8 Aronstam, R.S. *et al.* (1994) *Neurochem. Res.* 19, 1515–1520
9 Martin, D.C. *et al.* (1995) *Biochem. Pharmacol.* 49, 809–817
10 Clark, I.A. *et al.* (1981) *Infect. Immun.* 32 1058–1066
11 Clark, I.A. (1982) *Klin. Wochenschr.* 60. 756–758
12 Rockett, K.A. *et al.* (1994) *Parasite Immunol.* 16, 243–249
13 Warrell, D.A. *et al.* (1986) *Am. J. Trop. Med. Hyg.* 35, 882–889
14 Tiao, G. *et al.* (1994) *Surgery* 116, 332–338
15 Misko, T.P. *et al.* (1993) *Eur. J. Pharmacol.* 233, 119–125
16 Yoshida, M. *et al.* (1994) *Biochem. Biophys. Res. Commun.* 202, 923–930

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Will Reducing *Plasmodium falciparum* Malaria Transmission Alter Malaria Mortality among African Children?

Snow and Marsh[1] raise a crucial and timely issue concerning the relationship between malaria-related death rates and transmission intensity. However, we believe that the data they present might have been interpreted in a more critical way.

Both authors have played a leading role in questioning the validity of verbal autopsies (VA), and hence the ability to define malaria-specific mortality[2]. On the basis of their argument about the changing clinical picture of malaria with increasing transmission intensity, they might have questioned the estimates from the two studies that found virtually no malaria-related mortality[3,4]. In both these studies many of the deaths were reported as either 'non-measles/non-malaria' after a simple, unstructured questioning of the mother[3] or as 'unknown cause' after a similar superficial recall 2–5 years after the event occurred[4]. In both studies, the authors were unaware that malaria-related deaths could occur without a febrile/convulsive episode. When attempting to make such between-site (ecological) comparisons, studies in which key assessments are made with some consistency should be chosen. If studies that did not use a well-standardized VA procedure are eliminated, the picture that emerges is that of an initial increase followed by some sort of plateau.

Secondly, the authors fail to point out the inherent variability of mortality rates. Year-to-year variations as well as strong secular trends are well described in Africa and elsewhere. This is best illustrated by the mortality data from The Gambia cited by Snow and Marsh, in the range of 6–10 per 1000 per year, suggesting that as much variability is found within one small country as is found between the remaining sites. A further recent study in The Gambia found overall child mortality in children aged 1–4 years of 6.5 per 1000 per year, but with local variations ranging from 1.9 to 9.4 per 1000 per year[5].

Surely the most urgent question relating to entomological inoculation rate (EIR) and mortality is whether a reduction in EIR will increase child survival (by which we mean survival by the age of functional immunity, taken here to be the fifth birthday). The relationship between malaria-specific death rates and the overall risk of dying by the fifth birthday is not obvious[6]: it is possible that children protected from malaria will be at increased risk of other diseases, or alternatively that such children will have a better chance of survival. Therefore interventions which reduce EIR may have varying impact on child survival in different settings, depending on the relative contribution of other diseases to child mortality.

Given these issues, we believe that the question raised by Snow and Marsh is unlikely to be resolved through ecological comparisons. The long-term follow-up of large-scale transmission-reducing interventions is likely to be the only way forward. The VA lacks both sensitivity and specificity for malaria deaths, and thus estimation of malaria-specific effects is likely to be both biased and imprecise[2]. We would urge that such studies assess child survival (ie. risk of death by the fifth birthday) directly rather than through cause-specific mortality rate estimates.

References

1 Snow, R.W. and Marsh, K. (1995) *Parasitology Today* 11, 188–190
2 Snow, R.W. *et al.* (1992) *Lancet* 340, 351–355
3 Spencer, H.C. *et al.* (1987) *Ann. Trop. Med. Parasitol.* 81 (Suppl. 1), 36–45
4 Carme, B. *et al.* (1984) *Bull. Soc. Pathol. Exp.* 77, 104–114
5 D'Alessandro, U. *et al.* (1995) *Lancet* 345, 479–483
6 Vandenbroucke, J.P. (1985) *Am. J. Epidemiol.* 121, 627–628

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Is Reduction of Transmission Desirable for Malaria Control?

Snow and Marsh[1] question whether interventions that reduce *Plasmodium falciparum* transmission in Africa will result in reduction of life-threatening malaria and death. They focus on the dilemma that has existed since 1950, ie. whether or not transmission control is a desirable aim in areas with hyperendemic ('stable') malaria[2,3]. In 1950 it was decided to start a worldwide eradication of malaria, commencing in tropical African areas because of its most intense transmission there. One of the criteria of hyperendemicity was the presence of infective anopheline mosquito vectors causing at least ten infective bites per person per year*. Snow and Marsh interpret the stability criterion as 'year-to-year transmission', and include areas with more than one infection per inhabitant per year. It should be noted, however, that such low annual transmission rates are generally the result of intense transmission that only occurs during short periods, while during the rest of the year, and/or sometimes complete subsequent years, transmission is (virtually) absent.

Interventions aiming at reduction of malaria-related mortality should include the earliest possible induction of antidisease memory, which will be regularly boosted by natural infections thereafter. Antidisease immunity can be obtained either by infections acquired naturally during periods of increased risk for severe disease, or (preferably) by a future vaccine based on molecules from asexual stages of *P. falciparum*. All interventions, including impregnated bednets, sporozoite/liver-stage and sexual-stage vaccines, will reduce the chances of being exposed to asexual parasites, and so will diminish the opportunity to generate antidisease immunity. All these methods of control, directly or indirectly, result in a reduction of transmission.

To what level should transmission be brought down? In most parts of sub-Saharan Africa, the rate of transmission is so high that it is unrealistic to assume that a degree of coverage can be achieved that would be sufficient to reduce the number of severe cases. Under these circumstances, one could argue that transmission should be

*Malaria Conference in Equatorial Africa, 1951