused by a widespread use of a single class of insecticide. Current methods of malaria control are highly dependent on pyrethroids, which are the most commonly used compounds for indoor residual spraying and the only insecticide class used for long-lasting insecticidal nets.

According to the *World Malaria Report 2011*, which includes data on insecticide resistance for the first time, 45 countries around the world have identified resistance to at least one of the four classes of insecticides used for malaria vector control; 27 of these are in sub-Saharan Africa. Resistance has been reported from all WHO Regions except the WHO European Region. India and malaria-endemic countries in sub-Saharan Africa are of greatest concern due to widespread reports of resistance - in some areas to all classes of insecticides - combined with a high malaria burden.

In response to this emerging threat, WHO is currently working with a broad group of stakeholders to develop a Global Plan for Insecticide Resistance Management in malaria vectors, which will be released in early 2012.

Q: What is the current status of malaria vaccine research?

There are currently no licensed malaria vaccines. Over 20 research projects are in clinical trials. Of these, the most advanced is in Phase 3 clinical trials. This vaccine is called RTS,S/AS01 and it has been developed through a partnership between GlaxoSmithKline Biologicals and the PATH Malaria Vaccine Initiative (MVI), with funds from the Bill & Melinda Gates Foundation to MVI. RTS,S is at least 5-10 years ahead of other candidate malaria vaccines. RTS,S is a *Plasmodium falciparum* vaccine, with no protection expected against *P. vivax* malaria.

An effective vaccine against malaria has long been envisaged as a valuable addition to the available tools for malaria control. WHO is committed to working with malaria vaccine stakeholders towards the 2025 goal set out in the malaria vaccine technology roadmap – a vaccine with at least 80% efficacy against clinical malaria. WHO also participated in the malaria eradication R&D agenda (malERA) consultative process which supported the concept of a vaccine that can interrupt malaria transmission. The long-term goals for malaria vaccines will therefore include not only protection against clinical malaria, but also impact against malaria transmission as a core feature of vaccine performance.

Q: How well does RTS,S work?

The results of the Phase 3 trial will become available to WHO in three stages: late 2011, late 2012 and late 2014. A WHO recommendation for use will most likely be based on data from all three stages, and can be expected in 2015. The first of these interim reports became available in October 2011. The efficacy figure was 55% reduction in frequency of malaria episodes during the 12 months of follow-up in children 5-17 months of age at first immunization.

This is not the vaccine development partnership's stated target population, which is children aged 6-14 weeks of age, in co-administration with other vaccines. The efficacy in this target population is not yet known. Efficacy here means reducing how often vaccinated children get clinical malaria. It does not mean half of the children are completely protected. We do not know how long the vaccine's protection lasts, we do not know if a booster dose will be needed and we do not know whether this level of protection is the same in countries with different intensities of malaria transmission. We should have more information on all of these issues by the end of the Phase 3 trial in 2014.

Q: How is WHO involved in malaria vaccine research efforts ?

WHO's role is to advise and guide the malaria vaccine development activities of the global research community. Once Phase 3 clinical trial data become available, WHO convenes its technical group to assess the safety and effectiveness of the malaria vaccine, and considers a WHO policy recommendation and prequalification, if advised that these are supported by the data. The technical group advising WHO on Phase 3 trials of malaria vaccines is the Joint Technical Expert Group on Malaria Vaccines, convened by the Immunization, Vaccines, and Biologicals Department and the Global Malaria Programme.