Socioeconomic development as an intervention against malaria: a systematic review and meta-analysis

Lucy S Tusting, Barbara Willey, Henry Lucas, John Thompson, Hmooda T Kafy, Richard Smith, Steve W Lindsay

Summary

Background Future progress in tackling malaria mortality will probably be hampered by the development of resistance to drugs and insecticides and by the contraction of aid budgets. Historically, control was often achieved without malaria-specific interventions. Our aim was to assess whether socioeconomic development can contribute to malaria control.

Methods We did a systematic review and meta-analysis to assess whether the risk of malaria in children aged 0–15 years is associated with socioeconomic status. We searched Medline, Web of Science, Embase, the Cochrane Database of Systematic Reviews, the Campbell Library, the Centre for Reviews and Dissemination, Health Systems Evidence, and the Evidence for Policy and Practice Information and Co-ordinating Centre evidence library for studies published in English between Jan 1, 1980, and July 12, 2011, that measured socioeconomic status and parasitologically confirmed malaria or clinical malaria in children. Unadjusted and adjusted effect estimates were combined in fixed-effects and random-effects meta-analyses, with a subgroup analysis for different measures of socioeconomic status. We used funnel plots and Egger’s linear regression to test for publication bias.

Findings Of 4696 studies reviewed, 20 met the criteria for inclusion in the qualitative analysis, and 15 of these reported the necessary data for inclusion in the meta-analysis. The odds of malaria infection were higher in the poorest children than in the least poor children (unadjusted odds ratio [OR] 1·66, 95% CI 1·35–2·05, p<0·001, P=68%; adjusted OR 2·06, 1·42–2·97, p<0·001, P=63%), an effect that was consistent across subgroups.

Interpretation Although we would not recommend discontinuation of existing malaria control efforts, we believe that increased investment in interventions to support socioeconomic development is warranted, since such interventions could prove highly effective and sustainable against malaria in the long term.

Funding UK Department for International Development.

Introduction Malaria remains one of the most serious public health problems worldwide, with 2·57 billion people at risk of falciparum malaria in 2010.1 Although the burden of malaria is falling globally, morbidity and mortality remain high, with estimates of total reported deaths in 2010 between 655 0002 and 1·24 million,3 with an estimated 82·69 million disability-adjusted life years lost in 2010.4 In addition to direct health effects, malaria also has a serious negative effect on socioeconomic development, and indeed “where malaria prospers most, human societies have prospered least”5. This effect is shown by the relation between an index of income and education6 and rates of economic growth5 are lower in sizes.9 Indeed, these findings, together with others for inclusion in the meta-analysis. The odds of malaria infection were higher in the poorest children than in the least poor children (unadjusted odds ratio [OR] 1·66, 95% CI 1·35–2·05, p<0·001, P=68%; adjusted OR 2·06, 1·42–2·97, p<0·001, P=63%), an effect that was consistent across subgroups.

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Costs associated with the burden of malaria constitute 5·8% of the total gross domestic product of sub-Saharan Africa (roughly US$12 billion annually).7 Both national income and rates of economic growth are lower in malaria-endemic countries than in countries where the disease is not endemic. One estimate suggests that a 10% reduction in malaria is associated with 0·3% increased growth, and other research has shown similar effect sizes. Indeed, these findings, together with others for inclusion in the meta-analysis. The odds of malaria infection were higher in the poorest children than in the least poor children (unadjusted odds ratio [OR] 1·66, 95% CI 1·35–2·05, p<0·001, P=68%; adjusted OR 2·06, 1·42–2·97, p<0·001, P=63%), an effect that was consistent across subgroups.

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The honeymoon period for malaria control is threatened both by resistance and, in the wake of the recent economic crisis, by so-called donor fatigue, creating a serious risk of a resurgence of malaria, as has occurred repeatedly in the past. Other interventions must be considered, as is recognised in the integrated vector management strategies supported by WHO, which, through combining efforts to control several vector-borne diseases, can yield sustainable and cost-effective reductions in the transmission of malaria, lymphatic filariasis, dengue, and other diseases.

However, since malaria control in many countries has historically been achieved without such malaria-specific interventions, socioeconomic development could potentially provide an effective and sustainable means of control in malaria-endemic countries. Based on this hypothesis, we did a systematic review and meta-analysis of the evidence for the relation between risk of malaria infection and socioeconomic status in children aged 0–15 years.

Methods
Search strategy and eligibility criteria
We followed recommendations made by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). We searched Medline, Web of Science, Embase, the Cochrane Database of Systematic Reviews, the Campbell Library, the Centre for Reviews and Dissemination, Health Systems Evidence, and the Evidence for Policy and Practice Information and Coordinating Centre evidence library to identify studies published in English between Jan 1, 1980, and July 12, 2011. We selected synonymous terms and used these to develop the search strategy (appendix pp 3–4). Bibliographies of relevant studies retrieved from the searches were checked for additional publications. The search strategy was not limited by study design. We excluded reports published before 1980, since we sought to examine evidence from the period most applicable to the present status of malaria control.

Studies retrieved were eligible for inclusion if they satisfied all our criteria: the study population consisted of children aged 0–15 years; the association between socioeconomic status and malaria was assessed; and the outcome of interest was prevalence of microscopically confirmed or rapid diagnostic test-confirmed Plasmodium falciparum infection or clinical malaria (fever and P falciparum infection). Low socioeconomic status was defined as not owning defined household assets; a low household income; a low score in an asset-based index of socioeconomic status, constructed with principal components or factor analysis; or parents having an unskilled rather than a skilled occupation. Cross-sectional, case-control, and cohort studies were all included in the analysis. Studies with low response rates were included. Only studies done in local populations of countries classified as malaria-endemic were included, and studies with populations of migrants, displaced people, or military personnel were excluded. Studies in which the outcome was severe malaria, congenital malaria, or in which most infections were not P falciparum were also excluded.

Figure 1: Malaria burden and human development index for income and education in 43 countries in sub-Saharan Africa
Data for cumulative probability of malaria death per 1000 children aged 0–5 years are for 2010 and were taken from Murray and colleagues. "Our human development index for income and education is for 2011 and was calculated from the UN Development Programme website and was derived from three variables: gross national income per head in purchasing power parity terms for 2011 (constant international 2005 US$); expected years of schooling for children as of 2011; and mean years of schooling for adults as of 2011. Methods for the calculation are shown in the appendix (p 1)." All 43 countries in sub-Saharan Africa for which data for both variables were available were included.

Figure 2: Study selection

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6106 records identified through searching databases
4478 records excluded by screening title and abstract
4696 records after duplicates removed
4696 records screened
218 full-text articles assessed for eligibility
20 studies included in qualitative analysis
35 studies included in quantitative analysis (meta-analysis)
4 records identified from bibliographies of screened studies
198 full-text articles excluded
36 did not have required study population
75 did not include required exposure
69 did not include required outcome
10 records were reviews, commentaries or modelling papers
4 records for which full text could not be located
Data extraction
We first screened titles and abstracts, and then one reviewer (LST) screened the relevant full-text articles. SWL also reviewed 22 (10%) of the full-text articles screened, which were selected at random, with any discrepancies resolved by RS. One reviewer (LST) extracted study characteristics and unadjusted and adjusted effect sizes with 95% CIs and recorded the data in a standard form. We did quality and risk-of-bias assessments as recommended by Wells and colleagues.25

Statistical analysis
Studies that met the eligibility criteria and that reported unadjusted or adjusted odds ratios (ORs) with 95% CIs, or presented sufficient data for the calculation of unadjusted ORs and 95% CIs, were included in the meta-analysis.
### Study site | Study design | n | Participants | Recruitment of participants | Exposure | Outcome | Control group | Measure of effect | Un-adjusted effect (95% CI) | Adjusted effect (95% CI) | Factors adjusted for | Reason for exclusion from quantitative analysis
---|---|---|---|---|---|---|---|---|---|---|---|---
Ong’Echa et al,31 2006 | Kenya | Case-control | 374 | Aged 0–3 years (children with cerebral malaria and those with previous hospital visits were excluded) | Recruited when visiting district hospital with symptoms of malaria | Parents are farmers vs parents are not farmers | Incidence of clinical malaria (parasitaemia plus fever) | Healthy controls recruited from maternal and child health clinic | OR 3·85 (1·64–9·09) | 0·92 (0·41–2·04) | Child risk factors (auxiliary temperature ≥37·5°C), nutritional factors, house type, and mosquito control measures | NA
Pullan et al,32 2010 | Uganda | Cross-sectional | 1770 | Aged 0–15 years | Selected from all households in district | Lowest vs highest socio-economic status quintile | PPR | None | OR 1·25 (0·74–2·13) | NA | NA | NA
Ronald et al,33 2006* | Ghana | Cross-sectional | 296 | Aged 1–9 years | Randomly sampled from community | Decreasing household socioeconomic status | PPR | None | OR 3·22 (1·95–5·32) | 3·95 (2·26–6·90) | Age and travel to rural areas | NA
Slutsker et al,34 1996 | Malawi | Cross-sectional | 3915 | Aged 0–3 months | Infants’ mothers enrolled into a chemoprophylaxis study at four antenatal clinics | No electricity at home vs electricity at home | PPR | None | OR 1·80 (1·30–2·10) | NA | NA | NA
Villamor et al,35 2003 | Tanzania | Cross-sectional | 687 | Aged 6–60 months | Children were enrolled in a vitamin A supplementation trial when admitted to hospital with pneumonia | No electricity at home vs electricity at home | PPR | None | OR 1·84 (1·23–2·76) | NA | NA | NA
Winskill et al,36 2011* | Tanzania | Cross-sectional | 1438 | Aged 6 months to 13 years | Randomly selected from 21 hamlets | Decreasing household socioeconomic status | PPR | None | OR 1·15 (0·94–1·39) | NA | NA | NA
Yamamoto et al,37 2010 | Burkina Faso | Case-control | 283 | Aged 0–3 years | Recruited by passive case detection at central laboratory | Incidence of clinical malaria (parasitaemia plus fever) | Controls from demographic surveillance system database matched for age, sex, ethnicity, and residence | OR 0·47 (0·20–1·08) | NA | NA | NA

**Studies included in the qualitative analysis, but excluded from the meta-analysis**

Clark et al,38 2008 | Uganda | Cohort | 558 | Aged 1–10 years | Recruited from a census population in one parish | 1st and 2nd (lowest) vs 3rd and 4th wealth quartile (highest) | Incidence of clinical episodes of malaria per person-year at risk | None | RR 2·04 (1·54–2·70) | 1·30 (0·96–1·79) | Age, sickle cell trait, G6PD deficiency in girls, bednet use, household crowding, and distance from swamp | Not possible to calculate OR

(Continues on next page)
used the generic inverse-variance method for the meta-analysis, in which weight is given to each study according to the inverse of the variance of the effect, to minimise uncertainty about the pooled effect estimates. Both outcomes (\textit{P falciparum} infection and clinical malaria) were combined in the analysis. We allocated the included studies into four subgroups, according to the measure of socioeconomic status used: asset ownership; household wealth; socioeconomic index; or parents’ occupations. We did separate analyses for unadjusted and adjusted ORs. Missing data were not problematic since meta-regression of individual data was not done.

Initially we did a fixed-effects meta-analysis, but if \( I^2 \) was large (>50%), which suggests substantial heterogeneity between studies, we used random-effects analysis. Random-effects analysis adjusts the standard errors of each study estimate of effect to include a measure of variation in the effects reported between studies. We produced forest plots to visually assess the ORs and 95% CIs of each study, and used funnel plots to assess publication bias (with study size as a function of effect size). We used Egger’s linear regression method to test for funnel plot asymmetry (ie, to quantify the bias captured by the funnel plot).22 Analyses were done with Stata 11 and RevMan 5.

**Results**

Our initial search yielded 6106 records, of which 4696 remained after removal of duplicates (figure 2). 20 records met our inclusion criteria (table).23-42 and of these 15 contained the necessary data for inclusion in the quantitative analysis (meta-analysis). Five records were

<table>
<thead>
<tr>
<th>Study site</th>
<th>Study design</th>
<th>n</th>
<th>Participants</th>
<th>Recruitment of participants</th>
<th>Exposure</th>
<th>Outcome</th>
<th>Control group</th>
<th>Measure of effect</th>
<th>Un-adjusted effect (95% CI)</th>
<th>Adjusted effect (95% CI)</th>
<th>Factors adjusted for</th>
<th>Reason for exclusion from quantitative analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghana</td>
<td>Cross-sectional</td>
<td>1744</td>
<td>Aged 6–60 months</td>
<td>Randomly sampled from communities near (&lt;1000 m) and less near (&gt;1000 m) agricultural sites in Accra</td>
<td>Socio-economic status below vs above mean for the city</td>
<td>PfPR</td>
<td>None</td>
<td>Insufficient information provided</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Not possible to calculate OR</td>
</tr>
<tr>
<td>Ghana</td>
<td>Cohort</td>
<td>535</td>
<td>Aged 2–4 months</td>
<td>Recruited from nine villages after visiting health centre (children with chronic diseases excluded)</td>
<td>Family does not have good financial situation vs family has good financial situation</td>
<td>Incidence of clinical malaria (parasitaemia plus fever)</td>
<td>None</td>
<td>Incidence rate ratio</td>
<td>1.59 (1.33–1.89)</td>
<td>1.52 (1.27–1.82)</td>
<td>Sex, ethnicity, season of birth (dry or rainy season), sickle cell trait, mother’s education, mother’s occupation, knowledge of malaria, and protective measures</td>
<td>Not possible to calculate OR</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>Cross-sectional</td>
<td>672</td>
<td>Aged 0–15 years</td>
<td>Selected from farming and non-farming households</td>
<td>Low vs high socioeconomic status</td>
<td>PfPR</td>
<td>None</td>
<td>OR</td>
<td>NA</td>
<td>2.44 (0.88–10.00)</td>
<td>Age, agricultural zone, crops grown, irrigation, overnight stays in temporary farm huts, and distance to permanent ponds and fish ponds</td>
<td>Bayesian credible intervals reported only</td>
</tr>
<tr>
<td>Uganda</td>
<td>Cross-sectional</td>
<td>1844</td>
<td>Aged 5–15 years</td>
<td>All residents of four villages asked to participate, with 78% successfully enrolled</td>
<td>Decreasing household socioeconomic status</td>
<td>PfPR</td>
<td>None</td>
<td>OR</td>
<td>NA</td>
<td>2.27 (0.88–25.00)</td>
<td>Age, bednet use</td>
<td>Bayesian credible intervals reported only</td>
</tr>
</tbody>
</table>

OR=odds ratio. PfPR=Plasmodium falciparum parasite rate. RR=risk ratio. *Socioeconomic status analysed as a continuous variable.
excluded from the quantitative analysis either because Bayesian credible intervals were reported (n=2) or because ORs could not be calculated from the available data (n=3).

Despite substantial overlap between CIs for both unadjusted and adjusted results, high I² values from fixed-effects analysis suggested substantial heterogeneity between

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**Figure 3: Association between low socioeconomic status and clinical malaria or parasitaemia in children aged 0–15 years**

Pooled effects from random-effects meta-analyses for unadjusted (A) and adjusted (B) results are shown. Studies are divided into subgroups by measure of socioeconomic status used. Error bars show 95% CIs. df=degrees of freedom.

### A

<table>
<thead>
<tr>
<th>Socioeconomic index</th>
<th>Log (odds ratio)</th>
<th>SE</th>
<th>Odds ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-Taiar et al. (2009)</td>
<td>0.505314</td>
<td>0.191170</td>
<td>1.76 (1.21–2.56)</td>
<td>8.4%</td>
</tr>
<tr>
<td>Custodio et al. (2009)</td>
<td>0.275341</td>
<td>0.210820</td>
<td>1.69 (0.85–3.35)</td>
<td>8.0%</td>
</tr>
<tr>
<td>Pullan et al. (2010)</td>
<td>0.223144</td>
<td>0.271367</td>
<td>1.25 (0.73–2.13)</td>
<td>6.6%</td>
</tr>
<tr>
<td>Ronald et al. (2006)</td>
<td>1.169381</td>
<td>0.255894</td>
<td>3.22 (1.95–5.32)</td>
<td>7.0%</td>
</tr>
<tr>
<td>Slukter et al. (1996)</td>
<td>0.87787</td>
<td>0.166032</td>
<td>1.80 (1.30–2.49)</td>
<td>9.1%</td>
</tr>
<tr>
<td>Wenski et al. (2011)</td>
<td>0.139622</td>
<td>0.102621</td>
<td>1.15 (0.94–1.40)</td>
<td>10.5%</td>
</tr>
<tr>
<td>Yanamoto et al. (2010)</td>
<td>-0.756122</td>
<td>0.435365</td>
<td>0.47 (0.20–1.10)</td>
<td>4.0%</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td>1.49 (1.10–2.01)</td>
<td>53.5%</td>
</tr>
</tbody>
</table>

Subgroup heterogeneity: τ²=0.12; χ²=24.51, df=6 (p=0.0004); I²=76%

Test for overall effect: Z=2.56 (p=0.01)

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<table>
<thead>
<tr>
<th>Asset ownership</th>
<th>Log (odds ratio)</th>
<th>SE</th>
<th>Odds ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baragatti et al. (2009)</td>
<td>0.725499</td>
<td>0.325729</td>
<td>2.07 (1.10–3.90)</td>
<td>5.6%</td>
</tr>
<tr>
<td>Ghebreyesus et al. (2000)</td>
<td>-0.028422</td>
<td>0.249721</td>
<td>0.97 (0.60–1.59)</td>
<td>7.1%</td>
</tr>
<tr>
<td>Koram et al. (1995)</td>
<td>0.833909</td>
<td>0.238911</td>
<td>2.30 (1.43–3.77)</td>
<td>7.3%</td>
</tr>
<tr>
<td>Villamor et al. (2003)</td>
<td>0.197271</td>
<td>0.205363</td>
<td>1.15 (0.94–1.41)</td>
<td>8.1%</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td>1.70 (1.17–2.48)</td>
<td>28.2%</td>
</tr>
</tbody>
</table>

Subgroup heterogeneity: τ²=0.09; χ²=7.14, df=3 (p=0.07); I²=58%

Test for overall effect: Z=2.76 (p=0.006)

---

<table>
<thead>
<tr>
<th>Household wealth</th>
<th>Log (odds ratio)</th>
<th>SE</th>
<th>Odds ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarke et al. (2001)</td>
<td>0.862872</td>
<td>0.279963</td>
<td>2.34 (1.35–4.05)</td>
<td>6.4%</td>
</tr>
<tr>
<td>Gahutu et al. (2011)</td>
<td>0.463734</td>
<td>0.191170</td>
<td>1.59 (1.05–2.41)</td>
<td>8.0%</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td>1.85 (1.28–2.68)</td>
<td>14.4%</td>
</tr>
</tbody>
</table>

Subgroup heterogeneity: τ²=0.01; χ²=1.22, df=1 (p=0.27); I²=18%

Test for overall effect: Z=3.25 (p<0.0001)

---

<table>
<thead>
<tr>
<th>Parents’ occupation</th>
<th>Log (odds ratio)</th>
<th>SE</th>
<th>Odds ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ong’echa et al. (2006)</td>
<td>1.347074</td>
<td>0.434886</td>
<td>3.85 (1.64–9.02)</td>
<td>4.0%</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td>3.85 (1.64–9.02)</td>
<td>4.0%</td>
</tr>
</tbody>
</table>

Subgroup heterogeneity: NA

Test for overall effect: Z=3.10 (p=0.002)

---

<table>
<thead>
<tr>
<th>Total (all measures of socioeconomic status)</th>
<th>Log (odds ratio)</th>
<th>SE</th>
<th>Odds ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.579818</td>
<td>0.154177</td>
<td>1.79 (1.32–2.42)</td>
<td>27.4%</td>
<td></td>
</tr>
<tr>
<td>3.377517</td>
<td>0.284787</td>
<td>3.95 (2.66–6.00)</td>
<td>19.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td>2.56 (1.18–5.56)</td>
<td>46.3%</td>
</tr>
</tbody>
</table>

Subgroup heterogeneity: τ²=0.26; χ²=6.01, df=1 (p=0.01); I²=83%

Test for overall effect: Z=2.38 (p=0.02)

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<table>
<thead>
<tr>
<th>Asset ownership</th>
<th>Log (odds ratio)</th>
<th>SE</th>
<th>Odds ratio (95% CI)</th>
<th>Weight</th>
</tr>
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<tbody>
<tr>
<td>Baragatti et al. (2009)</td>
<td>0.615386</td>
<td>0.233766</td>
<td>1.85 (1.17–2.93)</td>
<td>22.1%</td>
</tr>
<tr>
<td>Koram et al. (1995)</td>
<td>0.947789</td>
<td>0.290486</td>
<td>2.58 (1.46–4.56)</td>
<td>18.6%</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td>2.11 (1.48–3.01)</td>
<td>40.7%</td>
</tr>
</tbody>
</table>

Subgroup heterogeneity: τ²=0.00; χ²=0.80, df=1 (p=0.37); I²=0%

Test for overall effect: Z=4.40 (p=0.0001)

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<table>
<thead>
<tr>
<th>Parents’ occupations</th>
<th>Log (odds ratio)</th>
<th>SE</th>
<th>Odds ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ong’echa et al. (2006)</td>
<td>-0.086278</td>
<td>0.410929</td>
<td>0.92 (0.41–2.05)</td>
<td>12.9%</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td>0.92 (0.41–2.05)</td>
<td>12.9%</td>
</tr>
</tbody>
</table>

Subgroup heterogeneity: NA

Test for overall effect: Z=0.21 (p=0.83)

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<table>
<thead>
<tr>
<th>Total (all measures of socioeconomic status)</th>
<th>Log (odds ratio)</th>
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<th>Weight</th>
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<td></td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td></td>
<td></td>
<td>2.06 (1.42–2.97)</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Subgroup heterogeneity: τ²=0.11; χ²=10.72, df=4 (p=0.03); I²=63%

Test for overall effect: Z=3.83 (p=0.0001)

Test for subgroup differences: χ²=4.40, df=2 (p=0.22); I²=32.83%

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Findings from Kenya and Nigeria suggest that the costs (unadjusted effect size $P=68\%$; adjusted effect size $P=63\%$). Therefore random-effects analysis was used.

The meta-analysis was restricted to comparisons between the highest (least poor) and lowest (poorest) socioeconomic groups. Subgroup analysis suggested that low socioeconomic status was associated with increased odds of malaria irrespective of the measure used for socioeconomic status, with the exception of one study in which parents’ occupations were used; we therefore judged that to pool all results would be appropriate. In the meta-analyses for both unadjusted and adjusted results, the odds of malaria infection were higher in the poorest children than in the least poor children (figure 3).

Visual assessment of funnel plots (appendix p 8) showed that the studies were distributed fairly symmetrically about the combined effect size, which suggests little publication bias. However, Egger’s test for bias suggested funnel plot asymmetry for the unadjusted results (bias coefficient $1.70$, $95\%$ CI $-0.97$ to $4.37$, $P=0.191$), which suggests that publication bias (delayed publication or location bias), small-study effects, selective outcome reporting, or selective analysis reporting might have been present. A test for funnel plot asymmetry was not possible for the adjusted effects, since only five studies were included in the meta-analysis. Overall quality assessment scores for risk of bias in studies included in the quantitative analysis ranged from two to seven, out of a maximum of eight (appendix p 6–7).

**Discussion**

Our findings suggest that low socioeconomic status is associated with roughly doubled odds of clinical malaria or parasitaemia in children compared with higher socioeconomic status, within a locality. This conclusion is supported by a similar size and direction of effect noted in the five studies excluded from the meta-analysis. Since our analysis represents a comparison of the very poorest children with the least poor children within highly impoverished communities, the difference in the odds of malaria in the poorest children would probably be even greater if the studies were expanded to include children from wealthier backgrounds. The association between socioeconomic status and malaria is not definitive evidence for the direction of causality, since the poorest households are not only more susceptible to the disease, but are also more vulnerable to its costs, such that the disease itself can induce poverty. For example, a significant positive association between low socioeconomic status and malaria parasitaemia has been reported in Tanzania, with causality in both directions. Findings from Kenya and Nigeria suggest that the costs of malaria treatment (as a proportion of non-food monthly income) and subsequent financial setbacks are greater for poorer than for more wealthy households. Costs also vary geographically; in Kenya and Papua New Guinea, the risk of clinical disease is greater in low-transmission districts, with subsequently greater loss of income.

Wealth is probably protective against malaria, since it renders prophylaxis and treatment more affordable and is positively associated with other beneficial factors, including better-educated parents (which improves prophylaxis and treatment for children), increased housing quality (which reduces house entry by malaria-transmitting mosquitoes), and improved nutritional status of children (which could increase their subsequent ability to cope with malaria infection). Malaria and poverty therefore constitute a vicious cycle for the poorest households, exacerbating differences in health and wealth.

A major limitation of our meta-analysis is that the measurement of risk factors was done with varying precision in the included studies, and although we did subgroup and random-effects analyses, these are unlikely to have fully accounted for heterogeneity in study design. Another important limitation is the poor quality of the studies included in the meta-analysis, which results from the nature of the study question (since randomisation for socioeconomic status would not be practically or ethically possible). However, the consistency of results across studies and settings suggests that the finding of increased odds of malaria in children of low socioeconomic status is robust. For our systematic review, the main limitation was the language of the search. In particular, not including publications in Spanish probably excluded much data from South America, such that our findings cannot be generalised to that region. Egger’s test suggested the presence of some forest plot asymmetry; however, statistical tests for forest plot asymmetry tend to have low power and asymmetry might not be attributable to publication bias—it might also have arisen from poor study quality leading to artificially inflated effects in the smaller studies, selective outcome or analysis reporting, or chance. Incomplete retrieval (four full-text studies could not be retrieved) might also have introduced bias.

On the basis of our findings, we advocate that development programmes should be an essential component of malaria control. Malaria elimination in many high-income countries was achieved without malaria-specific interventions; prevalence started to fall in Europe and North America as a by-product of improved living conditions and increased wealth, and after Ronald Ross deduced the mode of malaria transmission in 1897, more specific interventions became possible, including habitat modification (permanent elimination of breeding sites—eg, by installing and maintaining drains), habitat manipulation (temporary creation of unfavourable conditions for the vector—eg, by fluctuating the amount of water in reservoirs), and modifications to human habitation or behaviour to reduce human-vector contact, such as mosquito-proofing of houses. As a result, most of Europe and North America is now characterised by anophelism without malaria, which is testament to the effectiveness of these control efforts, together with a reduced innate receptivity to malaria transmission that stems from advances in nutrition, health care, and...
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development.59 Similar environmental management strategies, together with larval control, also helped to reduce malaria transmission in many developing countries during the 20th century, including Zanzibar, Indonesia, Malaysia, the Panama Canal, and the Copper Belt of Zambia.60,61 Thus, as transmission today falls in much of sub-Saharan Africa and elsewhere, development will contribute to the reduction and elimination of the disease. Several specific development interventions could contribute to malaria control (appendix p 5), which might be similar to malaria-specific interventions in terms of costs (appendix pp 9–10). An excellent example of how such interventions can work in practice can be seen in Khartoum, Sudan (appendix p 11).

This approach has three major constraints. First, accurate costing of the extent to which specific development interventions contribute to malaria control is difficult. Whereas measuring the effect of house screening is straightforward, measuring that of improved education or raised incomes is not. Second, the effectiveness of a development intervention depends on both the nature and intensity of malaria transmission. For example, house screening is probably most effective in areas of low to moderate transmission where vectors feed indoors. Countries that have eliminated malaria since 1900 have largely been temperate, subtropical, or islands,4 and the high malaria burden in many developing countries is not merely a product of poverty. Rather, the specific ecological requirements of both the malaria parasite and its mosquito vector help to determine the range of the disease.41 Interventions have to be highly effective and development should not be thought of as a standalone strategy, but as a complement to malaria-specific interventions such as LLINs, indoor residual spraying, and larval source management. Third, economic development gives rise to broader social, environmental, and ecological changes that might in some circumstances lead to an increase in the burden of malaria (appendix p 5), as has been seen in Sri Lanka (appendix p 12). Nonetheless, these constraints should not be treated as barriers to the use of socioeconomic development as an intervention against malaria (appendix p 5).

In addition to initiatives such as the Millennium Villages project, which is operating in 14 villages in ten African countries to examine the effects of socioeconomic development,42 further research is needed to address some important questions, and to galvanise specialists in both health and development to work more closely together on malaria control. For example, randomised controlled trials should be considered to assess the effectiveness of socioeconomic interventions (eg, improved education and nutrition) against malaria in different settings. We must also investigate the causal pathways that lead from development to successful malaria control, and vice versa, and develop an understanding of the relation between malaria control, birth rates, and population growth.

That malaria control remains largely the preoccupation of the health sector alone is a failing of both those who work in health and those who work in international development. The disease severely compromises socioeconomic development, and its control and elimination would improve economic prosperity worldwide. The effectiveness of available drugs and insecticides for malaria control will ultimately deteriorate with the emergence of parasites resistant to antimalarials and of vectors resistant to insecticides, and the development and procurement costs of replacements will be high. Donor fatigue is also an ever-present threat to interventions such as LLINs, indoor residual spraying, and intermittent preventive treatment, especially in view of the economic situation since the 2007–08 financial crisis.64 However, several specific development interventions could be introduced to aid both economic development and malaria control. Increased wealth and improved standards of living that stem directly from socioeconomic development could prove fundamental in ensuring that malaria transmission continues to fall in much of Asia, South America, and Africa, as it happened historically in Europe and North America. Socioeconomic development could prove to be a very effective and sustainable intervention against malaria in the long term.

Contributors
SWL and RS conceived of the study. SWL, RS, LST, HL, and JT developed the study design and the outline of the report. LST searched the scientific literature, did the meta-analysis, and prepared the first draft of the report. BW provided advice on the systematic review and meta-analysis. HTK contributed the case study from Sudan (appendix). All authors reviewed the final version of the report.

Conflicts of interest
We declare that we have no conflicts of interest.

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