

A conversation with Professor Christian Lengeler, August 20, 2015

Participants

- Professor Christian Lengeler – Head of Health Interventions Unit, Swiss Tropical and Public Health Institute
- Jake Marcus – Research Analyst, GiveWell

Note: These notes were compiled by GiveWell and give an overview of the major points made by Professor Christian Lengeler.

Summary

GiveWell spoke with Professor Christian Lengeler of the Swiss Tropical and Public Health Institute (Swiss TPH) about delayed mortality as part of the process of updating the intervention report on bed nets. The conversation focused on the evidence against the delayed mortality hypothesis.

The consensus on the delayed mortality hypothesis

A debate arose in the 1990s that insecticide treated nets (ITNs), by protecting children from mosquitoes, may not only reduce the short-term burden of malaria, but may also reduce opportunities for humans to acquire immunity, making them more susceptible to malaria over the long term. A “delayed mortality” effect, or an increase in mortality in children at older ages, could offset reductions in mortality at younger ages.

Professor Lengeler told us that there is a strong consensus among malaria experts that there is no delayed mortality effect. He has not seen any serious debate around the issue for the past decade, because of the lack of controversy over the evidence against the delayed mortality hypothesis.

Differences in mortality rates by transmission intensity

In support of the delayed mortality hypothesis, one study showed that high transmission areas have similar mortality rates to medium transmission areas with higher mortality rates for infants in high transmission areas but lower mortality rates for older children. Professor Lengeler finds this study unconvincing, because the proportion of malaria deaths occurring in a hospital varies widely and this variation may explain the differences in mortality rates between areas with different transmission intensities.

An analogous study, which Professor Lengeler co-authored and published in the American Journal of Tropical Medicine in 2004, relied on community-based surveys

instead of hospital data. This study found that high transmission areas had higher mortality rates than medium transmission areas with higher mortality rates for infants in high transmission areas and similar mortality rates for children aged 1-5.

The scale-up of malaria control has made these types of studies very difficult to conduct now.

Follow-ups of randomized control trials (RCTs) of ITNs

Follow-ups of RCTs conducted at 3 different sites provide strong evidence against the delayed mortality hypothesis.

The follow-ups of 5-7 years did not find any indication of a rebound in mortality. Even if the follow-ups had found the same percentage increase in the mortality rate at older ages as the percentage decrease found in the mortality rate at younger ages, the increase would not do much to offset the benefit of ITNs at younger ages, because so many more children die at younger ages than at older ages.

It is difficult to measure the mortality rate in children at older ages precisely, because of the low number of deaths. However, the point estimates don't provide any indication of a rebound in mortality.

Country experiences from the scale-up of malaria control

The scale-up of malaria control has led to substantial declines in child mortality with no indication of a delayed mortality effect even in high transmission areas. For example, the Democratic Republic of the Congo, where transmission intensity is high, has had a large reduction in child mortality in the past 10 years. Though there are methodological difficulties with isolating the impact of the scale-up of malaria control, it is not clear what else would explain these large reductions in child mortality.

One possible exception may be Western Kenya. A paper written 2-3 years ago by Dr. Mary Hamel, a medical epidemiologist at the U.S. Centers for Disease Control and Prevention (CDC), suggested that malaria control measures in Western Kenya have been less successful than in other places, but this may be due to insecticide resistance, human immunodeficiency virus (HIV), or other causes outside of delayed mortality.

Professor Lengeler had not seen evidence of malaria control failures in Uganda, but it's possible any issues with malaria control there could be related to the potential issues in Western Kenya.

The Roll Back Malaria (RBM) Partnership is a global platform for coordinated action against malaria. RBM's Progress and Impact Series includes Country Reports that

analyze the impact of malaria control in several countries and those reports will have citations for the original evaluations of scale-ups of malaria control.

Rebound in malaria morbidity

There may be a rebound in malaria cases after malaria control interventions. For example, studies have found that giving malaria prophylaxis to very young children results in a higher number of malaria episodes later in life. Jean-François Trape has also commented on this. However, this rebound in malaria cases does not imply a rebound in mortality, because older children are less likely to die from malaria than younger children. The lower case fatality rate for older children is due to a number of factors including better physiological reserves, immunity, and access to treatment.

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